Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (1L) chemotherapy (CTx) vs continuation of CTx for HER2-advanced gastric or gastroesophageal junction cancer (GC/GEJC).

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Background: We report the primary analysis of JAVELIN Gastric 100, which compared avelumab (anti–PD-L1) maintenance after 1L CTx vs continued CTx in patients (pts) with GC/GEJC. Methods: In this global, open-label, phase 3 trial (NCT02625610), eligible pts had previously untreated, unresectable, locally advanced/metastatic (LA/M) HER2-GE/GEJC. Pts without progressive disease (PD) after 12 weeks of 1L oxaliplatin/fluoropyrimidine induction were randomized 1:1 to avelumab 10 mg/kg Q2W switch maintenance or continued CTx, stratified by region (Asia vs non-Asia). Primary endpoint was overall survival (OS) post induction/randomization in all randomized or PD-L1+ (≥1% of tumor cells, 73-10 assay) pts. Results: 805 pts received induction CTx and 499 pts were randomized (avelumab, n = 249; CTx, n = 250). At data cutoff (Sep 13, 2019), minimum follow-up was 18 months. In the avelumab and CTx arms, median OS post induction/randomization was 10.4 months (95% CI 9.1-12.0) vs 10.9 months (95% CI 9.6-12.4), hazard ratio (HR) 0.91 (95% CI 0.74-1.11; p = 0.1779); 24-month OS rates were 22.1% (95% CI 16.8-28.0) vs 15.5% (95% CI 10.8-20.9), respectively. The HR for OS in PD-L1+ pts (n = 54) was 1.13 (95% CI 0.57-2.23). No OS trend was seen in Asian pts (n = 114; HR 0.90 [95% CI 0.59-1.36]) or other subgroups, except for a potential benefit with avelumab in pts with no metastatic sites at randomization (n = 60; HR 0.52 [95% CI 0.28-0.98]). Progression-free survival was similar between arms (HR 1.04 [95% CI 0.85-1.28]). In the avelumab vs CTx arms, objective response rates (post randomization only) were 13.3% (95% CI 9.3-18.1) vs 14.4% (95% CI 10.3-19.4), and 12-month rates for duration of response were 62.3% (95% CI 40.9-77.9) vs 28.4% (95% CI 13.2-45.7), respectively. Treatment-related adverse event rates (all grades/grade ≥3) were 61.3%/12.8% with avelumab and 77.3%/32.8% with CTx. Conclusions: Avelumab maintenance showed clinical activity and favorable safety vs continued CTx in pts with LA/M GC/GEJC; however, JAVELIN Gastric 100 did not meet its primary objective of demonstrating superior OS in the randomized or PD-L1+ population. Clinical trial information: NCT02625610. Research Sponsor: Merck KGaA, Darmstadt, Germany and Pfizer Inc.
Extensive peritoneal lavage after curative gastrectomy for gastric cancer study (EXPEL): An international multicenter randomized controlled trial.

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Background: Peritoneal recurrence of gastric cancer after curative surgical resection is common and portends a poor prognosis. Preliminary studies suggest extensive intraoperative peritoneal lavage (EIPL) may reduce the risk of peritoneal recurrence and improve survival. We sought to perform a randomized phase III study to definitively establish the role of performing EIPL after gastrectomy. Methods: This is a prospective, open-label, phase 3 multicentre randomised controlled trial involving 22 hospitals from Korea, China, Japan, Malaysia and Singapore. Patients aged between 21 to 80 years with cT3/4 stomach cancer undergoing curative resection were randomized to either surgery and EIPL (lavage with 10 litres of saline) or surgery alone. Comparison of DFS and OS were made via log-rank test. The cumulative incidence of peritoneal recurrence was compared using competing risks approach. All analyses were performed based on intention-to-treat. Results: Between March 2015 to August 2018, 800 patients were randomly assigned to surgery alone (n = 402) or EIPL (n = 398). Based on a median follow-up duration of 29 months, the 3-year cumulative incidence of all-cause mortality was 23.1% and 23.3% for EIPL and surgery alone respectively (hazard ratio [HR] = 1.09, 95% CI: 0.78 to 1.52, p = 0.615). Similarly, the 3-year cumulative incidence of recurrence were 28.0% and 25.9% respectively (HR = 1.01, 95% CI: 0.74 to 1.37, p = 0.947), and 7.9% and 6.6% respectively for peritoneal recurrence (Subdistribution HR = 1.33, 95% CI: 0.73 to 2.42, p = 0.347). Overall, the risk of adverse events was higher in EIPL as compared to surgery alone (relative risk = 1.58, 95% CI 1.07 to 2.33, p = 0.019). The most common adverse events were anastomotic leak, bleeding and intra-abdominal abscess. At the planned third interim analysis on 28 August 2019, the predictive probability of achieving even a 5% difference in 3-year OS in favour of EIPL at final analysis was < 0.4%. The trial was thus recommended to terminate on the basis of futility. Conclusions: EIPL does not show any survival benefit compared with surgery alone and is not recommended for patients undergoing curative gastrectomy for cancer. Clinical trial information: NCT02140034. Research Sponsor: National Medical Research Council Singapore.
Early results of the randomized, multicenter, controlled evaluation of S-1 and oxaliplatin as neoadjuvant chemotherapy for Chinese advanced gastric cancer patients (RESONANCE Trial).

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Background: Perioperative chemotherapy brings potential benefits to growing patients with gastric cancer based on several clinical trials including MAGIC, ACTS-GC, CLASSIC and INT-0116. However, the effect of neoadjuvant therapy before D2 gastrectomy remains pending. According to phase II clinical trials, SOX regimen as neoadjuvant chemotherapy is associated with increased rate of D2 lymph nodes dissection and R0 resection. We hypothesize that SOX regimen can improve survival of patients with gastric cancer. Methods: Through CT, EUS and laparoscopic exploration, patients with gastric cancer on the stage IIA-IIIC were included in the study and divided into 2 groups randomly. Patients in neoadjuvant group received 2-4 cycles of SOX before surgery and 4-6 cycles after surgery, while patients in no neoadjuvant group received 8 cycles after surgery. The primary endpoint was 3-y DFS and the secondary endpoint were 5-y OS, ORR, D2/R0 resection rate and side effect. Results: A total of 772 patients were enrolled in the study between September 2012 and July 2019. After neoadjuvant therapy, the downstaging was found in neoadjuvant group (261/386, 67.6%). The pathological efficiency rate and pCR rate of neoadjuvant group were 67.8% and 23.6% respectively. The R0 resection rate in neoadjuvant group was significantly higher than that in adjuvant group (73.1% vs 58.1%, p < 0.05). There was no difference in terms of surgical time, blood loss, postoperative complications and hospital stay. Conclusions: SOX makes increased rate of R0 resection, acceptable adverse effect and no impression on surgeries, which suggest that perioperative chemotherapy using SOX can prolong median survival time, DFS and OS. Clinical trial information: NCT01583361. Research Sponsor: Chinese PLA General Hospital.
A randomized controlled phase III multicenter study on dose escalation in definitive chemoradiation for patients with locally advanced esophageal cancer: ARTDECO study.

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Background: To analyze the effect of radiation dose escalation to the primary tumor on local control, locoregional control, survival and toxicity in definitive chemoradiation for esophageal cancer. Methods: Patients with clinical stage T2-4, N0-3, M0 carcinoma of the esophagus were randomized between a standard dose of 50.4 Gy/1.8 Gy/5,5 weeks to the tumor and regional lymph nodes (SD) versus the same dose combined with an integrated boost of 0,4 Gy per fraction (total 61,6 Gy) to the primary tumor (HD). Chemotherapy consisted of 6 weekly concurrent carboplatin (AUC 2) and paclitaxel (50 mg/m²) in both arms. The primary endpoint was local progression free survival (LPFS) and 260 patients were needed to detect a difference of 15% (power: 80%). Secondary endpoints were locoregional progression free survival (LRPFS), overall survival (OS) and toxicity. Patients were stratified for histological subtype. Results: Between September 2012 and June 2018, 260 patients were included. Reasons for inoperability were proximal localization and patient preference (44%), comorbidity (30%), unresectable lymph nodes (11%), T4 (5%), local recurrence 2% and combinations (7%). 61% of the patients had a squamous cell carcinoma (SCC) and 39% had an adenocarcinoma (AC). 94% completed radiation treatment and 85% had at least 5 courses chemotherapy. Median follow up time was 45 months. 3-year LPFS was 70% in the SD arm versus 76% in the HD arm (ns). LPFS for SCC and AC was 74% versus 81% and 62% versus 65% for SD and HD, resp. (ns). 3-year LRPFS was 53% and 63% for the SD and HD arm resp. (p = 0.08). 1 year any progression free survival was 60% for SCC and 50% for AC, without a significant difference between SD and HD (p = 0,5). 3-year OS was 41% versus 40% for SD and HD resp. Overall grade 4 and 5 CTC toxicity was 12% and 4% in the SD arm versus 14% and 10% in the HD arm, resp. Conclusions: In definitive chemoradiation for esophageal cancer, radiation dose escalation up to 61,6 Gy to the primary tumor did not result in a significant increase in local control over 50,4 Gy. Numerical improvement of locoregional control after HD was observed with an increase in toxicity and without improving OS. Clinical trial information: NL38343.018.11. Research Sponsor: Dutch Cancer foundation KWF.
Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study.

**Background:** Advanced OGA patients (pts) are treated with platinum-based 1st line chemotherapy but the role of maintenance therapy once disease control is obtained is unknown. **Methods:** PLATFORM is a prospective, open-label, adaptive phase II trial assessing maintenance therapy in OGA. HER2 negative pts with advanced OGA achieving response or stable disease on completion of 1st line platinum-based chemotherapy were initially randomised to surveillance (A1), capecitabine (A2) and durvalumab (A3). Rucaparib (A4) and capecitabine+ramucirumab (A5) were subsequently added as part of adaptive design. Primary endpoint is progression-free survival with target recruitment of 154pts/arm. A pre-planned futility interim analysis (IA) is triggered when 61 pts/arm are recruited and evaluable using 12-week progression-free rate (PFR). Individual arms will continue accrual if the upper limit of 1-sided 95% CI difference is >0 when compared to A1. Biomarker analyses of A1 and A3 IA patients include: PDL1 as tumour and immune cell combined proportion (TIP), multiplex IHC of tumour infiltrating lymphocytes (TILs), TMB and MSI status by whole exome sequencing. **Results:** To date, 1053 pts have registered prior to or during 1st line therapy and 356 pts randomised. Primary attrition was due to disease progression. Baseline demographics in the IA population (arms A1 to A3, n = 183) were male (81%); median age 65 yrs; metastatic disease (92%); Oesophageal (40%), OG junction (28%) and gastric (32%) primary. 12-week PFR were A1: 51% (95%CI: 38-64%); A2: 52% (95%CI: 40-65%); A3: 49% (95%CI: 36-62%). PFR differences to arm A1 were A2: 1.6% (95%CI: -13.2 to 16.5%); A3: -1.6% (95%CI: -16.5 to 13.3%). In A1, PFR was 53% vs 43% in PDL1 TIP >10%, 10% and $\leq$10%, respectively. In A3, PFR was 51% vs 100% in PDL1 TIP <10%, 10% and $\geq$10%, respectively. 3 pts in A3 had partial response; none were seen in A1 and A2. Density of TILs subsets, TMB and MSI data will be presented. **Conclusions:** PLATFORM IA did not indicate futility in maintenance capecitabine or durvalumab compared to surveillance in advanced OGA and will continue to target accrual. Incremental radiological responses were observed with maintenance durvalumab only. Clinical trial information: NCT02678182. Research Sponsor: The Royal Marsden NHS Foundation Trust sponsors this study. MedImmune LLC, Clovis Oncology and Eli Lilly provide durvalumab, rucaparib and ramucirumab respectively without cost and provide grants to assist with study costs and research sample collection.

Performance of a blood-based test for the detection of multiple cancer types.

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Background: Cancers of the esophagus, stomach, pancreas, gallbladder, liver, bile duct, colon and rectum will account for 17% of incident cancer diagnoses and 26% of cancer-related deaths in the US in 2019. We developed a methylation-based cfDNA early multi-cancer detection test that also can predict the tissue of origin (TOO) of these and other cancers types; performance of this test for gastrointestinal (GI) tract cancers is reported here. Methods: The Circulating Cell-free Genome Atlas (CCGA; NCT02889978) study is a prospective, multi-center, observational, case-control study with longitudinal follow-up, enrolling individuals with cancer (> 20 cancers, all stages, newly diagnosed) and without cancer. Plasma cfDNA was subjected to a cross-validated targeted methylation (TM) sequencing assay. Methylation fragments were combined across targeted genomic regions and assigned a probability of cancer and a predicted TOO. GI cancer classes were upper GI (esophagus/stomach, n = 67), pancreas/gallbladder/extrahepatic bile duct (n = 95), liver/intrahepatic bile duct (n = 29), and colon/rectum (n = 121). Results: Detection across all GI cancers was 82% (95% CI 77-86) at a > 99% pre-set specificity. Overall predicted TOO accuracy was 92% (88-95) among the samples for which TOO was predicted (6/255 had indeterminate predicted TOO). The table shows performance by GI cancer type. Conclusions: Simultaneous detection at high specificity (> 99%) of multiple cancer types, including GI cancers across stages at high sensitivity (82%), was shown using TM analysis of cfDNA. Accurate (92%) localization of cancers to specific regions of the GI tract was also achieved. Detection of multiple GI cancers from a single noninvasive blood test could be a practical method for detecting GI and other cancers, and may facilitate diagnostic work-ups. Clinical trial information: NCT02889978. Research Sponsor: GRAIL, Inc.

<table>
<thead>
<tr>
<th>GI Cancer Type</th>
<th>Sensitivity, % (n)</th>
<th>Predicted TOO Accuracy, % (n)</th>
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<tr>
<td>All Stage 1-3</td>
<td>Stage 4</td>
<td>All Stage 1-3</td>
</tr>
<tr>
<td>Upper GI</td>
<td>85 (30/40)</td>
<td>87 (6/24)</td>
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<tr>
<td>Pancreas/Gallbladder/Extrahepatic Bile Duct</td>
<td>82 (34/49)</td>
<td>92 (50/52)</td>
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<tr>
<td>Liver/Intrahepatic Bile Duct</td>
<td>86 (15/19)</td>
<td>85 (10/13)</td>
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<tr>
<td>Colon/rectum</td>
<td>79 (53/67)</td>
<td>96 (50/52)</td>
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<tr>
<td>All GI Cancers</td>
<td>82</td>
<td>96</td>
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</tbody>
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Access to care and outcomes for noncurative esophagogastric cancer: A population-based geographic study.

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Background: Esophagogastric cancer (EGC) carries a heavy mortality burden owing largely to high rates of unresectable disease at diagnosis. Among patients not undergoing curative-intent therapy, access to care may vary. We examined the geographic distribution of care delivery and survival across a jurisdiction, and its relationship with distance to cancer centres (CCs), for non-curative EGC.

Methods: We conducted a population-based analysis of adults with non-curative EGC from 2005-2017 using linked administrative healthcare datasets in Ontario, Canada. Outcomes were medical oncology consultation, receipt of chemotherapy, and overall survival (OS). We used geographic information system analysis to map locations of CCs and outcomes across census divisions. Regions of discordance between care use and OS were identified with bivariate choropleth maps. Multivariable modified Poisson models assessed the relationship between distance to the nearest CC and outcomes, adjusting for demographic, clinical, and socioeconomic factors.

Results: Of 10,228 patients surviving a median of 5.1 months (IQR: 2.0-12.0), 68.6% had medical oncology consultation and 32.2% received chemotherapy. Regions of comparable OS and care delivery were clustered throughout the province. CCs were distributed unevenly, with higher levels in Southern Ontario. Higher-level CCs clustered in regions with higher rates of consultation, chemotherapy use, and OS. Each increment in distance from location of residence to the nearest CC (11-50, 51-100, and $\geq101$ km) was associated with lower likelihood of seeing medical oncology and receiving chemotherapy, and inferior OS, compared to $\leq10$ km.

Conclusions: A third of patients with non-curative EGC did not see medical oncology, and the majority did not receive chemotherapy. Care delivery and OS exhibited high geographic variability. Location of residence influenced access to care and OS, with inferior outcomes for those living further from a CC. These findings are important for designing interventions and policies to reduce disparities in access to care and outcomes for non-curative EGC. Research Sponsor: Canadian Institutes of Health Research (CIHR) Partnerships for Health System Improvement (PHSI) grant.
The short-term outcomes from TOP-G trial: Randomized phase II noninferiority trial comparing gastrectomy with omentectomy and omentum preserving gastrectomy for advanced gastric cancer.

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Background: A complete resection of the omentum has been believed as a standard procedure for advanced gastric cancer. However, there was no evidence for survival significance of omentectomy. Therefore, we conduct the Phase II trial (TOP-G trial) comparing gastrectomy with omentectomy and omentum preserving gastrectomy. Here, we present the short-term outcomes which was a secondary endpoint of TOP-G trial. Methods: Enrollment criteria included histologically confirmed cT2-4a and N0-2 gastric adenocarcinoma. The extent of nodal dissection was performed based on the Gastric Cancer Treatment Guidelines in Japan. All procedure was performed through laparotomy. Laparoscopic approach was not accepted. Surgical outcomes morbidity, and mortality were compared between gastrectomy with omentectomy group (group A) and omentum preserving gastrectomy group (group B). Postoperative complication was evaluated with Clavien-Dindo classification. Results: A total of 251 patients were randomly assigned to group A (n = 125) or group B (n = 126) between April 2011 and October 2018. After excluding patients who received bypass or no surgery, 246 patients were analyzed as actual treatment group. There was no difference between two groups in patient characteristics and pathological findings. There was no difference in operation time (median 244 vs 204 min, p = 0.156) and in blood loss (median 260 vs. 210 ml, p = 0.371). Median number of totally retrieved lymph nodes was similar (median 36 vs. 37, p = 0.758). There was no difference in the incidence of any postoperative complication (28.9% vs. 25.8%, p = 0.584). There was no mortality in both groups. Conclusions: Omentum preserving gastrectomy for advanced gastric cancer was similar short-term outcomes with gastrectomy with omentectomy. Clinical trial information: UMIN000005421. Research Sponsor: None.
Comparing the accuracy of EUS and CT in staging of esophageal cancer.

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Background: Endoscopic ultrasound (EUS) is a suitable device for staging of esophageal cancers. However, chest computed tomography (CT) has traditionally been the standard diagnostic modality for malignancies. This study aimed to compare the accuracies of EUS and chest CT in T and N staging of esophageal cancers. Methods: We retrospectively analyzed 149 patients who had undergone EUS examination and 275 patients who had undergone chest CT before cancer surgery. The inclusion criteria were: 1) patients diagnosed with esophageal cancer on biopsy, 2) patients who had undergone EUS examination or chest CT before cancer surgery, and 3) patients who underwent cancer surgery at the Seoul National University Bundang Hospital from May 2003 to December 2018. We determined the accuracy of T and N staging on EUS examination and chest CT with the biopsy specimens. Results: The overall accuracies of EUS examination and chest CT were 72.5% (108/149) and 68.7% (189/275), respectively, for T staging ($p = 0.487$) and 64.4% (96/149) and 61.5% (169/275), respectively, for N staging, which was not statistically different ($p = 0.596$). For the substaging, the accuracy of EUS examination was not statistically different than that of chest CT for the T, N stage. Conclusions: EUS examination is not superior to chest CT for diagnosing T stage in esophageal cancers, whereas chest CT is not superior to EUS examination for diagnosing N stage in esophageal cancers. EUS examination and chest CT are not satisfactory for diagnosing T, N stage in esophageal cancers. Further study is needed for accurate T, N stage diagnosis in esophageal cancer. Research Sponsor: None.
Usefulness of laparoscopic narrow-band imaging for the evaluation of therapeutic effects on peritoneal metastasis in gastric cancer.

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Background: As recent advances in chemotherapy improved prognosis of gastric cancer (GC) patients with peritoneal metastasis (PM), accurate diagnosis of PM has become more important. However, the sensitivity of conventional imaging modalities such as CT or PET is not satisfactory. Staging laparoscopy (SL) is often used to diagnose PM in advanced GC patients, but accurate detection of PM can be difficult. In this study, we evaluate the usefulness of laparoscopic narrow-band imaging (NBI) versus conventional laparoscopic white-light imaging (WLI) for the diagnosis of PM and for the evaluation of therapeutic effect of chemotherapy. Methods: We excised 54 white nodules from the parietal peritoneum of 40 GC patients. Among them, 9 patients received chemotherapy for advanced or recurrent GC before SL, and 31 did not receive chemotherapy except for adjuvant chemotherapy with S-1. The WLI and NBI findings were compared with the pathological findings. Results: Intranodular vessels were evaluated by WLI and NBI for dilatation, tortuousness, heterogeneity, and brown spots. Detection of any one abnormal finding on NBI plus clear demarcation of the peritoneal nodules on WLI more properly diagnosed 42 peritoneal nodules of 31 patients who did not receive chemotherapy (sensitivity, 100%; specificity, 88.9%; accuracy, 95.2%). In contrast, diagnosis ability was poor for 12 peritoneal nodules of 9 patients who received chemotherapy before SL (sensitivity, 66.7%; specificity, 33.3%; accuracy, 58.3%). Conclusions: Laparoscopic NBI is a useful tool for the diagnosis of PM in advanced GC before chemotherapy, and disappearance of dilated vessels on laparoscopic NBI could be useful to evaluate the therapeutic effect. Research Sponsor: None.
Is D2 surgery necessary for clinical T1 gastric cancer with nodal swelling?

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**Background:** D2 surgery is required for clinical T1 gastric cancer with nodal swelling, however, D2 has a higher risk for morbidity than D1/D1+. Moreover, previous study demonstrated that the false positive rate for nodal diagnosis in clinical T1 was very high. To select optimal surgery with high probability, we explored risk factors for false positivity in clinical T1 disease. **Methods:** Patients who underwent radical gastrectomy for clinical T1 gastric cancer between April 2015 and June 2019 were enrolled. Accuracy, sensitivity, specificity, positive predictive value, and negative predictive values for nodal diagnosis were retrospectively investigated. The risk factors for false positivity were also analyzed by the following factors: age, sex, histological type, tumor size, tumor depth, location, tumor type, presence of ulcer, and timing of CT that is (1) the patients who underwent primary endoscopic mucosal dissection (ESD) but resulted in non-curative resection, then received CT to proceed to surgery (delayed CT group) or (2) the other patients who had received CT before primary surgery or before non-curative ESD (primary CT group). **Results:** A total of 679 patients were examined in the present study. The accuracy, sensitivity, specificity, positive predictive value, and negative predictive value were 83.5% (567/679), 14.3% (13/91), 94.2% (554/588), 27.7% (13/47), and 87.7% (554/632), respectively. The false positive rate was 72.3% (34/47). In univariate analysis, differentiated tumor ($p = 0.012$) and delayed CT ($p < 0.001$) were associated with the false positivity. Multivariate analysis revealed that delayed CT (OR, 4.534; $p < 0.001$) was a sole significant risk factor for false positivity. False positive rate was 100% (13/13) in the delayed CT group and 61.8% (21/34) in the primary CT group ($p = 0.009$). **Conclusions:** False positive rate was high in clinical T1 disease, especially when the patients received delayed CT after non-curative ESD. D2 surgery would be unnecessary even though nodal swelling was detected in CT after non-curative ESD. Research Sponsor: None.
Prediction of lymph node metastasis in early gastric cancer using artificial intelligence technology.

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**Background:** Early gastric cancer shows lymph node involvement in about 10-15% of patients. Despite this fact, we perform radical lymphadenectomy for all patients because predicting lymph node metastasis has yet to be successful. In this study, we hypothesize that image analysis using artificial intelligence (AI) technology may help solve the problem.

**Methods:** We retrospectively collected 82 patients with clinical T1N0 and pathological node negative and 82 patients with clinical T1N0 and pathological node positives and then divided the 164 patients into a training:validation set in ratio of 9:1. Endoscopic images of the early tumors were analyzed by transfer learning using AlexNet, a deep neural network containing 5 convolutional layers and 3 fully-connected layers. The model was validated with newly-collected 40 images from 20 clinical T1N0 and pathological node negative and 20 patients with clinical T1N0 and pathological node positives as a test set. For comparison, three methods of prediction were implemented: prediction at random, by logistic regression, and by skilled endoscopists.

**Results:** The AI predicted LNM with accuracy of 80.9% in the validation set and 66.9% in the test set. (48.3% for node negative cancers and 85.4% for node positive cancers) On the other hand, prediction at random, by logistic regression, and by 2 endoscopists resulted in 50.3%, 50.0%, and 47.5%, respectively.

**Conclusions:** Although the accuracy still needs to be improved, image analysis using the AI technology resulted in the best prediction of lymph node metastasis, indicating that AI is a promising technology for the diagnosis of lymph node metastasis in early gastric cancer. Research Sponsor: None.
Background: In patients with gastric cancer (GC), the most common double cancer is colorectal cancer (CRC). However, the meaning of screening colonoscopy has not been established. The aim of this retrospective study was to evaluate the useful of screening colonoscopy in preoperative patients with GC. Methods: This study included 689 patients who received screening colonoscopy before gastric surgery between 2012 and 2016. Multivariate analysis using logistic regression model was conducted to elucidate independent risk factors of CRC. Then, we investigated the clinicopathological factors for CRC. Results: Colorectal adenomas and CRC were observed in 315 patients (46%) and 37 patients (5.4%), respectively. The clinical T classification of the CRC were as follows; Tis: 24 patients (65%), T1: 8 patients (21%), T2: 2 patients (6%), and T3: 3 patients (8%). In multivariate analysis, male (OR 5.04, 95% C.I. 1.29-19.6, p = 0.020) was revealed as risk factor for affecting CRC. The treatments for CRC were as follows; EMR was performed in 27 patients, simultaneous resection with GC was performed in 9 patients, resection after gastrectomy was performed in 1 patient, respectively. Pathological stage of CRC was as follows; Stage 0: 24 patients, Stage I: 10 patients, and Stage IIA: 3 patients, respectively. As for the patients who underwent surgery for CRC, all of them received radical colectomy. No patient died for CRC who received colonoscopy before gastric surgery. Conclusions: Screening colonoscopy is useful for GC patients. Because most of the synchronous CRC were found early stage and curatively treated. Research Sponsor: None.
Trastuzumab + fluoropyrimidine maintenance in the frontline setting for non-progressing advanced HER-2 positive gastroesophageal adenocarcinoma.

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Background: In untreated patients with HER2 positive advanced gastroesophageal adenocarcinoma (AGEA), trastuzumab plus active cytotoxic combination is the standard of care. Our objective was to assess the role of maintenance therapy (trastuzumab + fluoropyrimidine) in the absence of cancer progression. Methods: We retrospectively analyzed HER2 positive AGEA patients (between August 2008 and October 2018) who received first-line trastuzumab-based therapy followed by maintenance therapy. The primary objectives were to assess the time to maintenance failure (TTMF), the first progression-free survival (PFS), and overall survival (OS). Results: Of 70 patients analyzed, 80% were men with a median age of 60.5 years. Primary tumor commonly involved the gastroesophageal junction (65.7%). More than 1 sites of metastases were frequent (88.6%). The best response was complete in 17%, partial in 70%, and stable in 11.4%. The median follow-up time for survivors was 2.1 years (range, 0.6 to 9.2). The median TTMF was 0.7 years (95% CI; 0.4 to 1.1 years). One-year TTMF-free rate was 41%. The median PFS was 1.3 years (95% CI, 0.8-1.6). The median OS was 3.2 years (95% CI, 2.3 years-4.5 years), with a 3-year survival rate of 55% (95% CI, 40%-67%). Conclusions: Our results showed that the OS of this unique population of HER2 positive AGEA patients who qualify for maintenance therapy is excellent. The contribution of the maintenance therapy can be clarified only by prospective investigations. Research Sponsor: None.
Propensity-score-matched analysis of a multi-institutional dataset to compare the postoperative complications after distal gastrectomy between Billroth I and Roux-en-Y.

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Background: Billroth I (B-I) or Roux-en-Y (R-Y) are common reconstruction technique after distal gastrectomy, each with advantages and disadvantages and which is the most successful remains unclear. The aim of the present study was to clarify the difference of postoperative complications between the two techniques. Methods: A multi-institutional retrospective database comprising clinical information of 3484 patients who received resection of gastric cancer from 2010 to 2014 at nine institutions. Using propensity scores to strictly balance the significant variables, and we compared the overall and severity postoperative complications. We considered Clavien–Dindo grade $\text{II}$ postoperative complications clinically relevant, and grade $\text{III}$ severe postoperative complications.

Results: After matching, we enrolled 1086 patients (n=543 in each group). The incidence of postoperative complications in the R-Y group was significantly higher vs the B-I group (28% vs 17%, respectively; $P<0.0001$). The incidence of intra-abdominal abscess (4.2% vs 1.7%, $P=0.0120$), pancreatic fluid leakage (3.1% vs 1.1%, $P=0.0204$), bowel obstruction (2.8% vs 0.7%, $P=0.0109$), and delayed gastric emptying (5.0% vs 0.9%, $P<0.0001$) in the R-Y group was significantly higher vs the B-I group, respectively; but not significant difference in leakage (3.2% vs 3.3%, respectively; $P=0.8636$). The incidence of severe postoperative complications in the R-Y group was also significantly higher vs the B-I group (15% vs 6.3%, respectively; $P<0.0001$). Multivariable analysis for severe postoperative complications found that R-Y reconstruction was an independent risk factor (odds ratio, 2.20, $P=0.0005$). Subgroup analysis found that R-Y reconstruction was associated with a greater risk of severe postoperative complications in most subgroups, but not the subgroup of patients receiving intraoperative transfusions. Conclusions: R-Y reconstruction was associated with increasing overall postoperative complications, as well as grade $\geq 3$ severe postoperative complications. Research Sponsor: None.
Health-related quality-of-life results from JCOG0912: A phase III noninferiority trial comparing open and laparoscopy-assisted distal gastrectomy for stage I gastric cancer.

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Background: Laparoscopy-assisted distal gastrectomy (LADG) was non-inferior to open (ODG) in patients with stage I gastric cancer in randomized phase 3 non-inferiority trial (JCOG0912). Here, we present the results of health-related quality of life (HRQoL) which was a secondary endpoint in JCOG0912. Methods: Among 33 institutions participated in JCOG0912, 4 major cancer centers were selected for HRQOL assessment. HRQoL was assessed using EORTC QLQ-C30 and the EORTC-STO22 before (baseline) and at 1, 3, 12, and 36 months after surgery. The primary HRQOL scale was QLQ-C30 global health status. We defined clinically meaningful decrease of HRQoL as decrease in 10 points or more from the baseline. Missing data were regarded as decrease. Assuming that expected %decrease of global health status at 3 months was 61% in ODG and 45% in LADG with 80% power and two-sided alpha of 0.05, sample size for HRQOL assessment was calculated to be 304. When this hypothesis at 3 months was confirmed, statistical comparison was tested in turn at 12 and 36 months. Results: Among 921 enrolled patients in JCOG0912 from Mar 2010 to Nov 2013, 592 were enrolled from the 4 centers in this HRQOL study. The %decrease of global health status at 3 months was different between ODG and LADG (37.2% (109/293) in ODG vs 29.2% (86/295) in LADG, odds ratio [OR] 0.65 (95% CI: 0.45-0.93, p = 0.020)), but was not different in 1 month (56.0% (164/293) vs 55.3% (163/295), OR 0.92 (0.61-1.32)), 12 months (26.3% (77/293) vs 27.8% (82/295) (OR 1.07 (0.73-1.56)) and 36 months (31.4% (91/293) vs 30.8% (91/295) (odds ratio, 0.96 (0.67-1.37))). Among the other subscales, LADG had significantly better symptom scores for pain at 1 and 3 months, constipation at 3 and 12 months, and eating restrictions at 3 months. Conclusions: Decrease of HRQoL was less frequently observed in LADG than ODG especially in the early phase after surgery. Considering non-inferiority and better HRQoL of LADG, LADG is strongly recommended for stage I gastric cancer. However, we have to be careful to expand the indication of LADG for advanced gastric cancer until a solid evidence is obtained. Clinical trial information: UMIN000003319. Research Sponsor: National Cancer Center; The Ministry of Health, Labour and Welfare of Japan; AMED.
Modified Controlling Nutritional Status score: A refined prognostic indicator depending on the stage of gastric cancer.

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**Background:** The role of controlling nutritional status (CONUT) score in predicting cancer survival remains uncertain. This study aimed to investigate the predictive value of the CONUT score and to develop a more appropriate scoring system beyond CONUT for gastric cancer (GC). **Methods:** We retrospectively reviewed 1307 patients who underwent curative gastrectomy between 2009 and 2015. The CONUT and three modified scores with modified lipid components (L-CONUT: albumin/total lymphocyte count [TLC]/low density lipoprotein, H-CONUT: albumin/TLC/high density lipoprotein, and T-CONUT: albumin/TLC/triglyceride) were calculated. The predictive value of each scoring system on long-term survival was assessed. **Results:** The values of the four nutritional scores were categorized into three groups (low, medium, and high). The CONUT (P < 0.001), L-CONUT (P < 0.001), H-CONUT (P < 0.001), and T-CONUT (P < 0.001) scores showed significant differences in overall survival in the three groups. Survival analysis according to the pathological stage showed that advanced age, Eastern Cooperative Oncology Group performance status, male sex, and high H-CONUT score (HR, 3.93; 95% CI, 1.81–8.55; P = 0.001) were independent worse prognostic factors for overall survival in the stage I group. In the stage II group, CONUT score (HR, 5.077; 95% CI, 1.65–15.65; P = 0.005) was significantly associated with poor prognosis. In the stage III group, no scoring system showed significant results. **Conclusions:** In advanced GC (beyond stage II), the prognostic impact of the nutritional scoring system was uncertain. However, the H-CONUT score is a promising indicator of prognosis in stage I GC, and the CONUT score is useful for predicting long-term survival in stage II GC. Research Sponsor: None.

Prognostic value of modified Glasgow Prognostic Score (mGPS) and neutrophil-lymphocyte ration (NLR) after curative resection for gastric cancer.

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**Background:** Several biomarkers based on serum chemistry have been reported to be associated with the prognosis of several types of cancers. This retrospective study aimed to investigate the prognostic value of preoperative mGPS and NLR after curative resection for gastric cancer.

**Methods:** A total of 295 patients who underwent curative gastrectomy for primary gastric cancer at our institution from January 2013 to December 2017 were enrolled in this study. The mGPS was calculated by CRP and Alb using standard thresholds (> 0.5 mg/dL for CRP and < 3.5 g/dL for Alb). The NLR was defined as absolute neutrophil count divided by absolute lymphocyte count. The survival curves of patients stratified by each parameter were plotted by the Kaplan-Meier method and compared by log-rank test. Multivariate Cox proportional hazards regression models were used to select parameters independently correlated with prognosis.

**Results:** The median follow-up time was 36.7 months, and 29 patients died during follow-up. The estimated 5-year survival rate was 83.1%. Results from the univariate analyses showed mGPS2 (CRP > 0.5 mg/dL and Alb < 3.5 g/dL) was associated with poor survival while NLR and NLRc was not (P = 0.001, P = 0.506, and P = 0.423, respectively). In the multivariate analyses, the mGPS2 was identified as an independent predictive factor for OS in gastric cancer patients after curative resection (HR: 2.624; 95% CI: 1.058-6.505; P = 0.037).

**Conclusions:** Preoperative mGPS2 was associated with worse survival after curative resection of gastric cancer patients. Based on our study, those with mGPS2 may be warranted to receive additional therapy or nutritional support to acquire better survival. Research Sponsor: None.
The impact of single-hetero UGT1A1 on clinical outcomes of irinotecan monotherapy in gastric cancer after fluoropyrimidine, platinum, and taxanes: Multicenter retrospective study.

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Background: Japanese gastric cancer treatment guidelines (5th edition) recommend irinotecan (IRI) after fluoropyrimidine, platinum and taxanes as a third line chemotherapy. We previously reported that patients with UGT1A1 single heterozygous (SH) had significantly high frequency of severe hematological adverse events (AEs) compared to patients with UGT1A1 wild type (WT) in IRI monotherapy for advanced gastric cancer (AGC). However, it remains unclear that UGT1A1 SH affect efficacy and safety of IRI after fluoropyrimidine, platinum and taxanes compared to WT as a salvage line. Methods: We retrospectively analyzed the clinical data of patients who received IRI monotherapy after fluoropyrimidine, platinum and taxanes in the multi-institutional retrospective study. From January 2010 to December 2017, 69 eligible patients were registered from 8 centers in Japan. Results: Forty one patients with UGT1A1 WT and 28 patients with UGT1A1 SH were included in this study. In WT/SH patients, performance status 0/1/2 was 12/25/4 and 5/17/6, treatment line 3rd/4th or later was 33/8 and 26/2, HER2 status positive/negative was 12/29 and 5/23, respectively. In WT/SH patients, rate of initial dose reduction was 22 and 28% (P = 0.363), median relative dose intensity (RDI) was 82% and 80% (P = 0.309). Of 88 patients who have measurable lesions, the overall response rate (ORR) was 5.7% and 4.2% (P = 1.000), disease control rate (DCR) was 54% and 38% (P = 0.289). Median progression free survival was 3.2 and 2.1 months (HR 0.607, P = 0.058) and median overall survival from initial day of IRI monotherapy was 10.0 and 7.0 months (HR 0.618 P = 0.086). In WT/SH patients, severe hematological AEs (G3) were observed more frequently in patients with UGT1A1 SH (WT: 43% and SH: 68%, P = 0.050), although frequency of severe non-hematological AEs (G3) were not significantly different in both groups (13% and 25%, P = 0.211). Conclusions: Compared to UGT1A1 WT, UGT1A1 SH status may be associated with poor efficacy and be a risk factor of higher frequency of severe hematological AEs. Research Sponsor: None.
Improved efficacy to cytotoxic agents chemotherapy after immune checkpoint inhibitors exposure in metastatic gastric cancer.

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Background: An association between improved responses to chemotherapy after exposure to vaccine-based immunotherapy has been previously reported in other cancers. However, it is unclear whether the chemotherapy response improves after exposure to immunotherapy, such as immune checkpoint inhibitors (ICIs). The objective of this retrospective study was to evaluate whether chemotherapy (4th-line) would yield improved efficacy when given after exposure to anti-PD-1 antibody in metastatic gastric cancer (mGC).

Methods: We investigated retrospectively clinical characteristics at baseline of mGC patients who received chemotherapy after progression of anti-PD-1 antibody (Nivolumab) between February 2018 and July 2019. Anti-PD-1 antibody was adapted as third-line therapy. Inclusion criteria for the analysis reported herein: histologically proven adenocarcinoma; ECOG PS 0-2; adequate organ functions; and received chemotherapy including 5-fluoropyrimidines (5-FU), platinum, and taxane or irinotecan. We evaluated efficacy outcomes, including ORR, DCR by RECIST version 1.1, PFS, and OS.

Results: Out of 27 treated with anti-PD-1 antibody, 10 patients were evaluable for responses and eligible to be included in this analysis. Patient characteristics were as follows: median age (range), 72 (50-88) years; male/female, 8/2; ECOG PS (0/1/2), 4/5/1; HER2 (+/-), 5/5; histology (differentiated/undifferentiated), 5/5; metastatic lesions (LN/peritoneum/liver/lung), 5/3/1/3; number of metastatic sites (1/≥2), 5/5; number of prior CTx regimens (3/4/5), 10/0/0; median period (range) from first line CTx, 18.8 (7.9-47.1) months; and CTx regimens (CPT-11/PTX/S-1+Oxaliplatin), 7/2/1; Among the 10 patients, 1 achieved a partial response, giving an ORR of 10.0%. Six patients had stable disease and three had progressive disease. The DCR was 70%. Median PFS and OS were 5.5M and 8.5M, respectively. There were no new irAEs appeared during CTx.

Conclusions: In mGC patients, our study demonstrated that increased efficacy to cytotoxic agents chemotherapy given after exposure to ICI was higher as compared to our historical data from the pre-anti-PD1 era. Updated results will be presented. Research Sponsor: None.
Conversion gastrectomy for stage IV unresectable gastric cancer: A retrospective cohort study.

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**Background:** Stage IV Gastric cancer (GC) is a heterogeneous biological condition with a mixture of distant metastases, including hematologic, lymph nodal and/or peritoneal. In the recent classification introduced by Yoshida et al with the proposal to identify objective principles for conversion surgery, stage IV GC patients were subdivided into 4 new categories. In this study, we retrospectively investigated the efficacy of conversion gastrectomy for stage IV GC patients, with particular focus on the Yoshida's classification.

**Methods:** A retrospective, single center cohort study was performed in patients who had undergone conversion gastrectomy between 2005 and 2018. Data were extracted from Hokkaido Cancer Center database including all metastatic gastric cancer patients submitted to surgery. Only stage IV unresectable tumors/metastases which became resectable after chemotherapy were included in this analysis.

**Results:** Forty-two resected stage IV GC patients were included in this analysis. Median overall survival (OS) was 40.0 months and 1-, 3- and 5-year survivals were 92.9, 70.7 and 57.7%, respectively. Univariate analysis among the patients with conversion gastrectomy identified macroscopic type, clinical response to 1st line therapy, pathological tumor depth, pathological nodal stage, R0 resection as significant prognostic factors. The MSTs of the patients with conversion gastrectomy for each category were 50.1 months for category 1, 46.6 months for category 2, 22.7 months for category 3 and 17.2 months for category 4.

**Conclusions:** Unresectable stage IV GC patients could benefit from radical surgery after chemotherapy and achieve long survivals. Adequate selection of stage IV GC patients for conversion therapy may be an important role. Research Sponsor: None.
Impact of gastric cancer treatment pathways on patient outcomes in a community oncology practice setting.

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Background: Gastric cancer (GC, including gastroesophageal junction adenocarcinoma) pathways have been implemented and refined since 2010 in the US Oncology Network (USON), a community-practice-based network. This study was designed to evaluate the impact of 4 pathway periods (PP): pre-pathway: pre-Aug ’10; Level 1: Sept ‘10-Nov ‘14; Clear Value, Dec ‘14-Feb ‘17; Value: After Mar ‘17, on treatment heterogeneity, treatment duration, and overall survival (OS).

Methods: Adult patients were eligible if they were treated at a participating USON site and were diagnosed with and treated for GC; follow up was through Mar 2019. Heterogeneity was measured by the Herfindahl-Hirschman Index (HHI), which is evaluated from 0.0 to 1.0 (complete to no heterogeneity). Time to treatment failure (TTF) was defined as initiation of the line of therapy until start of the subsequent line of therapy or death. OS was estimated from start of first-line (1L) therapy. Time-to-event outcomes were estimated using Kaplan-Meier.

Results: Of 3191 eligible patients, 2297 received treatment for advanced/metastatic disease. Of these, patient median age was 65.3 years, 60% were male, 70% were initially diagnosed with stage IV disease. Pre-pathway, common 1L regimens were single-agent fluorouracil (15%) and docetaxel-cisplatin-fluorouracil (14%); FOLFOX (45%) was most frequent during the value PP, 941 (41%) received second-line (2L) therapy. During Level 1 PP, single-agent irinotecan (11%) was most common during 2L, whereas in Value PP, ramucirumab+paclitaxel (43%) was most common. HHI and TTF are presented in the table. Median OS was 12.6 months (95% confidence interval, CI: 11.9, 13.5), which did not change significantly over PPs.

Conclusions: 1L and 2L heterogeneity was initially high, and was reduced over time; TTF showed modest increase. OS data are limited by high levels of censoring in the latter PPs, which reduces the ability to evaluate changes in more recent years. Research Sponsor: Eli Lilly and Company.

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Perioperative FLOT in resectable gastric cancer: Italian real-world data from the RealFLOT study.

Elisa Giommoni, Ferdinando De Vita, Irene Pecora, Francesco Iachetta, Antonia Strippoli, Maria Antonietta Satolli, Carmelo Pozzo, Michele Prisciandaro, Samantha Di Donato, Angelica Petrillo, Silvia Catanese, Giuseppe Tirino, Daniele Lavacchi, Lorenzo Antonuzzo, On behalf of GOIRC (Gruppo Oncologico Italiano di Ricerca Clinica); Medical Oncology, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy; Division of Medical Oncology, Department of Precision Medicine, University of Study of Campania “L. Vanvitelli”, Naples, Italy; Medical Oncology, Azienda Ospedaliero-Università Pisana, Pisa, Italy; Medical Oncology Unit, Clinical Cancer Center, AUSL-IRCCS, Reggio Emilia, Italy; Medical Oncology, Fondazione Policlinico Universitario “A. Gemelli”, IRCCS, Rome, Italy; Department of Medical Oncology, University of Turin, Turin, Italy; University Hospital of Modena, Modena, Italy; Medical Oncology Department, University Hospital, University of Cagliari, Cagliari, Italy; Oncology Unit - Dipartimento di Oncologia Clinica e Sperimentale Istituto Oncologico Veneto IOV-IRCCS, Padua, Italy; Medical Oncology, Usl Toscana Sudest, Arezzo, Italy; Internal Medicine Department "Tor Vergata" University Hospital, Rome, Italy; Medical Oncology, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Reggio Emilia, Italy; Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Medical Oncology, Department Nuovo Ospedale-Santo Stefano Instituto Toscano Tumori, Prato, Italy; Division of Medical Oncology, Department of Precision Medicine, University of Study of Campania “L. Vanvitelli”, Naples, Italy

Background: Perioperative treatments have significantly improved survival in patients with resectable gastric cancer, increasing 5-year overall survival from 23% with surgery alone to 45% with FLOT (fluorouracil, oxaliplatin, docetaxel). Pathological regression is a prognostic marker of better survival. Methods: In this observational, retro- and prospective study we collected data from patients with resectable gastric or gastro-oesophageal junction (GEJ) adenocarcinoma treated, as clinical practice, with perioperative FLOT. All patients had clinical T2 or higher and/or nodal involvement, according to FLOT4-AIO trial. Results: A total of 206 patients received perioperative chemotherapy with FLOT at 15 Italian centres, between September 2016 and September 2019. Overall, 186 (90.3%) patients completed the preoperative phase, 190 (92%) underwent surgery, and 142 (68.9%) started the postoperative phase. Among patients who started the postoperative phase, 105 (51.0%) received FLOT, while 37 (18%) received less intensive regimens (e.g. FOLFOX or De Gramont), depending on performance status after surgery or toxicity in the preoperative phase. Pathological complete response (pCR) was obtained in 7.3% of cases. In the preoperative phase, grade (G) 3-4 hematological and gastrointestinal adverse events (AEs) were reported in 42 (20.4%) and 13 (6.3%) patients, respectively. Conclusions: These real data confirmed the feasibility of perioperative FLOT in a less-selected population, representative of the clinical practice. The pCR rate was lower than in the FLOT4-AIO trial. The survival outcomes, potential predictive or prognostic factors and comprehensive safety data will be included in the final analysis. Research Sponsor: None.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients (n = 206)</th>
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<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>141 (68%)</td>
</tr>
<tr>
<td>Female</td>
<td>65 (32%)</td>
</tr>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>Gastric</td>
<td>114 (55%)</td>
</tr>
<tr>
<td>GEJ</td>
<td>92 (45%)</td>
</tr>
<tr>
<td>cT</td>
<td></td>
</tr>
<tr>
<td>T3-4</td>
<td>180 (87%)</td>
</tr>
<tr>
<td>T1-2</td>
<td>26 (13%)</td>
</tr>
<tr>
<td>cN</td>
<td></td>
</tr>
<tr>
<td>N+</td>
<td>174 (85%)</td>
</tr>
<tr>
<td>N0</td>
<td>32 (15%)</td>
</tr>
<tr>
<td>Compliance</td>
<td></td>
</tr>
<tr>
<td>Completed preoperative phase</td>
<td>186 (90%)</td>
</tr>
<tr>
<td>Started postoperative phase</td>
<td>142 (69%)</td>
</tr>
<tr>
<td>Received 4 courses of postoperative FLOT without dose reduction</td>
<td>29 (14%)</td>
</tr>
<tr>
<td>Pathological response</td>
<td></td>
</tr>
<tr>
<td>ypNO</td>
<td>60 (29%)</td>
</tr>
<tr>
<td>ypCR</td>
<td>15 (7.3%)</td>
</tr>
<tr>
<td>AEs in preoperative phase</td>
<td></td>
</tr>
<tr>
<td>Hematological G3-4</td>
<td>42 (20.4%)</td>
</tr>
<tr>
<td>Gastrointestinal G3-4</td>
<td>13 (6.3%)</td>
</tr>
</tbody>
</table>

SOURCE: Prediction models for overall survival in patients with metastatic and potentially curable esophageal and gastric cancer.

Héctor G. van den Boorn, Ameen Abu-Hanna, Nadia Haj Mohammad, Maarten C.C.M. Hulshof, Suzanne S. Gisbertz, Bastiaan R. Klarenbeek, Marije Slingerland, Laurens Victor Beerepoot, Tom Rozema, Mirjam A.G. Sprangers, Rob H. A. Verhoeven, Aeilko H. Zwinderman, Martijn G.H. van Oijen, Hanneke W.M. Van Laarhoven; Academic Medical Center, Amsterdam, Netherlands; Utrecht UMC, Utrecht University, Department of Medical Oncology, Utrecht, Netherlands; Amsterdam UMC, University of Amsterdam, Department of Radiotherapy, Cancer Center Amsterdam, Amsterdam, Netherlands; Amsterdam UMC, University of Amsterdam, Department of Surgery, Cancer Center Amsterdam, Amsterdam, Netherlands; Radboud University Nijmegen, Department of Surgery, Nijmegen, Netherlands; Leiden University Medical Center, Leiden, Netherlands; Elisabeth Tweesteden Hospital, Tilburg, Netherlands; Verbeeten Institute, Department of Radiotherapy, Tilburg, Netherlands; Department of Medical Psychology, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, Netherlands; Department of Clinical Epidemiologic Biostatics, Academic Medical Center, Amsterdam, Netherlands; Department of Medical Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; Amsterdam UMC, University of Amsterdam, Department of Medical Oncology, Cancer Center Amsterdam, Amsterdam, Netherlands

Background: Prediction models in cancer care can provide personalized prediction outcomes and can aid in shared decision making. Existing prediction models for esophageal and gastric cancer (EGC), however, are mostly aimed at predicting survival after a curative treatment has already been completed. The aim of this study is to develop prediction models, called SOURCE, to predict overall survival at diagnosis in potentially curable and metastatic EGC patients. Methods: The data from 12,756 EGC patients diagnosed between 2014-2017 were retrieved from the prospective Netherlands Cancer Registry. Four Cox regression models were created for potentially curable and metastatic cancers of the esophagus and stomach. Predictors, including treatment type, were selected using the Akaike Information Criterion. The models were validated with temporal cross-validation on their concordance-index (c-index) and calibration. Results: The validated model’s c-index is 0.76 for potentially curable cancer. For the metastatic models, the c-indices are 0.71 and 0.70 for esophageal and gastric cancer, respectively. The calibration intercepts and slopes lie in the 95% confidence interval of 0 and 1, respectively. The included model variables are given in Table. Conclusions: The SOURCE prediction models show fair c-indices and an overall good calibration. The models are the first in EGC to include treatment as a predictor. The models predict survival at diagnosis for a variety of treatments and therefore could have a high clinical applicability. Future research is needed to demonstrate the effect on shared decision making in clinical practice. Research Sponsor: Dutch Cancer Society (KWF), grant number 2014-7000.

<table>
<thead>
<tr>
<th>Overview of included model variables.</th>
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<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>Performance status</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>cT</td>
</tr>
<tr>
<td>cN</td>
</tr>
<tr>
<td>Tumor topography</td>
</tr>
<tr>
<td>Morphology</td>
</tr>
<tr>
<td>Differentiation grade</td>
</tr>
<tr>
<td>HER2 status</td>
</tr>
<tr>
<td>Only distant lymph node metastasis</td>
</tr>
<tr>
<td>Liver metastasis</td>
</tr>
<tr>
<td>Peritoneal metastasis</td>
</tr>
<tr>
<td>Number of metastatic sites</td>
</tr>
<tr>
<td>Treatment type</td>
</tr>
</tbody>
</table>
Impact of intraoperative staging of gastric cancer on long-term survival.

Keisuke Koumori, Kazuki Kano, Hayato Watanabe, Yota Shimoda, Hirohito Fujikawa, Takanobu Yamada, Yasushi Rino, Munetaka Masuda, Takashi Oshima, Takashi Ogata; Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan; Kanagawa Cancer Center, Yokohama, Japan; Yokohama City University, Yokohama, Japan; Department of Surgery, Yokohama City University, Yokohama, Japan

**Background:** The preoperative stage and intraoperative stage of gastric cancer were unified as the clinical stage in the 8th edition of the TNM classification (UICC). Although there are some reports about the relationship between preoperative stage and prognosis, the relationship between intraoperative stage and prognosis remains unclear. The aim of this study was to clarify the impact of intraoperative diagnosis and staging on long-term survival. **Methods:** Overall survivals were examined in 915 patients who underwent curative resection for gastric adenocarcinoma between April 2011 and March 2019 in our hospital. **Results:** The median age of the patients was 69 years (27-90 years), including 585 male and 330 female. The median follow-up period was 33.6 months (0.1-86.7 months). The number of the patients according to intraoperative stage were 641(70.1 %) in stageI, 15(1.6%) in stageIIA, 135(14.8%) in stageIIB, 111(12.1%) in stageIII, 12(1.3%) in stageIVA and 1(0.1%) in stageIVB. The hazard ratios of intraoperative stage for overall survival were as follows (ref: StageI); StageIIA, 6.990 (95% CI: 2.473-19.760, p = 0.001), StageIIB, 2.234 (95% CI: 1.220-4.092, p = 0.009), StageIII, 4.091 (95% CI: 2.416-6.928, p = 0.001), StageIVA, 6.061 (95% CI: 2.150-17.080, p < 0.001), StageIVB, 14.92 (95% CI: 2.035-109.3, p = 0.008). **Conclusions:** The survival of intraoperative StageIIA was poorer than StageIIIB/III. Intraoperative positive lymph node metastasis could be negative impact of survival, even if tumor invasion was T1 or T2. Research Sponsor: None.
**Treatment burden following standard of care open versus robotic D2 gastrectomy plus neoadjuvant chemotherapy (NAC) for locally advanced gastric cancer (LAGC).**

Mariana Juanita Rodriguez, Ana Sofia Ore, Khoschy Schawkat, Kevin F. Kennedy, Andrea J. Bullock, Jonathan F. Critchlow, James Moser; Beth Israel Deaconess Medical Center, Brookline, MA; Beth Israel Deaconess Medical Center, Boston, MA; Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA

**Background:** Phase III trials demonstrate improved short-term outcomes after laparoscopic gastrectomy for LAGC compared to open. We hypothesized that robotic D2 gastrectomy after NAC (NAC/RG) yields benefits across multiple outcome domains vs standard of care treatment for LAGC. **Methods:** Single institution, interrupted time series comparing SOC plus open gastrectomy (OG,2008-2013) for LAGC (T2-4Nany/TanyN+) vs universal neoadjuvant plus RG (2013-2018). Treatment burden was a composite of adverse events affecting: efficiency (postoperative length of stay, reoperation or 90 d readmission), oncology (positive margins, < 16 resected nodes), cumulative major morbidity (90 d comprehensive complication index) and pain (narcotic consumption). Predictors were evaluated via multivariate modeling, and 2-year overall survival was estimated by Kaplan-Meier/log-rank tests. **Results:** After exclusions, 87 subjects underwent surgical resection (55 OG; 32 RG) with equivalent baseline characteristics: demographics, BMI, comorbidity (Charlson), tumor size, and clinical AJCC staging; male sex was more likely in RG (69% vs. 44%, p = 0.02). NAC administration increased from 35% in SOC/OG cohort to 100% in NAC/RG. All four domains of efficiency, oncologic efficacy, morbidity, and pain (narcotic use) improved. Treatment burden declined from 86% in OG to 56% after RG (p = 0.003). Multivariable modeling demonstrated OR 0.23 for treatment burden in RG compared to OG (95% CI 0.07-0.72, p = 0.012), whereas sex, extent of resection (total vs subtotal), tumor size, and T stage had no effect. These differences persisted in NAC subgroup (n = 51) comparisons between RG and OG treatment burden, as well as pathologic T stage, tumor size, and AJCC stage. No detriment in 2-year overall survival was observed after adoption of NAC/RG (80% RG vs. SOC 60%, p = 0.048). **Conclusions:** After NAC, robot-assisted D2 gastrectomy was associated with decreased treatment burden relative to OG. Frequencies of unfavorable hospitalization, adverse oncological outcomes, major morbidity, and narcotic consumption all improved after RG in this interrupted time series. Prospective trials are needed. Research Sponsor: None.
Real-world outcomes of first-line U.S. patients with unresectable advanced or metastatic gastroesophageal adenocarcinoma by primary tumor location.

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**Background:** Gastric cancer clinical trials are inconsistent in their inclusion of esophageal adenocarcinoma (EAC). Thus it is uncertain if outcomes are similar among subgroups of gastroesophageal adenocarcinoma. The aim of this study was to compare baseline characteristics and clinical outcomes of US patients with EAC versus Gastroesophageal Junction Cancer (GEJC) and Gastric Cancer (GC) treated in real world clinical settings. **Methods:** Adult patients with unresectable, advanced or metastatic GC, GEJC, or EAC diagnosed between January 2011 and November 2018 were identified from the Flatiron Health database. Patients with a positive HER2 test, or who received trastuzumab, were excluded. Overall survival (OS) was defined as time from first-line (1L) treatment initiation to death or loss of follow-up. Survival analyses were conducted using Kaplan-Meier methods with log-rank test and Cox models. **Results:** A total of 3052 patients (969 EAC and 2083 GEJC/GC) met eligibility criteria. Out of all EAC patients, 90% were males and 76% were white. Within the GEJC/GC patients, 67% were males and 57% were white. Median age was 66 years for both cohorts while proportion with ECOG PS of 0 or 1 was 78% for EAC and 84% for GEJC/GC among patients with ECOG scores. The proportion of patients receiving 1L treatment was comparable (78% for EAC, 76% for GEJC/GC) across groups with FOLFOX being the most frequent treatment (25% for EAC and 29% for GEJC/GC). There was no significant difference in OS between the two groups, with median OS of 9.1 and 9.6 months for EAC and GEJC/GC, respectively (HR 0.957, 95% CI: 0.863 - 1.062, p = 0.41). **Conclusions:** In this US real-world analysis, OS did not differ significantly between patients with EAC and patients with GEJC/GC who received 1L treatment, suggesting that these two populations may have comparable survival benefit from systemic therapy. Research Sponsor: Bristol-Myers Squibb.
The impact of additional treatment after endoscopic submucosal dissection for esophageal squamous cell carcinoma in real-world clinical practice.

Nanako Sakaguchi, Toshifumi Yamaguchi, Yasunobu Ishizuka, Hiroyuki Kodama, Takahiro Miyamoto, Tetsuji Terazawa, Yuichi Kojima, Takayuki Kii, Makoto Sanomura, Masahiro Goto, Kazuhide Higuchi; Second Department of Internal Medicine, Osaka Medical College, Osaka, Japan; Department of Cancer Chemotherapy Center, Osaka Medical College Hospital, Osaka, Japan; Hokusetsu General Hospital, Osaka, Japan

Background: Endoscopic submucosal dissection (ESD) is the standard therapy for the T1a-EP/LPM esophageal squamous cell carcinoma (ESCC), although it is difficult to diagnose the invasion depth accurately before ESD. The incidence of lymph node metastases in ESCC involving the muscularis mucosae (pT1a-MM) and the submucosa (pT1b-SM) is reported to range from approximately 10% to 30%. For the patients with MM, SM or involving LVI or positive vertical margin after ESD, additional treatment (AT) is recommended to prevent local recurrence. However, the AT is not always performed to the frail or elderly patients. The aim of this study is to investigate the outcome of AT and non-AT (NAT) after ESD for ESCC in the real-world clinical practice. Methods: We retrospectively reviewed the ESCC patients who were pathologically confirmed T1a-MM or T1b-SM (UICC-TNM7th) after ESD at Osaka medical college hospital between 2004 and 2016. Results: Among 224 patients who received ESD, 52 patients were pT1a-MM (n = 36; 69.2%) or pT1b-SM (n = 16; 30.8%). Twelve of 52 patients (23%) received AT and forty patients (77%) received NAT. Six patients (AT group: 2 patients, NAT group: 4 patients) had local lymph node recurrence. Five of them underwent salvage therapy. Median follow up time were 54.3 months (range: 48.4-62.4). The 3-, 5-year RFS rate and the 3-, 5-year OS rate were 83.8% [95%CI: 68.2- 92.6], 73.4% [95%CI: 56.0- 85.7] and 94.7% [95%CI: 81.3- 98.6], 91.7% [95%CI: 77.1- 97.3] in all patients, respectively. The 5-year RFS and OS rate were 77.8%, 90.0% in the AT group and 71.6, 92.2% in the NAT group. Conclusions: Although the AT tended to prevent local recurrence, the OS was comparable with NAT because of salvage therapy. The active surveillance is recommended for T1a-MM or T1b-SM ESCC. Research Sponsor: None.
Change in neutrophil-to-lymphocyte ratio (NLR) in response to immune checkpoint inhibitor for advanced gastric cancer.

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Background: We intended to evaluate the utility of neutrophil-to-lymphocyte (NLR) in advanced gastric cancer patients treated with immune checkpoint inhibitor (ICI). Methods: We examined NLR at baseline and 6 (±2) weeks later in 139 patients between August 2015 and April 2019. Landmark analysis at 6 weeks was conducted to explore the prognostic value of NLR change on progress-free survival (PFS), overall survival (OS), objective response rate (ORR), and disease control rate (DCR). Cox and logistic regression models were adjusted for tumor differentiation, Lauren classification, line of therapy, type of anti-PD-1/PD-L1 therapy, and baseline NLR. Results: Median duration on therapy was 6 cycles. Median NLR was 3.33 (IQR: 2.26-4.84) at baseline and 2.93 (IQR: 1.67-4.83) at week 6. Patients with a higher baseline NLR showed a trend toward lower DCR, shorter PFS, and shorter OS. Higher NLR at 6 weeks was significantly associated with inferior PFS [hazard ratios (HRs) 1.03, 95% confidence interval (CI): 1.00-1.06 ] and inferior OS (HR 1.08, 95%CI: 1.03-1.12). Relative NLR decrease by ≥ 25% from baseline to 6 weeks after ICI therapy was an independent prognostic factor for ORR (OR 8.11,95% CI:2.40-27.4), DCR (OR 20.03, 95% CI: 3.32-121), PFS (HR 0.37, 95% CI: 0.20-0.68), and OS (HR 0.26, 95% CI: 0.10-0.65). Conclusions: Early decline of NLR (and NLR at 6 weeks) were associated with improved clinical outcomes in advanced gastric cancer patients treated with ICI. Research Sponsor: None.

<table>
<thead>
<tr>
<th>Association of NLR with survival in advanced gastric cancer patients.</th>
<th>PFS</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of events</strong></td>
<td>Univariate HR (95% CI)</td>
<td>Multivariate HR* (95% CI)</td>
</tr>
<tr>
<td>Continuous NLR (baseline)</td>
<td>139 96</td>
<td>1.03 (0.99-1.07) 1.02 (0.97-1.06)</td>
</tr>
<tr>
<td>Continuous NLR (6-weeks)†</td>
<td>121 92</td>
<td>1.03 (1.00-1.05) 1.03 (1.00-1.06)</td>
</tr>
<tr>
<td>NLR-change [6 weeks]‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decrease ≥ 25%</td>
<td>46 24</td>
<td>0.47 (0.27-0.81) 0.37 (0.20-0.68)</td>
</tr>
<tr>
<td>No change (&lt;25% decrease to &lt;25% increase)</td>
<td>35 27</td>
<td>1 (reference) 1 (reference)</td>
</tr>
<tr>
<td>Increase ≥ 25%</td>
<td>40 31</td>
<td>1.21 (0.72-2.02) 0.97 (0.53-1.77)</td>
</tr>
</tbody>
</table>

Treatment patterns and long-term clinical outcomes in Chinese patients with nonmetastatic gastric cancer: Results from the non-interventional EVIDENCE registry study.

Jiafu Ji, Shukui Qin, Xin Wang, Weiping Zhou, Lin Chen, Zhichao Zheng, Wuyun Su, Helong Zhang, Jianhua Wang, Qi Luo, Yong Tang, Lin Shen; Peking University Cancer Hospital and Institute, Beijing, China; PLA Cancer Center of Bayi Hospital Affiliated to Nanjing University of Chinese Medicine, Nanjing, China; Xijing Hospital, Xi’an, China; Department of Gastrointestinal Surgery, Hainan General Hospital, Haikou, China; Chinese PLA General Hospital, Beijing, China; Liaoning Cancer Hospital and Institute, Shenyang, China; Affiliated Hospital Inner Mongolia Medical University, Huhhot, China; Tangdu Hospital, Fourth Military Medical University, Xi’an, China; Shanxi Provincial People’s Hospital, Xi’an, China; First Affiliated Hospital, Xiamen University and Xiamen Cancer Center, Xiamen, China; Affiliated Tumor Hospital of Xinjiang Medical University, Urumqi, China; Department of Gastrointestinal Oncology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital and Institute, Beijing, China

**Background:** Although gastric cancer (GC) is a leading cause of cancer-related death in China, important questions about optimal management remain unanswered. The EVIDENCE registry study evaluated data from patients with GC in China to assess the pattern of treatments and long-term clinical outcomes. **Methods:** Five cohorts of patients with different HER2 and metastatic status were evaluated from April 2013 to June 2018 in this prospective, multicenter, non-interventional, real-world study. Data from patients with operable non-mGC are reported: Cohort III (HER2+) and Cohort V (HER2−). Outcome measures included overall survival (OS), event-free survival (EFS), and disease-free survival (DFS). **Results:** Cohorts III/V included 758 patients (Cohort III, 271; Cohort V, 487); 75.5% were male and the mean age was 58.8 years. The majority of Cohort III/V patients (538/758; 71.0%) received only adjuvant treatment, with 215/758 (28.4%) receiving S1+oxaliplatin. Neoadjuvant or adjuvant trastuzumab was administered to 43/758 patients (Cohort III, 42; Cohort V, 1). Radiation during neoadjuvant or adjuvant treatment was administered to 23/758 (3.0%) patients. The median duration of follow-up was 515 days, during which 72 (9.5%) patients died due to progressive disease. OS rates (95% CI) for Cohorts III and V were 94% (89–96) and 95% (92–97) at 1 year, and 76% (67–83) and 70% (64–75) at 3 years, respectively. Respective EFS rates were 82% (76–87) and 86% (83–89) at 1 year, and 62% (53–70) and 57% (51–63) at 3 years; and respective DFS rates were 88% (82–93) and 86% (81–89) at 1 year and 69% (58–78) and 62% (55–68) at 3 years. Multivariate analysis indicated that the primary tumor site (p = 0.004) and overall cancer stage (p < 0.001) were associated with DFS. Regarding the primary tumor site, there was a trend towards better DFS for antrum tumors (hazard ratio 0.59; 95% CI 0.32–1.07) when evaluated against gastroesophageal junction tumors. **Conclusions:** This longitudinal analysis of clinicopathologic characteristics and outcomes of Chinese patients with non-mGC will provide critical information that will help to inform disease management. Clinical trial information: NCT01839500. Research Sponsor: Shanghai Roche Pharmaceuticals Ltd., China.
A nationwide population-based study comparing survival in unresectable advanced or synchronous metastatic esophageal and gastric adenocarcinoma.

Background: Similarities between esophageal and gastric adenocarcinomas have been identified in terms of genomic characteristics. There is however no consensus on the combined or stratified inclusion of esophageal adenocarcinoma (EAC) within gastric cancer (GC) clinical trials. The aim of our study was to compare patient and tumor characteristics, first-line treatment regimens and overall survival (OS) of patients with EAC and GC.

Methods: We selected patients with unresectable advanced and/or synchronous metastatic EAC (n = 1554) or GC (including junction tumors; n = 2095) diagnosed in the period 2015-2017 from the nationwide Netherlands Cancer Registry. Patients with a positive HER2 test result and/or receiving trastuzumab as a first-line treatment were excluded. Data on OS were analyzed using Kaplan-Meier curves with Log-Rank test.

Results: The EAC patient population had significantly more male patients (83% vs 66%), lower median age (68 vs 71 years) and higher median BMI (25.4 vs 24.5). Significant differences in location of metastases were identified, with higher percentages in non-regional lymph nodes (48% vs 28%), liver (50% vs 35%), lung (21% vs 9%) and bone (19% vs 7%) and lower in peritoneum (5% vs 42%), in EAC versus GC patients respectively. EAC patients more often received any type (supportive or active systemic) of treatment (76% vs 60%). Median OS was longer in EAC than GC patients (EAC: 4.8 vs GC: 4.1 months; p < 0.01). The percentages of patients receiving first-line systemic treatment were equal in both groups (43%). The number of patients receiving CapOx or FOLFOX was not significantly different (43% vs 47%). Carboplatin+paclitaxel was more frequently given in EAC versus GC (34% vs 3%), while EOX or ECC was given less frequently (12% vs 30%). No significant difference was observed in median OS between EAC and GC patients receiving first-line active systemic treatment (8.0 vs 7.6 months; p = 0.28).

Conclusions: Patient characteristics, tumor characteristics, treatment regimens and OS differ between EAC and GC patients. Despite these differences, in patients receiving first-line active systemic treatment no significant differences in OS were found. Research Sponsor: Bristol-Meyers Squibb.
Association of real-world agreement between HER2 expression and ERBB2 amplification with trastuzumab therapy benefit in advanced gastric/esophageal (adv GE) cancer patients (pts).

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**Background:** Trastuzumab (T) plus chemotherapy is standard of care for pts with HER2+ adv GE cancer. Selection for T relies on HER2+ result by immunohistochemistry (IHC) +/- in-situ hybridization (ISH); ERBB2 amplification by comprehensive genomic profiling (CGP) also predicts benefit. As CGP use increases, it is important to explore associations of IHC/ISH and CGP result agreement with clinical outcomes in pts with adv GE cancer. **Methods:** Pts with adv GE cancer were selected from the Flatiron Health-Foundation Medicine (FMI) clinico-genomic database (CGDB), a nationwide de-identified EHR-derived clinical database linked to FMI genomic data. Pts treated from 01/2011-12/2018 with CGP data for tissue specimens collected before 1L were included. Agreement between HER2 status by IHC +/- ISH v ERBB2 amplification by CGP was assessed. For 1L containing T, time to tx discontinuation (TTD) and overall survival (OS) from 1L start stratified by HER2:ERBB2 agreement and ERBB2 copy number (CN) [ERBB2+ = CN >4] were estimated with unadjusted Kaplan-Meier analysis and adjusted (practice type, sex, age at adv dx) hazard ratios (aHR) from Cox proportional hazards models. **Results:** Of 596 HER2-tested pts with adv GE cancer in CGDB, 174 (29%) were HER2+ by IHC/ISH. Median age at adv dx was 63 y; 76.5% were male and 97% had adenocarcinoma. Overall HER2:ERBB2 agreement was 91%. Of 123 HER2+ 1L T-treated pts, median TTD and OS were longer for HER2+:ERBB2+ (concordant; n = 93) v HER2+:ERBB2- pts (discordant; n = 30): TTD, 5.2 v 0.8 months, aHR 0.46 (0.29-0.70); OS 14.8 v 7.5 months, aHR 0.38 (0.21-0.68). Median OS was 22.0 vs 8.4 months for 1L T-treated pts with ERBB2 CN > 30 (median) v CN ≤30 (aHR 0.69 [0.37-1.27]). **Conclusions:** In this large real-world clinico-genomic dataset, HER2:ERBB2 agreement was high in tested pts with adv GE cancer. 1L T-treated pts with discordant tests (HER2+: ERBB2-) had significantly shorter TTD and OS. Pts with higher ERBB2 CN had longer OS, but this finding was not significant after adjusting for covariates. Further research is needed to explore associations between HER2:ERBB2 agreement and clinical outcomes in this population. Research Sponsor: None.
Clinical impact of postgastrectomy sarcopenia on the prognosis in patients with gastric cancer.

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**Background:** There is a lack of research on newly developed sarcopenia postoperatively. The purpose of this study was to investigate the risk factors and the clinical impact of postgastrectomy sarcopenia on the prognosis in patients undergoing radical gastrectomy for gastric cancer (GC).

**Methods:** We retrospectively reviewed clinicopathological data from 430 consecutive GC patients who underwent surgical resection at Chung-Ang University Hospital between January 2011 and December 2015. Their skeletal muscle mass and abdominal fat volume were measured by abdominal CT imaging.

**Results:** A total of 425 patients were analyzed in the study. The mean age was 62 years old and male were 301 (70.8%). Of these, 42 patients (9.9%) were diagnosed as pre-operative sarcopenia. Compared with non-sarcopenic group, pre-operative sarcopenia groups showed more female, higher BMI, less alcoholic, and less smoking. However, there was no significant difference in 5-year overall survival and disease free survival between the groups (p = 0.836 and p = 0.638, respectively). Among 381 non-sarcopenic patients, 48 patients (12.6%) were diagnosed as newly developed sarcopenia in one year after gastric resection. Compared with non-sarcopenic group, the newly developed sarcopenic group showed more male, more undifferentiated tumor, lower hemoglobin level, less alcoholic, less smoking, and presence of diabetes mellitus. However, there was no significant difference in the 5-year overall survival and disease free survival among non-sarcopenic, sarcopenic, and newly developed sarcopenic groups (p = 0.521 and p = 0.534, respectively). The relationship between preoperative body fat volume and postoperative muscle mass showed a significant correlation (rho = 0.296, p < 0.001), but only BMI was significantly associated with long term survival.

**Conclusions:** Although newly developed sarcopenia after surgery did not affect the survival rate, patients with nutritional risk of sarcopenia after surgical resection may require early evaluation of nutritional status and nutritional support. 

Research Sponsor: None.

Development and validation of a pretreatment nomogram to predict disease-specific mortality in gastric cancer.

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Background: The American Joint Committee on Cancer (AJCC) has increasingly recognized the need for individual risk prediction model. The AJCC has emphasized the attractiveness of disease-specific mortality (DSM), which can properly control for competing events, as an endpoint of risk model, as well as overall survival (OS) and disease-specific survival (DSS). For the era of tailored therapy, we aimed to develop a new pretreatment gastric cancer nomogram for prediction of DSM.

Methods: The nomogram was developed using data of 5,231 patients with primary gastric cancer treated at Shizuoka Cancer Center (Shizuoka, Japan), and it was created with a Fine and Gray competing-risks proportional hazards regression model. Fifteen clinical variables, which were obtained at pretreatment, were collected and registered, to develop the nomogram. Data of independent cohort of patients from the University of Verona (Italy; 389 patients) formed the external validation cohort. The model was validated internally and externally using measures of discrimination (Harrell’s C-index), calibration and decision curve analysis.

Results: In the development procedure, multivariable analysis for DSM selected 14 variables for constructing the nomogram. The developed nomogram showed good discrimination, with a C-index of 0.887 (95% CI; 0.881-0.894); that of the American Joint Committee on Cancer (AJCC) clinical stage was 0.794 (0.784-0.804). In the external validation procedure, the C-index was 0.713 (0.680-0.746) (AJCC, 0.582, 0.539-0.622) in the University of Verona cohort. The nomogram performed well in the calibration and decision curve analyses when applied to both the internal and external validation cohorts.

Conclusions: This new pretreatment risk model accurately predicts DSM in gastric cancer and can be used for patient counseling in clinical practice and stratification in clinical trials.

Research Sponsor: None.
Retrospective comparison of neoadjuvant chemoradiation (nCRT) +/- surgery using the CROSS trial regimen and definitive chemoradiation (dCRT) with carboplatin (C) and paclitaxel (P) in esophageal (EC), and gastroesophageal junction cancer (GEJC) in Canada.

Sidra Khalid, Wilma M. Hopman, Kiran Virik; Department of Medical Oncology-Queen's University, Kingston, ON, Canada; Department of Public Health Sciences-Queen's University, Kingston, ON, Canada

Background: Trimodality therapy using the CROSS trial protocol is an accepted standard of care for locally advanced EC and GEJC. For medically inoperable patients (pts), CRT has been a standard. CRT with C and P is an option in the definitive setting. This single institution review aims to assess the application and outcomes of the CROSS trial protocol in our real world population. Methods: From June 2012 until June 2018, a retrospective review was undertaken of 83 pts who underwent CRT with C and P with trimodality or upfront definitive intent. 65 pts underwent nCRT; 40 proceeded to surgery. 18 had upfront dCRT. Pt demographics, clinical, pathological, treatment and surgical characteristics were assessed. These factors and outcomes were analyzed in exploratory analyses. Results: Of the 83 pts: median (m) age was 69 yrs (range 48-82), 34% were ≥ 75 yrs, 80% were male, 21% had CAD, 43% GERD, 23% Barrett’s, 77% adenocarcinoma, m tumor length was 5 cm, 36% had BMI > 30 and 80% were Siewert I tumors. The m RT dose was 50.4 Gy, m chemo doses were 5, m time to CRT was 69 days and m time from CRT to surgery was 66 days. 23% nCRT pts and 72% dCRT pts were ≥ 75 yrs and 49% and 33% of these respectively had no interruptions to CRT. Pts who underwent surgery were younger (p = 0.04) and weighed more (p = 0.05). Pts ≥75 yrs were likely to have dCRT (p = 0.001). For nCRT and surgery, nCRT only and dCRT respectively, median overall survival (mOS) was 35.5, 12.1 and 17.1 months (M) (log rank p = 0.08), PFS was 32.2, 10 and 9.6M (log rank p = 0.01). Compared to the other 2 groups, pts who underwent surgery had: no COPD (p = 0.004), less CAD (p = 0.003), less renal impairment (p = 0.023) and had lower esophageal tumors (p = 0.027). mOS for pts who had nCRT was 28.9M and 17.1M for dCRT (log rank p = 0.70). Further correlative outcome data will be presented. Conclusions: Despite the broadening of CROSS trial eligibility criteria in our real world data, there appears to be a survival benefit with trimodality therapy. The use of C and P in dCRT may be of value especially in the elderly, and requires further study. Research Sponsor: None.
Relationship between perioperative change of total psoas muscle area and cancer prognosis in esophageal carcinoma.

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Background: As surgery for esophageal carcinoma in the elderly people has been increasing, sarcopenia is a severe problem not only in complications, but also in long-term prognosis. However, the relationship between perioperative skeletal muscle loss especially in the early postoperative period and long-term prognosis has not been clarified. Methods: This study retrospectively analyzed 152 patients with thoracic esophageal carcinoma who had undergone radical esophagectomy in our institution from April 2008 to March 2015 (Patients with postoperative hospital stay longer than 6 weeks were excluded). As an index of perioperative sarcopenia, total psoas muscle area (TPA) was measured before surgery (as baseline), at postoperative day (POD) 7 and postoperative month (POM) 6 from CT images. We investigated the correlation between the change of TPA and the postoperative survival. Results: Of 152 patients, 52 (34.2%) showed a TPA decrease from baseline to POD 7, and 98 (64.5%) showed a TPA decrease from baseline to POM 6. At the time of POD 7, overall survival (OS) decreased significantly in a TPA decrease group (P = 0.008, 5-year survival rate: non-decrease group 82.3% / decrease group 56.8%). Recurrence free survival (RFS) was also significantly decreased in a TPA decrease group (P < 0.001, 5-year recurrence free survival rate: non-decrease group 73.7% / decrease group 44.9%). On the other hand, at the time of POM 6, OS and also RFS had no significant difference between decrease and non-decrease groups. In univariate analysis for OS, pStage $\geq 3$ and TPA decrease at POD 7 had poor prognosis. In multivariate analysis for OS, pStage $\geq 3$ (HR:5.516, P < 0.001, 95%CI:2.634-11.551) and TPA decrease at POD 7 (HR:2.036, P = 0.047, 95%CI:1.104-3.416) were also independent poor prognostic factors. In univariate analysis for RFS, pStage $\geq 3$, TPA decrease at POD 7 and age $\geq 60$ years had poor prognosis. In multivariate analysis, pStage $\geq 3$ (HR:3.831, P < 0.001, 95%CI: 2.182-6.728) and TPA decrease at POD 7 (HR:1.942, P = 0.021, 95%CI:1.104-3.416) were independent poor prognostic factors. Conclusions: Our findings suggest that the TPA decrease early in a postoperative period has poor prognosis on OS and also RFS. Research Sponsor: None.

Impact of palliative care in patients with metastatic esophageal cancer declining chemotherapy.

Nicholas Manguso, Sungjin Kim, Michelle Guan, Veronica Placencio-Hickok, Haesoo Kim, Jar-Yee Liu, Andrew Eugene Hendifar, Samuel J. Klempner, Miguel Burch, Alexandra Gangi, Joseph Chao, Mitchell Kamrava, Katelyn Mae Atkins, Jun Gong; Cedars-Sinai Medical Center, Department of Surgery, Los Angeles, CA; Cedars-Sinai Medical Center, Los Angeles, CA; Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA; Cedars-Sinai Medical Center, West Hollywood, CA; The Angeles Clinic and Research Institute, Los Angeles, CA; City of Hope Comprehensive Cancer Center, Duarte, CA; Cedars-Sinai Medical Center, LA, CA; City of Hope, Duarte, CA

Background: Palliative care has been associated with improved overall survival (OS), but limited data exist in metastatic esophageal cancer (mEC). We investigated the impact of palliative care in patients with mEC who declined chemotherapy (CTX).

Methods: The National Cancer Database was used to identify patients between 2004-2015. Patients with M1 disease who declined CTX and had known palliative care status (surgery, radiotherapy [RT], pain management, or any combination of) were included. Cases with unknown CTX, RT, or nonprimary surgery status were excluded. Kaplan-Meier estimates of OS were calculated. Univariable and multivariable Cox regressions were performed. Results: Among 140,234 EC cases, we identified 1,493 patients who declined CTX and had complete data. Median age was 70 years, most (66.3%) had a Charlson Comorbidity Index (CCI) of 0, and 37.1% were treated at an academic center. Most (72.7%) did not receive palliative care. Median OS was 2.53 months (mos), with no statistically significant difference in median OS between those receiving palliative care (2.83 mos, 95% confidence interval [CI] 2.53-3.12) vs. no palliative care (2.37 mos, 2.2-2.56; p = 0.288). On univariable analysis, treatment at an academic center (hazard ratio [HR] 0.90, 0.80-1.00) and CCI ≥2 (HR 1.20, 1.00-1.42) were predictive of OS (p < 0.05). On multivariable analysis, male sex (HR 1.23, 1.08-1.40), South geographic region (HR 1.23, 1.04-1.46), CCI of 1 (HR 1.17, 1.03-1.32), higher grade (HR 1.21, 1.07-1.38), and higher T stage (HR 1.39, 1.12-1.73) were associated with poor OS (p < 0.05). Conclusions: Palliative care conferred a numerically higher, but not statistically significant difference in OS among patients with mEC declining CTX. Quality of life metrics, inpatient status, and subgroup analyses are important for examining the role of palliative care in mEC and future studies are warranted. Research Sponsor: None.
Baseline features predicting receipt of chemotherapy in metastatic esophageal cancer: A National Cancer Database analysis of 12,370 patients.

Nicholas Manguso, Sungjin Kim, Andrew Eugene Hendifar, Samuel J. Klempner, Joseph Chao, Michelle Guan, Veronica Placencio-Hickok, Haesoo Kim, Jar-Yee Liu, Miguel Burch, Alexandra Gangi, Katelyn Mae Atkins, Mitchell Kamrava, Jun Gong; Cedars-Sinai Medical Center, Department of Surgery, Los Angeles, CA; Cedars-Sinai Medical Center, Los Angeles, CA; Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA; The Angeles Clinic and Research Institute, Los Angeles, CA; City of Hope Comprehensive Cancer Center, Duarte, CA; Cedars-Sinai Medical Center, West Hollywood, CA; Cedars-Sinai Medical Center, LA, CA; City of Hope, Duarte, CA

Background: We investigated predictors for chemotherapy (CTX) and prognostic variables in a large metastatic esophageal cancer (mEC) patient data set. Methods: We interrogated the National Cancer Database between 2004-2015 and included patients (pts) with M1 disease who had known CTX status (received or did not receive CTX). Univariable and multivariable analyses were performed, and a logistic regression model was used to estimate the effect of CTX with adjustment for potential confounders. Results: We included 12,370 mEC patients with available CTX status for multivariable analyses. Predictors for CTX treatment included year of diagnosis 2010-2014 (odds ratio (OR) 1.29, 95% confidence interval (CI) 1.17-1.43), median income > $46,000 (OR 1.49, 1.27-1.75), and node-positivity (OR 1.35, 1.20-1.52; all p < 0.05), while female gender (OR 0.86, 0.76-0.98), black race (OR 0.76, 0.67-0.93), uninsured (OR 0.41, 0.33-0.52), and Charlson Comorbidity Index (CCI) ≥2 (OR 0.61, 0.50-0.74) predicted for lower odds of receiving CTX (all p < 0.05). Median OS for pts receiving CTX was 9.53 mos (9.33-9.72) vs. 2.43 mos (2.27-2.60) with no CTX (p < 0.001). Modeling the effect of CTX to OS using a time-dependent coefficient showed that CTX was associated with improved OS up to 10 months, after which there is no significant effect on OS. Independent predictors of OS included treatment at an academic center (hazard ratio (HR) 0.91, 0.87-0.94), CCI =2 (HR 1.16, 1.07-1.26), and uninsured status (HR 1.20, 1.09-1.31). Conclusions: We identified several predictors for receipt of CTX and OS in pts with mEC. The benefit of CTX on OS is time-dependent and favors early initiation. Focused outreach in lower income and underinsured patients is critical as receipt of CTX is associated with improved OS. Research Sponsor: None.
Real-world treatment attrition rates in advanced esophagogastric cancer.

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Background: Over the last decade, multiple agents have demonstrated efficacy for advanced esophagogastric cancer (EGC), including ramucirumab, irinotecan, trifluridine/tipiracil, and immunotherapy. Despite the availability of later lines of therapy, there remains limited real-world data about the treatment attrition rates between lines of therapy. We sought to characterize the use and attrition rates between lines of therapy for patients with advanced EGC. Methods: We identified patients who received at least one cycle of chemotherapy for advanced EGC between July 1, 2017 and July 31, 2018 across 6 regional centers in British Columbia (BC), Canada. Clinicopathologic, treatment, and outcomes data were extracted by chart review. Results: Of 169 patients who received at least one line of therapy, median age was 65.2 years (IQR 58-72) and 128 (76%) were male, ECOG PS 0/1 (84%), gastric vs GEJ (35% vs 65%). Histologies included adenocarcinoma (76%), squamous cell carcinoma (10%) and signet ring (14%), with 26% HER2 positive. 62% presented with de novo disease, and 35% had received previous chemoradiation. There was a high level of treatment attrition, with patients receiving only one line of therapy (n = 73, 43%), two lines (n = 65, 38%), three lines (n = 25, 15%), and four lines (n = 6, 4%). Kaplan-Meier survival analysis demonstrated improved survival with increasing lines of therapy (median overall survival 9.6 vs. 18.5 vs. 25.8 vs. 40.7 months, \( p < 0.05 \)). On multivariable Cox regression, improved survival was associated with better baseline ECOG, longer duration of first-line therapy, and increased lines of therapy (\( p < 0.01 \)). Conclusions: The steep attrition rates between therapies highlight the unmet need for more efficacious earlier-line treatment options for patients with advanced EGC. Research Sponsor: None.

<table>
<thead>
<tr>
<th>Hazard Ratio (95% CI)</th>
<th>( p )-value</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>1.01 (0.99-1.03)</td>
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<tr>
<td>Gender (Male vs. female)</td>
<td>0.94 (0.61-1.44)</td>
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<tr>
<td>Baseline ECOG</td>
<td>1.53 (1.09-2.14)</td>
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<tr>
<td>Recurrent disease (vs. de novo)</td>
<td>0.83 (0.56-1.21)</td>
</tr>
<tr>
<td>Duration of first-line treatment</td>
<td>0.92 (0.89-0.94)</td>
</tr>
<tr>
<td>Lines of treatment</td>
<td>0.51 (0.40-0.65)</td>
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Helicobacter pylori-negative gastric cancer in Guatemala: Incidence, clinical characteristics, treatment modalities, and outcomes.

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Background: Gastric cancer (GC) in Guatemala is the second most common cancer diagnosis and the second leading cause of cancer death in both sexes. It is difficult to determine the exact incidence rate of H. pylori infection-negative gastric cancer (HPIN-GC) because H. pylori detection rates decrease with the progression of gastric atrophy and intestinal metaplasia. The aim of this study was to evaluate the incidence, clinicopathologic characteristics, treatment modalities and outcomes. Methods: A retrospective review of the medical records of 210 pts with histological diagnosis of gastric cancer evaluated at the General Hospital of Diseases from the Guatemalan Social Security Institute (IGSS) from January 2010 to December 2018. Helicobacter pylori infection status was evaluated by histology, a rapid urease test Current H. pylori infection was defined as positive results from histology. Overall survival was estimated by Kaplan Meier method and compared by Log-rank test. P value < 0.05 was considered significant. Results: The rate of HPIN-GC occurrence was 36% (n = 76). Sex, age, location of the tumor, Lauren’s classification and treatment modalities were not different according to H. pylori infection status. However, HPIN-GC had a more advanced pT classification (T3/T4; 58 vs 28%, p=.019) and a more advanced stage (more than stage I; 64 vs 44%, p=.033) than H. pylori-positive gastric cancer. Treatment modalities: 22% gastrectomy, 24% palliative care, 54% systemic chemotherapy at any time of disease course, 33% initial palliative surgery (derivative o gastrectomy), gastrectomy at any time in 16% (n 7). For those patients who received systemic chemotherapy (n 113) objective response rate was 38% and disease control rate 66%.Median OS was 26 months: 47 m for localized, 18 for locally advanced, and 8 m for advanced disease (P=.0001). Only 17% of patients received second line chemotherapy and 4% a third line. Conclusions: At least 36% cases of gastric cancer were H. pylori negative. HPIN-GC looks like to have a poorer prognosis than H. pylori-positive cases. Chemotherapy can be offered to less than a half of patients. the earliest stages are associated with better survival. Research Sponsor: None.

Treatment modalities and oncological outcomes in Mexican patients with localized gastric cancer.

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Background: gastric cancer is common in Mexico. Evaluation of treatment strategies is greatly important in early gastric cancer. National institutions rarely report their outcomes, limiting feedback and policy improvements. Methods: single-center retrospective review of patients with histologically confirmed localized gastric cancer diagnosed from Jan 2005 to Dec 2017. Overall survival (OS) and recurrence-free survival (RFS) were estimated by Kaplan-Meier curves and compared with log-rank rest. A p value < 0.05 was significant. Results: we included 78 cases, median age 63 years, 52.6% men. Surgery was the initial treatment in 46 patients (59%) and 87% achieved R0 resection. Adjuvant treatment was administered to 63% of patients. 29 patients (37.2%) started perioperative chemotherapy with 86.2% of them being resected, and 75.9% having R0 resection. 13 patients (44.8%) also received postoperative chemotherapy. Better performance status (p=0.036) and lower albumin levels (p=0.039) were found in patients with initial surgery vs those with perioperative chemotherapy. At the time of surgery, most patients had stage III disease in both groups but 5 patients had M1 disease despite negative initial laparoscopy in the chemotherapy group and 5 patients did not require adjuvant tx given early stage in the surgery first group. Median OS and RFS are reported in table. Conclusions: Most patients in our center undergo initial surgery. We report a differential survival according to initial treatment. More advanced disease in chemotherapy first group may explain differences. Given non-random assignment, we could not show survival benefit of chemotherapy treated patients. Research Sponsor: None.

<table>
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<tr>
<th></th>
<th>Median OS (mo)</th>
<th>p</th>
<th>Median RFS (mo)</th>
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<tr>
<td>All patients (n 78)</td>
<td>29.5</td>
<td>0.018</td>
<td>18.8</td>
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<tr>
<td>Initial treatment</td>
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<tr>
<td>Surgery (n=46)</td>
<td>43.6</td>
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<td>No (n=13)</td>
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<tr>
<td>I-II (n=36)</td>
<td>83.8</td>
<td>0.001</td>
<td>84.0</td>
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<td>III-IV (n=35)</td>
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<tr>
<td>Neo+ adjuvant chemotherapy</td>
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<td>Yes (n=13)</td>
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<td>14.1</td>
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<td>No (n=62)</td>
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Impact of postoperative complications on recurrence in pathological stage II/III gastric cancer patients who received curative resection followed by adjuvant S-1 chemotherapy.

Hayato Watanabe, Tsutomu Hayashi, Keisuke Koumori, Kazuki Kano, Yota Shimoda, Hirohito Fujikawa, Takanobu Yamada, Yasushi Rino, Munetaka Masuda, Takashi Ogata, Takashi Oshima; Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan; Department of Gastric Surgery, National Cancer Center Hospital, Tokyo, Japan; Kanagawa Cancer Center, Yokohama, Japan; Yokohama City University, Yokohama, Japan; Department of Surgery, Yokohama City University, Yokohama, Japan

Background: Postoperative complications increased recurrence in gastric cancer (GC) patients. However, there was no study evaluating impact of postoperative complication among patients receiving adjuvant chemotherapy. The aim of present study was to investigate the impact of postoperative complications in pStage II/III GC patients who received adjuvant S-1 chemotherapy. 

Methods: The present study retrospectively examined GC patients who received curative gastrectomy followed by adjuvant S-1 chemotherapy between January 2000 and December 2011 at Kanagawa Cancer Center. The patients with postoperative complications were classified into PC group, and those without postoperative complications were into NC group. Clinicopathological characteristics and recurrence-free survival (RFS) were compared between the groups. 

Results: 226 patients were included in this study. Postoperative complication occurred in 30 patients (13.3%). Age (Median, range) is significantly higher in NC group (64, 24-86) than in PC group (59, 36-82) (p = 0.033). Total gastrectomy was predominant type of surgery in the PC group (73.3%) than in NC group (52.0%) (p = 0.031). There was no difference in gender, ASA score, tumor location, pathological stage (TNM 7th) and pathological type between two groups. 

Conclusions: Postoperative complications were an independent risk factor for RFS in pStage II/III GC patients who received curative gastrectomy followed by adjuvant S-1 chemotherapy. Research Sponsor: None.
Should signet-ring cell histology alter the treatment approach for clinical stage I gastric cancer?

Michael K. Turgeon, Adriana C. Gamboa, Manali Rupji, Rachel M. Lee, Jeffrey M. Switchenko, Maria C. Russell, Kenneth Cardona, David A. Kooby, Charles A. Staley, Shishir K. Maithel, Mihir M. Shah; Winship Cancer Institute, Division of Surgical Oncology, Department of Surgery, Emory University, Atlanta, GA; Winship Cancer Institute, Emory University, Atlanta, GA; Emory University, Department of Biostatistics and Bioinformatics, Atlanta, GA; Emory University, Atlanta, GA

Background: Upfront surgery is standard of care for stage I gastric cancer. Despite this, many clinicians administer preoperative therapy for clinical stage I disease with signet ring cell histology, given its aggressive biology. We aimed to assess the validity of this practice. Methods: The National Cancer Database (2004-2015) was reviewed for pts with non-metastatic signet ring cell gastric cancer who underwent treatment with surgery alone, perioperative chemotherapy, neoadjuvant therapy, or adjuvant therapy. Analysis was stratified by preoperative clinical stage and pathologic stage. Primary outcome was overall survival (OS). Results: Of 3000 pts, median age was 61 (IQR: 51-70). 34% were clinical stage I (n = 1018) of which 53% received surgery alone (n = 542), 5% perioperative chemotherapy (n = 47), 12% neoadjuvant therapy (n = 125), and 30% adjuvant therapy (n = 304). Median follow-up was 26 mos. For clinical stage I disease, surgery alone was associated with improved median OS (108 mos) when compared to perioperative chemotherapy (80 mos), neoadjuvant therapy (41 mos), or adjuvant therapy (73 mos, all p < 0.001). For pathologic stage I, surgery alone had equivalent survival to perioperative and adjuvant therapy (5-yr OS: 81 vs 82 vs 79%, p = 0.22). Concordance between clinical and pathologic stage I was 56%, specifically, 41% of clinical stage I pts were upstaged to pathologic stage II (44%) and stage III (56%). Adjuvant therapy for these pts was associated with improved median OS compared to pretreatment (perioperative chemotherapy / neoadjuvant therapy) for those upstaged to pathologic stage II (122 vs 37 mos, p < 0.001) or stage III (40 vs 18 mos, p < 0.001) disease. Conclusions: Our stage-stratified study demonstrates improved survival with upfront surgery for clinical stage I signet ring cell gastric cancer. Despite 41% of clinical stage I pts being upstaged to stage II or III on final pathology, adjuvant therapy offers a favorable rescue strategy, with improved outcomes compared to those treated preoperatively. Surgery alone also affords similar survival for pathologic stage I disease compared to multimodal therapy. This study challenges the intrinsic bias to overtreat stage I signet ring cell gastric cancer. Research Sponsor: U.S. National Institutes of Health.
Efficacy and safety of nab-paclitaxel plus ramucirumab versus paclitaxel plus ramucirumab as second-line treatment for patients with advanced gastric cancer: A single institutional experience.

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Background: Nanoparticle albumin-bound (nab)-paclitaxel (PTX) was non-inferiority to solvent-based paclitaxel as second-line for advanced gastric cancer (AGC) with fewer infusion-related reactions and a trend toward improved overall survival (OS) in patients (pts) with peritoneal metastasis (PM) or ascites in ABSOLUTE trial (Shitara K et al. Lancet Gastroenterol Hepatol. 2017). Furthermore, safety and efficacies of nab-PTX plus ramucirumab (RAM) was reported in a phase II trial (Bando H, et al. EJC 2018), although no randomised trial with PTX plus RAM is reported so far.

Methods: We retrospectively reviewed consecutive pts with AGC receiving nab-PTX plus RAM or PTX plus RAM as second-line chemotherapy from June 2015 to January 2019 at the National Cancer Center Hospital East. Adverse events were evaluated using Common Terminology Criteria for Adverse Events (CTCAE) v4.0. Progression-free survival (PFS) was calculated using the Kaplan-Meier method, and the differences were evaluated using the log-rank test. Results: A total of 257 pts were included for analysis with 118 pts treated with nab-PTX plus RAM and 139 pts with PTX plus RAM. 151 pts (59%) had peritoneal metastasis and 76 pts (30%) were associated with moderate or massive amounts of ascites. Objective response rates were similar between two groups (nab-PTX plus RAM 34.1% vs. PTX plus RAM 28.0%, p = 0.36). There were no significant differences in PFS (median 3.9 vs. 3.9 months, log-rank p = 0.34; hazard ratio [HR] = 1.14). HR of PFS was 0.96 in pts with PM and 0.79 in pts with moderate or massive ascites. The major grade 3 or higher adverse events were neutropenia (nab-PTX plus RAM 55.1% vs. PTX plus RAM 55.4%), leucopenia (28.8 vs. 35.3%), thrombocytopenia (5.1 vs. 2.9%), and febrile neutropenia (5.1 vs 9.4%). Conclusions: Efficacy and safety of nab-PTX plus RAM were comparable to those of PTX plus RAM in pts with AGC in clinical practice. nab-PTX plus RAM is a treatment option as second-line treatment in pts with AGC. Research Sponsor: None.
Should adenosquamous esophageal carcinoma be treated like adenocarcinoma or squamous cell carcinoma?

Adriana C. Gamboa, Benjamin I Meyer, Jeffrey M. Switchenko, Manali Rupji, Rachel M. Lee, Michael K. Turgeon, Maria C. Russell, Kenneth Cardona, David A. Kooby, Shishir K. Maithel, Mihir M. Shah; Winship Cancer Institute, Division of Surgical Oncology, Department of Surgery, Emory University, Atlanta, GA; Division of Surgical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; Emory University, Department of Biostatistics and Bioinformatics, Atlanta, GA; Winship Cancer Institute, Emory University, Atlanta, GA; Emory University School of Medicine, Atlanta, GA; Emory University, Atlanta, GA

Background: Adenocarcinoma and squamous cell carcinoma of the esophagus have distinct outcomes, treatment strategies, and response profiles to therapy. Adenosquamous carcinoma (ASC) is thought to behave more aggressively than each of its counterparts. Our aim was to determine if ASC is best managed as adenocarcinoma or squamous cell carcinoma. Methods: The National Cancer Database (2004-15) was queried for patients with non-metastatic, esophageal ASC. Analysis was stratified by clinical node negative (cN0) or node positive (cN1-3) according to AJCC 8th edition. Treatment types were categorized into chemoradiation alone, surgery alone, or preoperative chemoradiation followed by surgery. Primary outcome was overall survival (OS). Results: Among 352 pts, median age was 67 yrs, 80% were male (n = 281). Median f/u was 46 mos. 43% were cN0 (n = 151), 57% were cN1-3 (n = 201). 55% had chemoradiation alone (n = 194), 15% had surgery alone (n = 53) and 30% had preoperative chemoradiation (n = 105). Of pts who had preoperative chemoradiation, 20% had pathologic complete response (n = 17). For either cN0 or cN1-3, Charlson-Deyo Comorbidity Index did not differ among the treatment groups (all p > 0.05). On KM analysis for cN0 disease, treatment with surgery alone had a comparable 5-yr OS to preoperative chemoradiation (47 vs 34% p = 0.5) and each had improved 5-yr OS compared to chemoradiation alone (30%; p = 0.02; p = 0.06). On UV analysis for patients with cN0 disease, clinical T-stage was not associated with 5-yr OS. For patients with cN1-3 disease, however, preoperative chemoradiation was associated with improved 5-yr OS when compared to chemoradiation alone or surgery alone (27 vs 19 vs 0% p < 0.001). This persisted even when accounting for age and clinical T-stage (HR 0.45 p < 0.001). Conclusions: Esophageal adenosquamous carcinoma behaves more like adenocarcinoma both in response to chemoradiation and survival outcomes based on the treatment modality. The complete response rate to chemoradiation is only 20% unlike what has been shown for squamous cell carcinoma, where chemoradiation is an acceptable definitive therapy. Esophageal adenosquamous carcinoma should be managed like adenocarcinoma and not squamous cell carcinoma. Research Sponsor: Katz Foundation.
Blood-based-inflammation-markers, body mass index, and survival of nonmetastatic esophageal cancer.

Wanning Wang, Joelle Soriano, Tyler Soberano, Katrina Hueniken, M. Catherine Brown, Kirsty Taylor, Jaspreet K. Bajwa, George Dong, Eric Xueyu Chen, Jennifer J. Knox, Raymond Woo-Jun Jang, Rebecca Wong, Gail Elizabeth Darling, Wei Xu, Micheal McInnis, Dmitry Rozenberg, Elena Elimova, Aline Fusco Fares; Princess Margaret Cancer Center, Toronto, ON, Canada; Princess Margaret Cancer Centre, Toronto, ON, Canada; Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada; Department of Medical Imaging, Toronto, ON, Canada; Joint Department of Medical Imaging (JDMI), Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; University of Toronto, Department of Medical Imaging, Toronto, ON, Canada; Department of Biostatistics, Princess Margaret Cancer Centre, Toronto, ON, Canada; University of Texas MD Anderson Cancer Center, Houston, TX; Princess Margaret Hospital, Toronto, ON, Canada

Background: Blood-based-inflammation-markers (BBIM) and Body Mass Index (BMI) have been associated with overall survival (OS) in a number of cancers. Inflammation and obesity have biological interactions. We evaluated the role of Neutrophil-to-Lymphocyte-Ratio (NLR), Platelet-to-Lymphocyte-Ratio (PLR) and Systemic-Inflammation-Index (SII) in conjunction with BMI as predictors of OS in localized/locally-advanced-esophageal cancer (LEC/LAEC).

Methods: LEC/LAEC patients treated from 2006-2014 had the following variables analyzed both as continuous and categorical: BMI (low $< 25$ kg/m², high $\geq 25$ kg/m²), NLR (low $< 4$, high $\geq 4$), PLR (low $< 232$, high $\geq 232$), and SII (low $< 1375$, high $\geq 1375$), with OS. Univariate (UVA) and Multivariate analysis (MVA) were analyzed using Cox regression (adjusted hazard ratios, aHR; 95% Confidence Intervals, CI). MVA models of OS were built, assessing different categorical combinations of BBIM factors with and without BMI.

Results: Of 411 pts, 79% were males, median age was 63.5 years, 67% were adenocarcinomas; Stage I/II/III: 14%, 28%, 59%; Median BMI was 26.5kg/m² and BMI distribution was: 3% underweight, 40% normal weight, 37% overweight and 20% obese. After a median follow-up of 87 months, 204 pts recurred, and 257 died. In MVA, BMI alone had no impact on OS (aHR 0.89, CI 0.7-1.1, p=0.15); individually as continuous variables, higher SII (p=0.03) and higher NLR (p=0.006) were inversely associated with OS whereas higher PLR was not (p=0.10). In an MVA of categorical combinations of BMI and BBIM on OS, patients in the high-BMI/low-PLR group were at lower risk of death when compared to all other groups (aHR=0.65, 95%CI:0.5-0.8, p=0.007). Similar non-statistically significant trends were shown when SII and NLR were individually combined with BMI (aHR=0.77, 95%CI:0.6-1.0, p=0.09; aHR=0.74, 95%CI:0.5-1.0, p=0.05, respectively).

Conclusions: Our results suggest that in LEC/LAEC pts, high BMI and low PLR together are associated with improved OS when compared to pts with low BMI and/or high PLR. NLR and SII alone were associated with OS. Further studies evaluating the underlying mechanisms of BBIM, in particular PLR and inflammation/obesity are warranted. Research Sponsor: None.
Clinicopathological features and treatment outcomes of young patients with gastric and esophageal cancers.

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Background: Gastric and esophageal (GE) cancers most commonly occur in older adults in their 60s. There are inconsistent reports about prognosis in adolescent and young adult (AYA) pts, and treatment patterns and outcomes in this population have not been well characterized. Methods: A retrospective analysis was performed for AYA (age < 40) pts with GE cancers who presented to Princess Margaret Cancer Centre from 2008 to 2016. The Kaplan-Meier method was used to analyze progression free (PFS) and overall survival (OS). Results: We identified 57 AYA GE cancer pts (30 gastric, 27 esophageal). Features at diagnosis included: median age 35, 51% female (70% in gastric, 30% in esophageal), 82% with performance status 0-1, 83% Charlson Comorbidity Index 0, 54% stage IV. For gastric pts, 53% had diffuse histology and 47% had signet ring adenocarcinoma. There was a negative family history of gastric or esophageal cancer in 77% of pts. Curative intent treatment was used in 23 pts, palliative in 34. In curative pts, 48% had neoadjuvant therapy, 52% had upfront surgery. Of pts who underwent surgery, 57% had T3 or T4a disease and 38% had N2 or N3 disease. Median OS in curative pts was 39.9 months (95% CI 19.7-69.9), with a 5-year OS rate of 37% (95% CI 20-67). Of the palliative pts, 91% had chemotherapy. First line chemotherapy was a triplet regimen in 80%, doublet in 13%. The median number of treatment cycles on first line chemotherapy was 6, with a median PFS of 7.4 months (95% CI 5.4-10.5). At progression, 14 pts had second line treatment, 3 pts had third line and only 1 pt was treated beyond third line. Median OS in palliative pts was 12.1 months (95% CI 8-21.3). Conclusions: Consistent with the literature, our gastric AYA pts had increased female predominance and diffuse histology. Many AYA pts had advanced disease at diagnosis, with over half of pts presenting with metastatic disease. In both the curative and palliative setting, AYA pts did not have better survival outcomes despite being young with few comorbidities, suggesting they may have more aggressive biology. Research Sponsor: University Health Network, Other Foundation.
Age-related outcomes in patients with esophageal cancer: A propensity score matched analysis.

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Background: Esophageal cancer is increasing in incidence worldwide. It is estimated that there will be 17,650 new cases of esophageal cancer diagnosed, with 16,080 dying from the disease in the United States in 2019. There has been an increase in younger patients diagnosed with esophageal cancer. We sought to evaluate the outcomes in younger patients diagnosed with esophageal cancer. Methods: Utilizing the National Cancer Database we identified patients with esophageal cancer. We then stratified by age, <50, 51-60, 61-70, and >70 years. Baseline univariate comparisons were made for continuous variables using both the Mann-Whitney U and Kruskal Wallis tests as appropriate. Pearson's Chi-square test was used to compare categorical variables. Unadjusted survival analyses were performed using the Kaplan-Meier method. All statistical tests were two-sided and p < 0.05 was significant. Propensity score matched analysis was performed and only exact matches were allowed. Results: We identified 20,324 patients (<50, 2157), (51-60, 5387), (61-70, 7853), and (>70, 4927). T-stages and N stages were higher in the younger age groups p < 0.001 and p < 0.001 respectively. Median lymph nodes positive were highest in the <50 group (2.2 vs 1.8 vs 1.6 vs 1.7) p < 0.001. Additionally, tumor size was largest in this age cohort (3.7 vs 3.5 vs 3.4 vs 3.2) p = 0.002. Neoadjuvant therapy was administered in 69.4% of patients in the <50, 68.5% (51-60), 65.5% (61-70), and 49.5% > 70 patients, p < 0.001. The <50 age group was however more likely to receive adjuvant therapy (22.9% vs 20.5% vs 16.9% vs 13.4%) p < 0.001. Median and overall survival was 49.8 mo and 45% (<50), 45.4mo and 43% (51-60), 45.4mo and 43% (61-70), and 35.8mo and 39% >70, p < 0.001. After propensity score matching, multivariate analysis found that age <50, male gender, GEJ tumor location, grade, Charleson Deyo score, T-stage N stage, margin, facility volume, neoadjuvant and adjuvant therapy were predictors of survival. Conclusions: Although younger patients present with larger tumors, higher T-stages, and N stages, they are more likely to receive neoadjuvant and adjuvant therapies. It is these therapies which are most likely contributing to improved survival compared to their older counterparts. Research Sponsor: None.
Morbidity associated to advanced gastric cancer and its impact on overall survival.

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Background: Advanced gastric cancer (GC) is a disease with high morbidity and poor prognosis. We hypothesize that different sites of metastasis have different impact in terms of symptoms and complications. We sought to evaluate if site specific morbidity in our patients impacted treatment and survival. Methods: Medical records from patients with advanced GC treated from Jan 2005 to Dec 2015 were retrospectively reviewed. Morbidity was defined as having any symptom by metastases in a specific site. OS was estimated by Kaplan Meier method and compared by Log-rank test. P value < 0.05 was considered significant. Results: We included 180 consecutive patients, median age at diagnosis was 56 years (21-90), 55% were women. Most common sites of metastases were: peritoneum 76.1%, non-regional lymph nodes 38.9%, liver 22.8%, lung 26.7%, bone 9.4% and ovary 12.8%. Regarding morbidity, at diagnosis 68% of patients presented morbidity by the primary tumor: obstruction 56%, bleeding 27%, obstruction and bleeding 3%, other 14%. Disease by peritoneum caused morbidity in 30%, by lung in 8%, by ovarian in 4.4%, by lymph nodes in 3.3%, and by other sites in 5.6% of patients. OS in the global cohort was: 3.53 months (2.2 to 4.8), nevertheless by univariate analysis we found that OS was affected by morbidity at some sites as it is show in table. More patients with peritoneal morbidity could not receive treatment vs those without peritoneal morbidity (p = 0.042). Conclusions: We found that morbidity in peritoneum, lung and ovary adversely affected prognosis of patients with advanced GC. Moreover, peritoneal morbidity preclude patients from receiving oncological treatment. Research Sponsor: None.

<table>
<thead>
<tr>
<th>Site of morbidity (n)</th>
<th>OS with vs without morbidity (months)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary tumor (124)</td>
<td>3.1 vs 4.2</td>
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</tr>
<tr>
<td>Lymph nodes (6)</td>
<td>0.8 vs 3.5</td>
<td>0.52</td>
</tr>
<tr>
<td>Peritoneum (52)</td>
<td>1 vs 4.1</td>
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<tr>
<td>Liver (8)</td>
<td>12 vs 3.6</td>
<td>0.09</td>
</tr>
<tr>
<td>Lung (14)</td>
<td>11 vs 3.5</td>
<td>0.03</td>
</tr>
<tr>
<td>Ovary (8)</td>
<td>0.7 vs 4.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Other (17)</td>
<td>35 vs 3.5</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Patterns of disease, treatment, and outcomes of esophageal cancer arising within a previous radiation treatment field.

Lucy Xiaolu Ma, Peiran Sun, Osvaldo Espin-Garcia, Chihiro Suzuki, Di Maria Jiang, Charles Henry Lim, Kirsty Taylor, Bryan Anthony Chan, Hao-Wen Sim, Akina Natori, Eric Xueyu Chen, Geoffrey Liu, Jennifer J. Knox, Jonathan Yeung, Gail Elizabeth Darling, John Kim, Sangeetha Kalimuthu, Elena Elimova, Raymond Woo-Jun Jang; Princess Margaret Cancer Centre, Toronto, ON, Canada; Princess Margaret Hospital, Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; University of Toronto, Toronto, ON, Canada; Royal Brisbane and Women’s Hospital, Brisbane, ON, Canada; The Kinghorn Cancer Centre, St Vincent’s Hospital Sydney, Sydney, Australia; St Lukes Int’l Hosp, Koto-Ku, Japan; Department of Radiation Oncology, Princess Margaret Cancer Centre, Toronto, ON, Canada; University Health Network, Toronto, ON, Canada

Background: Esophageal cancer arising within a previous radiation treatment field (ECRF) is rare. The patterns of disease, treatment and outcomes in these patients (pts) have not been well characterized. Methods: A retrospective analysis was performed for pts treated for esophageal cancer at the Princess Margaret Cancer Centre from 2002-2016. Electronic medical records of all pts with a histologic diagnosis of esophageal cancer occurring within the field of previous radiotherapy were reviewed. The Kaplan-Meier method was used to calculate progression free survival (PFS) and overall survival (OS). Results: Of 31 ECRF pts identified, the most common prior cancer was head and neck (45%), median radiation (RT) dose 50Gy, median time to diagnosis of esophageal cancer 12 years. Features at diagnosis of ECRF included: median age 71 years, 58% male, 87% with performance status (PS) 0-1, 77% squamous cell carcinoma, 19% stage IV. Treatment intent was curative in 16 pts, palliative in 15 (Table). Reasons for palliative treatment were: 40% metastatic, 53% comorbidities/PS, 7% anatomic factors. Of resected pts, 36% had a pT1-2 tumour, 55% pN0, 69% R0. For curative pts, median PFS was 26.2 months (95%CI 10.9-34.4) with a 3 year PFS rate of 35% (95% CI 15-81). Median OS for curative pts was 26.4 months (95%CI 17.8-105.5) with a 3 year OS rate of 43% (95% CI 22-83). Most palliative pts were unable to have chemotherapy due to comorbidities and PS. Median OS for palliative pts was 9.5 months (95% CI 3.6-15.4). Conclusions: Most ECRF pts presented with earlier stage disease; however, more than a third of these could not have aggressive curative treatment due to comorbidities and/or PS. Most curative pts had surgery alone. Few palliative pts had chemotherapy, largely due to poor clinical status. Our data suggest that outcomes in both curative and palliative ECRF pts may be limited by the ability to tolerate standard of care treatments. Research Sponsor: Princess Margaret Cancer Centre.

<table>
<thead>
<tr>
<th>Treatment Intent</th>
<th>Curative n=16</th>
<th>Palliative n=15</th>
<th>Total n=31</th>
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<tr>
<td>Chemo</td>
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<td>4</td>
</tr>
<tr>
<td>RT</td>
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<tr>
<td>Supportive</td>
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<td>3</td>
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</tbody>
</table>
Patterns of gastric cancer metastasis within the United States.

Joseph Sirody, Amy H. Kaji, Danielle M. Hari, Kathryn Tzung-Kai Chen; Harbor UCLA Medical Center, Torrance, CA; Harbor-UCLA Medical Center, Torrance, CA

Background: There are few reports on the epidemiology of gastric cancer metastasis, although outcomes are known to be uniformly poor. Here we describe the patterns of gastric cancer metastasis and treatment in the United States (US). Methods: Patients with gastric adenocarcinoma histologies were identified in the National Cancer Database (NCDB) from 2004-2016. We describe univariate associations between different sites of metastasis and clinicopathologic characteristics and treatment modalities, using the chi-square and Kruskal-Wallis tests. Kaplan-Meier curves were constructed for the estimation of overall survival (OS) by metastatic site. Results: Due to changes in the coding of metastatic disease, we were limited to the year 2016 for evaluation of patterns of disease. Twenty-six percent (n = 1228) of gastric cancer patients presented with liver metastases, 20% (n = 941) with distant nodes, 43% (n = 2028) with other distant site metastases (including peritoneum), and the rest to bone, brain or lung. On univariate analysis, when compared to liver metastases, other distant site metastases were significantly more likely to arise from an antral primary site (28% v. 16%); to be of Hispanic origin (16% v. 7%); female (42% v. 29%); associated with signet ring histology (34% v. 6%); lymphovascular invasion (LVI) (58% v. 27%); and tumor grade III/IV (85% vs. 60%) (p < 0.0001 for all). There were no significant differences in how patients with metastatic disease were treated in terms of systemic therapy. With regard to OS, due to how metastatic sites were coded prior to 2016, it was not possible to compare peritoneal metastases against other sites; however, patients with distant nodal disease had improved median overall survival compared to those with any other metastatic site (7.9 v. 5.2 months, p < 0.0001). Conclusions: The majority of US patients with metastatic gastric cancer present with presumed peritoneal disease. Predictive factors for peritoneal metastases vs. liver metastases included adverse prognostic features, including signet ring histology, higher tumor grades, and LVI. Although it was not possible to compare OS of peritoneal disease against other sites, continued follow up is needed, as this may impact future staging. Research Sponsor: None.
Senior resident versus fellow participation during complex cancer operations.

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Background: Teaching hospitals that train both general surgery residents and fellows in complex general surgical oncology have become more common. Despite ACGME dictums, attending surgeons may favor either residents or fellows assisting on operations of greater complexity, depending upon a variety of factors, including local surgical culture. This study investigates whether participation of a senior resident versus a fellow impacts outcomes of complex cancer surgery.

Methods: Patients who underwent esophagectomy, or gastrectomy with assistance from either a senior resident (PGY-4 or 5) or a fellow (PGY-6 to 8) were identified from the American College of Surgeons' National Surgical Quality Improvement Program (2007-2012). Analyses were performed separately for each operation. Propensity-scores were created for the odds of undergoing the operation assisted by a fellow. Patients were matched based on propensity score, and outcomes were compared after matching.

Results: In total, 1,160 esophagectomies and 2,432 gastrectomies were identified. Senior resident participation was reported in 60.2% and 86.6%, respectively. Resident involvement was associated with non-white race (17.0% vs. 13.8%; p < 0.001), and lower rates of neoadjuvant chemotherapy (6.4% vs. 11.7%; p < 0.001). After matching, rates major complication rates were slightly higher for patients who underwent esophagectomies involving a resident compared to fellow (38.1% vs. 31.8%; p = 0.0447). However, major complications rates were similar for gastrectomy (21.2% vs. 22.1%; p = 0.775). In addition, operative time was shorter for gastrectomy (212 vs. 232 min; p = 0.009) involving a resident compared to a fellow, but comparable for patients who underwent esophagectomy (327 vs. 337 min; p = 0.310).

Conclusions: The results of this study suggest that senior resident participation in complex cancer operations does not negatively impact operative time or outcomes, compared to involvement of a surgical oncology fellow. Although confounding by operative autonomy may exist, these findings indicate that senior residents should be given the same opportunities as fellows to participate in these potentially more challenging operations. Research Sponsor: None.
First-line chemotherapy versus chemoradiation for resectable distal esophageal adenocarcinoma.

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Background: Multiple randomized controlled trials have shown that both neoadjuvant chemotherapy (CT) and chemoradiation (CRT) convey survival benefit as compared to upfront surgery in patients with esophageal adenocarcinoma. However, international practice remains variable. Therefore, the present study compares the outcomes of first-line CT to CRT for patients with adenocarcinoma arising from the distal esophagus. Methods: Patients with clinical stage T2-T3, N0-N+ esophageal adenocarcinoma originating from the distal esophagus who received first-line CT or CRT were identified from the National Cancer Data Base (2006-2014). Propensity-score were created for the odds of receiving CRT. Patients were matched 1:1 based on propensity score. Subset analysis was performed in patients who underwent esophagectomy. Pathological complete response was defined as ypT0N0M0. Results: In total, 709 and 8,877 patients who received first-line CT and CRT were identified, respectively. CT was associated with stage cT2 (27.2% vs. 23.3%; p = 0.017), and treatment at a high-volume center (27.2% vs. 20.2%; p < 0.001). After matching, resection rates were comparable for patients who received first-line CT and CRT (62.2% vs. 63.7%; p = 0.545). However, median overall survival was slightly lower for patients who receive CT compared to CRT (23.7 vs. 28.4 months; p = 0.044). Among patients who underwent esophagectomy, time to surgery (135 vs. 134 days; p = 0.689) and median overall survival (37.0 vs. 40.5 months; p = 0.630) was similar between matched cohorts. However, complete response (15.8% vs. 25.8%; p < 0.001) and negative margin (94.3% vs. 88.9%; p = 0.004) rates were significantly lower after CT compared to CRT. Conclusions: In patients with esophageal adenocarcinoma, first-line CRT results in significantly higher pathological complete response rates, negative resection margins rates, and improved survival. These findings suggest that first-line CRT is preferable over CT when tolerated in patients with esophageal adenocarcinoma. Research Sponsor: None.
Tumor size and the risk for lymph node metastases in T1 esophageal adenocarcinoma.

Meena Sadaps, Neal Mehta, Michael J. McNamara, Alok A. Khorana, Amit Bhatt; Cleveland Clinic, Cleveland, OH; Cleveland Clinic Foundation, Cleveland, OH; Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH; Cleveland Clinic- Taussig Cancer Institute, Cleveland, OH

Background: Adjuvant therapy after endoscopic resection (ER) of T1 EAC in non-surgical candidates is largely based on the risk of LNM. Risk factors for LNM in T1 EAC are not clearly defined. Our aim is to evaluate risk factors for LNM in T1 EAC patients following esophagectomy or ER with ≥ 5 years of follow-up. Methods: This is a retrospective analysis at a large tertiary referral center. Our pathology database identified patients who underwent esophagectomy or ER with ≥ 5 years follow-up, with histologically proven T1 EAC from 2010-2017. Patients were excluded if they (a) received chemoradiation prior to esophagectomy or before/after ER (b) had any other primary cancer treated within the previous 5 years. Specimens were reviewed by an expert GI pathologist for accuracy. Results: Of 80 patients (85% males), 61 (76%) underwent esophagectomy and 19 (24%) underwent ER. Twelve (15%) developed LNM per study criteria. Tumor size was significantly (p-value 0.014) associated with risk of LNM (Table). No other factors including lymphovascular invasion, differentiation on pathology, macroscopic appearance, infiltration growth pattern, or tumor distance from the gastroesophageal junction were significant risk factors for LNM. Conclusions: In T1 EAC, tumor size appears to be a significant risk factor for LNM at five years following surgical or endoscopic resection. Adjuvant therapy should be considered in patients with larger tumor size. None.

Comparison of Patients with and without LNM.

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</tr>
<tr>
<td>3</td>
<td>66</td>
<td>54</td>
<td>81.82</td>
<td>12.188</td>
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*Median [P25, P75]; ^Percentage; \*Mean (95% CI); ^C. Pearson’s Chi-squared test with Yates’ continuity correction (CC); W: Wilcoxon rank sum test with CC.
Relationship of periodic methylation patterns in the gastric mucosa and periodic stem cell replacement.

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Background: The role of *Helicobacter pylori*-associated methylation in the inactivation of tumour-suppressor genes has been previously investigated. However, the relationship between *H. pylori*-associated methylation and gene inactivation is unclear. Stem cells are replaced periodically every 8 years in the gastrointestinal mucosa. Hence, age-related methylation in the gastric mucosa was studied to understand the stabilization of new stem cell phenotypes. Methods: Endoscopic biopsy specimens of the antral mucosa were obtained from 148 *H. pylori*-negative and 124 *H. pylori*-positive subjects. The methylation-variable sites of 4 housekeeping genes (*CDH1*, *ARRDC4*, *MMP2*, and *CDKN2A*) and 2 stomach-specific genes (*TFF2* and *TFF3*) were examined using radioisotope-labelled methylation-specific polymerase chain reaction. Age-related methylation was evaluated at an interval of 2 years. Results: The 4 housekeeping genes were more frequently methylated in *H. pylori*-positive subjects than in *H. pylori*-negative subjects. Periodic changes in the housekeeping gene methylation were obscure. *TFF2*, which is highly expressed in the stomach, was periodically methylated to attain peaks at the age of 40–41, 48–49, 56–57, and 64–65 years in both *H. pylori*-negative and -positive subjects. *TFF3*, which is weakly expressed in the stomach, was methylated at the age of 46–47, 54–55, 66–67, and 72–73 years in *H. pylori*-negative subjects. The methylation of stomach-specific genes periodically fluctuated approximately at 8-year intervals in the gastric mucosa. Conclusions: Periodic methylation changes in the gastric mucosa may be used to estimate the replacement of new stem cells. Research Sponsor: None.
Safety, pharmacokinetics, and efficacy of RC48-ADC in a phase I study in patients with HER2-overexpression advanced solid cancer.

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Background: HER2 overexpression is common in many malignancies and contributes to tumor growth. Unlike the varied options of anti-HER2 target therapies for breast cancer, there is a huge unmet medical need for HER2 overexpressing non-breast solid tumor (NBST) such as gastric cancer and urothelial cancer. Therefore, we conducted the first study of RC48-ADC, a novel humanized anti-HER2 antibody conjugate, in NBST. Methods: This was an open-label, dose-escalation and expansion study in patients with HER2-overexpression (IHC 2+ and 3+) advanced solid cancers after failure of standard treatment. The dose escalation consisted of accelerated (0.1 and 0.5 mg/kg) and "3+3" titrations (1.0, 2.0, 2.5 and 3.0 mg/kg). In dose expansion stage, patients were given RC48-ADC at 2.0 mg/kg, Q2W. Results: As of Aug 20, 2019, 57 patients (including 47 with gastric cancer and 4 with urothelial cancer) were treated at 0.1 (1 patient), 0.5 (1 patient), 1.0 (3 patients), 2.0 (6 patients in dose escalation and 32 patients in dose expansion), 2.5 (11 patients), and 3.0 mg/kg (3 patients), respectively. Most of them were Stage IV (91.2%) or with metastasis (96.5%). DLT was observed in 1, 2, and 1 patient at 2.0, 2.5, and 3.0 mg/kg, respectively. The MTD was 2.5 mg/kg. Most commonly reported TRAEs were WBC count decreased (66.7%), fatigue (56.1%), neutrophil count decreased (54.4%) and hemoglobin decreased (52.6%). Grade 3/4 TRAEs were reported in 28 patients (49.1%). Confirmed ORR was 21.1% (8/38) for 2.0 mg/kg, and 17.5% (10/57) for all patients. DCR was 52.6% and 49.1%, respectively. PFS was 3.6 months (95% CI: 4.1, 11.3) for 2.0 mg/kg. Subgroup ORR was 20.7% (6/29) at 2.0 mg/kg and 18.2% (2/11) at 2.5 mg/kg for gastric cancer, and 50.0% (2/4) for urothelial cancer. Conclusions: RC48-ADC demonstrated a good safety profile and promising anti-tumor activity in the late stage solid tumor including gastric cancer and urothelial cancer. Response and PFS benefits were clinical meaningful at 2.0 mg/kg and 2.5 mg/kg. Phase 2 pivotal study (NCT03556345) in gastric cancer is ongoing. Clinical trial information: NCT02881190. Research Sponsor: RemeGen, Ltd.
Exploring the epidemiology of gastric cancer in a Tibetan population.

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Background: Gastric cancer is the 3rd leading cause of death from cancer and the 5th most common cancer world-wide. It is the primary cause of death for people of Tibetan origin in the Himalayan belt, with incidence (and death) rates between 60-140/100,000 people per year. Despite such a high disease burden, the epidemiology of gastric cancer has not been studied in this population. In this study, we explore gastric cancer risk factors among Tibetan refugees residing in India. Methods: Patients diagnosed with gastric cancer were identified by reviewing admission, discharge and out-patient endoscopy records between 2013-2019 at the Tibetan Delek hospital in Dharamshala, India. Risk factors not captured in the records were collected through interviews of patients or their relatives. Results: A total of 52 gastric cancer cases were identified, mostly males (77%). Median age was 78 (range: 30-91 years). Of the gastric cancer cases, 32% (n = 12/37) were retired military, 19% (n = 7/37) were monks or nuns, and 95% (n = 36/38) were born in Tibet. Sixty-five percent (n = 34/52) of the cases had histories of dyspepsia, 49% (n = 21/43) had used alcohol, and 40% (n = 17/43) were past smokers. Ninety-five percent (n = 20/21) of cases had been treated with traditional Tibetan medicines for various reasons in the past. Of the 17 patients (or relatives) interviewed for dietary risk factors, 76% (n = 13) reported frequent ingestion of stale and unrefrigerated food, 30% (n = 5) did not eat fresh fruit, and 47% (n = 8) reported intake of fresh fruit < 3 times per month. Most (83%, n = 24/29) patients had non-cardia cancers located in the fundus/body (n = 12) and antrum/pylorus (n = 12). Fifty-two percent (n = 16/31) had been treated with either chemotherapy, radiotherapy, or surgery, and 34% (n = 11/32) of the patients were receiving traditional Tibetan medicine as treatment for gastric cancer. Conclusions: Tibetan people have socio-cultural, behavioral and dietary risk factors that may be associated with gastric cancer. Investigations of causal factors (genetic, infective (Helicobacter pylori), environmental) with possible synergistic interactions could inform clinical and public health practice for this population and globally. Research Sponsor: Henry and Marsha Laufer; Stony Brook International Research Fellowship.
Screening and treatment strategy for double cancer for esophageal cancer surgery patients.

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Background: Esophageal cancer treatment, especially esophagectomy, is highly invasive, so treatment strategies are considered in view of existing double cancers. On the other hand, in Japan, 90% of esophageal cancers are squamous cell carcinoma, and it is known that there are a large proportion of head and neck cancers for double cancers as field cancerization. Methods: The aim of this study is to investigate the types of double cancer, simultaneous/metachronous, and the frequency and treatment policy of head and neck cancer as a particularly high coexistence rate for esophageal cancer surgery patient. The subjects were 304 patients who underwent esophagectomy performed from April 2010 to December 2017. All patients were examined with high-definition endoscopy with NBI by certificated endoscopist at the first visit as a search for simultaneous double cancer from the pharynx to the stomach. And after esophagectomy, endoscopy was also performed to check for metachronous double cancers in the remaining esophagus, gastric tube, and pharynx at least every 2 years. Results: The number of double cancer cases was found in 94 cases (30.9%), and the total number of double cancer cases was 122. Head and neck cancer (33 cases), stomach cancer (16 cases), and colon cancer (12 cases) were observed as the main course of double cancers. In double cancer cases, 47 cases (50.0%) were metachronous, 35 cases (37.2%) were simultaneous, and 12 cases (12.8%) were both synchronous. The most common double cancer was head and neck cancer (33 cases: 35.1%), and 23 cases were simultaneous, 10 cases were metachronous. As treatment strategy for head and neck cancer, endoscopic laryngo-pharyngo surgery (ELPS) were 19 cases. 10 cases (52.7%) were synchronous cancers, and 9 cases (47.3%) were metachronous cancers which were detected during follow-up after esophagectomy. Conclusions: Head and neck cancer associated with esophageal cancer surgery is the most common type of double cancer, and 1/3 of ELPS cases have been detected by follow-up endoscopy after esophagectomy, so endoscopic surveillance was also considered important. Research Sponsor: None.
Multiple primary cancers in patients with gastric cancer: A retrospective study in China National Cancer Center.

Qi Lei, Runfeng Zhang, Xi Zou, Aiping Zhou, Chun-Xia Du; Peking Union Medical College Hospital, Chinese Academy of Medical Science and Peking Union Medical College, Beijing, China; National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

**Background:** Gastric cancer (GC) is common in China. With the total incidence of cancer keeping rising in China, the occurrence of multiple primary cancers with GC is growing. Early detection and diagnosis of second or more primary cancers are vital for patients’ survival. **Methods:** Patients with multiple primary cancers containing gastric adenocarcinoma treated in China National Cancer Center from January 2010 to December 2017 were included. A 6-month interval was used to separate synchronous and metachronous cancers (according to IARC/IACR criteria). **Results:** 479 patients met the criteria were included, with 452 (94.4%), 24 (5.0%), 3 (0.6%) patients having two, three or more primary cancer sites respectively, contributing a total of 510 cancer sites besides stomach (Table). Malignancies at 257 (50.4%) sites occurred with GC synchronously, while 253 (49.6%) occurred metachronously. The median age at the diagnosis of first cancer was 59 (interquartile range [IQR], 53-66) years. The median interval between the diagnosis of first primary cancer and metachronous second one was 50.3 (IQR, 23.7-97.0) months. Cancers outside gastrointestinal (GI) tract were more likely to occur with GC metachronously, while GI tract cancers were more likely to occur synchronously ($\chi^2=55.36$, p<0.001). Out of 479 patients, there were 352 (73.6%) male and 127 (26.4%) female. The most common associated cancer was esophagus cancer (142, 40.3%) in male, and breast cancer (31, 25.4%) in female. 236 (49.8%) patients were current smokers or ex-smokers, and 190 (40.1%) were regular alcohol consumers. 110 (23.2%) had first-degree relative cancer family history, with 84 (17.7%) having GI tract cancer family history. **Conclusions:** GI tract including esophagus and colorectum should be carefully scrutinized during GC peri-operation period. Further genetic research is warranted to explore the potential pathogenesis of multiple primary cancers. None.

<table>
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<th>Distribution of sites in patients with GC.</th>
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<th>Total N. of sites</th>
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<td><strong>N. of sites</strong></td>
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<td>Before GC</td>
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<tr>
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<td>257</td>
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Per oral vitamin B12 replacement therapy after gastrectomy and its optimal dose (retrospective study) and our protocol of a prospective clinical trial.

Yasushi Rino, Toru Aoyama, Norio Yukawa, Haruhiko Cho, Takashi Oshima, Takanobu Yamada, Yosuke Atsumi, Kentaro Hara, Masakatsu Numata, Keisuke Kazama, Hiroshi Tamagawa, Tsutomu Sato, Takaki Yoshikawa; Yokohama City University, Yokohama, Japan; Department of Surgery, Yokohama City University, Yokohama, Japan; Kanagawa Cancer Center, Yokohama, Japan; Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan; Kanagawa Cancer Center, Kanagawa, Japan

Background: Postgastrectomy vitamin B12 deficiency is common metabolic sequel and worsens the quality of life of gastric cancer survivors. Recently, oral vitamin B12 replacement is reported. Therefore, we investigated retrospectively the efficacy of oral vitamin B12 replacement for gastric cancer patients with vitamin B12 deficiency after total gastrectomy. Methods: We reviewed 73 patients with gastric cancer who underwent total gastrectomy and were treated vitamin B12 replacement. Patients were consisted of 56 males and 17 females and median age was 70 y/o. We investigated initial treatment of vitamin B12 replacement and improvement of vitamin B12 deficiency. Results: Initial treatment of vitamin B12 replacements were intramuscular injection for 42 patients, per oral replacement for 28 patients and intravenous injection for 3 patients. Finally, all patients were treated with per oral replacement and the serum vitamin B12 levels became within normal range. Final vitamin B12 doses of replacement therapy were 500 µg of 20 out of 73 pts, respectively. Conclusions: Vitamin B12 replacement therapy should be necessary and continued. According to our results, one vitamin B12 tablet a day is enough. The vitamin B12 deficiency symptoms could be prevented. 500 micrograms vitamin B12 replacement orally is maybe effective and necessary. Our prospective clinical protocol (UMIN000030727): In this study, an oral vitamin B12 preparation (1500 µg/day, administered daily) was set as the control treatment, and a specific clinical trial was started to determine whether 500 µg/day daily administration would be sufficient for replacement therapy. Clinical trial information: UMIN000030727. Research Sponsor: Taiho Pharma & Daiichi Sankyo.
Economic impacts of care by high-volume providers for noncurative esophagogastric cancer: A population-based analysis.

Julie Hallet, Nicole Look Hong, Victoria Zuk, Laura Davis, Vaibhav Gupta, Craig Earle, Nicole Mittmann, Natalie Coburn; Odette Cancer Centre, Toronto, ON, Canada; Sunnybrook Research Institute, Toronto, ON, Canada; University of Toronto, Toronto, ON, Canada; Ontario Institute for Cancer Research, Toronto, ON, Canada; Cancer Care Ontario/Sunnybrook Research Institute, Toronto, ON, Canada; Odette Cancer Centre, Sunnybrook Hospital, Toronto, ON, Canada

Background: Esophagogastric cancer (EGC) is one of the deadliest and costliest malignancies to treat. Care by high-volume providers can provide better outcomes for patients with EGC. Cost implications of volume-based cancer care are unclear. We examined the cost-effectiveness of care by high-volume medical oncology providers for non-curative management of EGC. Methods: We conducted a population-based cohort study of non-curative EGC over 2005-2017 by linking administrative healthcare datasets. High-volume was defined as >11 patients/provider/year. Healthcare costs ($USD/patient/month-survived) were computed from diagnosis to death or end of follow-up from the perspective of the healthcare system using validated costing algorithms. Multivariable quantile regression examined the association between care by high-volume providers and costs. Sensitivity analyses were conducted by varying costing horizons and high-volume definitions. Results: Among 7,011 non-curative EGC patients, median overall survival was superior with care by high-volume providers with 7.0 (IQR: 3.3-13.3) compared to 5.9 (IQR: 2.6-12.1) months (p < 0.001) for low-volume providers. Median costs/patient/month-lived were lower for high-volume providers ($5,518 vs. $5,911; p < 0.001), owing to lower inpatient acute care costs, despite higher medication-associated and radiotherapy costs. Care by high-volume providers was independently associated with a reduction of $599 per patient/month-lived (95% confidence interval: -966 to -331) compared to low-volume providers. The incremental cost-effectiveness ratio was -393. Care by high-volume providers remained the dominant strategy when varying the high-volume definition and the costing time horizon. Conclusions: Care by high-volume providers for non-curative EGC is associated with superior survival and lower healthcare costs, indicating a dominant strategy that may provide an opportunity to improve cost-effectiveness of care delivery. Research Sponsor: CIHR.
An economic evaluation of palliation of dysphagia in esophageal cancer: Analysis of the TROG 03.01/NCIC ES.2 phase III study in advanced esophageal cancer in patients treated with radiotherapy versus chemoradiotherapy.

Michael Gordon Penniment, Paolo De Ieso, Rebecca Wong, Hossein Afzali; Royal Adelaide Department of Radiation Oncology, Kensington Park, SA, Australia; Department of Radiation Oncology, Peter MacCallum Cancer Centre, Parkville, Australia; University of Toronto, Toronto, ON, Canada; Flinders University, Adelaide, Australia

Background: In advanced oesophageal cancer (OC), 90% of patients have dysphagia as a principal symptom. The randomised TROG 03.01 trial reported no significant overall survival or dysphagia relief difference between 15 fractions (#) radiotherapy alone (RT) or RT plus chemotherapy (CRT). Future studies may consider RT hypofractionation, different chemotherapy, esophageal stenting, and best supportive care. Comparing costs and outcomes, economic evaluation often informs public funding decisions in countries such as Australia and the UK. The objective of this analysis was to derive baseline cost and outcome for further studies. Methods: Given equal outcomes (non-inferiority) between treatment arms, cost-minimisation analysis (CMA) was used to evaluate cost-effectiveness, cost a deciding factor if no other benefit was predicted. We explored 15 and 10 # courses used in TROG 03.01 and alternatives, 1 or 5 # Study design and uncertainty analyses were provided. Sub-analysis assessed salvage therapy for local and systemic progression. The EQ-5D (and SF-12) was used to determine utility values to estimate Quality-Adjusted Life years (QALYs) for evaluation. Results: From a health system perspective, costs and outcomes of RT were estimated at $4,700 AUD (15 # course). If, compared with RT alone, an alternative option is more costly but more effective, then a cost-utility analysis (CUA) is preferred economic evaluation. Intervention and in/outpatient costs, initial phase and post treatment were considered for stent insertion and alternative chemotherapy regimens. Alternatively, autocontoured CT planning and machine learning were modelled to reduce RT planning cost (est. $650/p). Total cost for 5 # is $3200 could be further reduced through process efficiency savings using CMA approach. Conclusions: The value of palliative approaches in common malignancies is difficult to assess. This study uses economic analysis to guide paying authority decisions. RT can be simplified from the TROG 03.01 approach to lessen cost and simplify treatment. The clinical efficiency of 1 or 5 # should be evaluated. Research Sponsor: NHMRC australia and NCI canada sponsored the original source trial.

Synchronous pulmonary and esophageal cancers: Is combined esophagectomy and anatomic lung resection appropriate?

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Background: Resection is the best treatment for both esophagus and lung cancer, however, concerns that a combined resection of synchronous lung/esophagus tumors might be associated with higher morbidity may preclude surgical therapy. We sought to review a multi-institutional experience on combined esophagus/lung cancer resections. Methods: Patients undergoing esophagectomy and those with concurrent anatomic resection for bronchogenic carcinoma between 1997-2018 at three high-volume North American centers were identified from prospectively collected databases. Combined resection cases (E+L) were matched in a 1:3 ratio to patients who underwent esophagectomy alone (E), based on age, sex, stage, neoadjuvant therapy, procedure (2/3hole), and approach (MIE/open). Patient demographics, tumour characteristics, and post-operative outcomes were compared. Statistical analysis was performed using unpaired t-test or Wilcoxon sum-rank test for continuous variables and Fisher’s exact test for categorical data. Statistical significance was defined as p < 0.05. Results: Of over 2500 patients undergoing esophagectomy, synchronous anatomic lung resection was performed in 20; 4 were excluded due to incomplete data (n = 16). Matching yielded 48 patients and 4 duplicates were removed (n = 44); there were no significant differences in patient demographics, neoadjuvant therapy, clinical stage, or procedure. Anatomic resection consisted of lobectomy (16/20), segmentectomy (3/20) and pneumonectomy (1/20), combined with 2-hole (14/20), 3-hole (4/20), or left thoraco-abdominal (2/20) esophagectomy. The proportion of patients with any complication in E+L was 50%, and 66% in E (p = 0.42). Pulmonary complications were 19% and 27% in the respective groups (p = 0.74). Mortality did not differ (E+L = 0/16; E = 1/44)NS. The median length of stay for both groups was similar (E+L = 10.5 days (IQR 5.7); E = 10.0 days (IQR 8.7))NS. Conclusions: Patients with synchronous localized lung and esophageal cancer, although rare, should not be biased towards nonsurgery therapy, as the morbidity associated with combined esophagectomy and anatomic lung resection does not differ significantly from esophagectomy alone. Research Sponsor: None.
Cryotherapy in addition to chemotherapy for palliation of inoperable esophageal cancer: A multicenter prospective study.

Toufic Kachaamy, Neil R. Sharma, Rahul Pannala, Jeffrey Weber, Kimberly Gorsuch, Yashika Young, Christina Salas, Christina M. Zelt, Heather Werling, Digant Gupta, Pankaj G. Vashi; Cancer Treatment Centers of America, Zion, IL; Parkview Health, Fort Wayne, IN; Mayo Clinic, Scottsdale, AZ; Western Regional Medical Center, Cancer Treatment Centers of America, Goodyear, AZ; Cancer Treatment Centers of America, Phoenix, AZ; Parkview Research Center, Fort Wayne, IN; Parkview, Fort Wayne, IN; Cancer Treatment Centers of America, Midwestern Regional Medical Center, Zion, IL

**Background:** Palliation of dysphagia (Dys) in patients with inoperable esophageal cancer (EC) can be challenging. The major goal of palliation therapy is to improve patient’s quality of life (QoL) and Dys and allow adequate caloric intake. The most commonly used palliative modalities for Dys are radiation therapy (RT) and esophageal stenting. However, RT is limited by total dose and adverse events (AE) in patients receiving systemic therapy (ST), and stenting suffers from a high rate of AE including reflux and chest pain. A relatively new modality of liquid nitrogen endoscopic spray cryotherapy (cryo) has been reported in retrospective studies to improve Dys in patients receiving systemic therapy. We prospectively evaluated Dys and QoL of patients with inoperable EC undergoing cryo in addition to ST for palliation. **Methods:** A prospective multicenter study of 24 adult inoperable EC patients undergoing cryo and ST for palliation at 4 specialized cancer centers from Sep 2017 to Aug 2019. QoL was assessed using a modified EORTC QLQ-OES18 questionnaire (score 18 to 72, with higher scores indicating worse QoL). Dys was measured using a 4-point Likert scale: 0, no Dys; 1, Dys to solids; 2, Dys to semi-solids; 3, Dys to liquids; 4, Dys to saliva. Paired t-test was used to evaluate change in QoL and Dys between pre- and post-cryo. **Results:** There were 19 males and 5 females (17 stage IV, 5 stage III, and 2 stage II at diagnosis). Among 24 patients, a total of 71 cryo were performed, with a mean of 2.9 treatments per patient. After a median follow-up of 2 months, the mean EORTC score improved significantly from 35.4 at baseline to 25.5 at last follow-up ($p < 0.001$). Similarly, the Dys score improved significantly from 2.0 at baseline to 0.87 at last follow-up ($p < 0.001$). Grade 3 or higher AE were seen in only one patient (4%) who had GI bleeding 2 weeks after cryo and was diagnosed with bleeding from severe reflux esophagitis related to gastric outlet obstruction. **Conclusions:** The analysis of this multicenter prospective study shows that cryo in addition to ST for palliation of EC is well tolerated with significant improvement in Dys and QoL. Research Sponsor: None.
Variation in treatment patterns and outcomes for resected esophageal cancer at designated thoracic surgery centers.

Vaibhav Gupta, Jordan Levy, Biniam Kidane, Alyson Mahar, Jolie Ringash, Rinku Sutradhar, Gail Elizabeth Darling, Natalie Coburn, PRESTO Research Group; University of Toronto, Toronto, ON, Canada; Department of General Surgery, University of Toronto, Toronto, ON, Canada; University of Manitoba, Winnipeg, MB, Canada; Department of Radiation Oncology, Princess Margaret Cancer Centre, Toronto, ON, Canada; Institute for Clinical Evaluative Sciences, Toronto, ON, Canada; Odette Cancer Centre, Sunnybrook Hospital, Toronto, ON, Canada

Background: Ontario regionalized thoracic surgery to designated centers to provide high-volume care for patients undergoing esophageal cancer resection. The objective of this study was to assess variation in treatment patterns and outcomes across thoracic centers, and to compare their performance to non-thoracic centers. Methods: A retrospective, population-based cohort study (2002-2014) was conducted in Ontario, Canada (population 13.6 million). Adults with resected esophageal cancer were identified through the PRESTO database. Case mix, use of neoadjuvant therapy, surgical outcomes (lymph node yield and margin rates) and survival were described across thoracic centers. Multivariable regression was used to estimate the effect of having surgery at a regionalized thoracic surgery center on perioperative (in-hospital & 90-day post-discharge) mortality and long-term survival, adjusting for case mix. Results: Of 3,880 patients meeting study criteria, 2,213 had pathology data available and were included in the analysis. Average age was 64 years, 85.7% had adenocarcinoma, 50.2% were pT3, and 38.4% were pN0. Most (82.6%) had surgery at one of 15 thoracic centers. Across thoracic centers, rates of neoadjuvant therapy varied 16.4-81.6%, positive margin rates varied 8.2-29.6%, median lymph node harvest varied from 7-20 nodes, perioperative mortality varied 2.6-20.5%, and 2-year survival varied from 48-80%. There was a trend toward reduced perioperative mortality, but no difference in long-term survival, with having surgery at a thoracic center. Conclusions: Even at designated thoracic centers, there is significant variability in treatment patterns, surgical outcomes, and survival. Looking beyond center volume, and translating best practices from high-performing hospitals to other hospitals, may improve patient outcomes. Research Sponsor: Sherif and MaryLou Hanna Chair in Surgical Oncology at Sunnybrook Health Sciences Center, Toronto, Canada.
Early implementation of a postoperative nutrition support pathway for patients undergoing esophagectomy.

Rebecca Carr, Christina Stella, Diana Glauner, Erin Kenny, Lianne Russo, Meghan Garrity, Matthew Bott, James M. Isbell, Bernard Park, Smita Sihag, David Randolph Jones, Daniela Molena; Memorial Sloan Kettering Cancer Center, New York, NY

**Background:** A significant risk of malnutrition burdens patients with esophageal cancer undergoing esophagectomy as tumor-related dysphagia and side effects of chemoradiation impair the patients’ ability to maintain adequate nutrition. Moreover, patients lose 10% or more of their preoperative body weight in the first year following surgery. Implementation of nutrition protocols may reduce postoperative weight loss and enhance recovery in these patients. **Methods:** This is a retrospective study examining a postoperative nutrition protocol initiated in August of 2017. Patients with esophagogastric cancer who underwent Ivor Lewis esophagectomy from July 2016 to July 2019 were identified from a prospectively collected database. Patients that underwent surgery after implementation of this protocol were compared to those operated prior to it. **Results:** Patients’ and tumor characteristics were similar between the two groups. The protocol included preoperative evaluation by a dietician, postoperative feeding pathway, and regular post-discharge follow up by phone with a dietician. In the post protocol group, we observed a reduction in time to initiation of diet and decreased weight loss at patient follow up (Table). There was no difference in incidence of postoperative complication, length of stay, 30-day readmission, or in hospital mortality. **Conclusions:** In conclusion, postoperative nutrition support programs may help reduce postoperative weight loss and may have a role in the prevention of malnutrition in these patients. Initial results suggest that more aggressive nutritional supplement program is feasible and may lead to improved postoperative outcomes in patients undergoing esophagectomy. Research Sponsor: None.

<table>
<thead>
<tr>
<th></th>
<th>Pre Protocol</th>
<th>Post Protocol</th>
<th>p-value</th>
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<tr>
<td><strong>Length of Stay</strong></td>
<td>9 (7-11)</td>
<td>8 (7-11)</td>
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<td><strong>Weight Loss at Follow Up</strong></td>
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<td><strong>Days to NG Removal</strong></td>
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<td>4 (3-5)</td>
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<tr>
<td><strong>Days to Clear Liquid Diet Initiation</strong></td>
<td>8 (6-9)</td>
<td>7 (6-8)</td>
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<td><strong>Days to Jejunostomy Removal</strong></td>
<td>25 (20-35)</td>
<td>25 (10-28)</td>
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<td><strong>Hospital Mortality</strong></td>
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<tr>
<td><strong>Postoperative Complication</strong></td>
<td>56 (60.9%)</td>
<td>93 (54.7%)</td>
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<td><strong>Serious Complication</strong></td>
<td>22 (23.8%)</td>
<td>44 (25.9%)</td>
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<td><strong>Anastomotic Leak</strong></td>
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<td>29 (17.1%)</td>
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<td><strong>30 Day Readmission</strong></td>
<td>13 (14.1%)</td>
<td>24 (14.1%)</td>
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Impact of inaccurate clinical staging for gastric cancer on patient survival outcomes.

Michelle Ju, Matthew R. Porembka; UT Southwestern, Dallas, TX; Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX

Background: Accurate clinical staging (CS) in gastric cancer is critical for appropriate treatment selection and prognostication, but CS remains highly ineffective. Our study aims to evaluate the factors associated with inaccurate CS, the impact of inaccurate CS on patient outcomes, and effect of adjuvant therapy in patients with inaccurate CS. Methods: We conducted a retrospective review of the NCDB of patients diagnosed with clinical early-stage gastric adenocarcinoma based on AJCC 8th edition (cT1-2, N0, M0) between 2004-2016. Those who did not undergo upfront surgery or had missing pathologic staging data were excluded. Patients were classified into 3 groups: accurately staged (AS) if pathologic staging confirmed early-stage cancer, inaccurately staged with receipt of adjuvant therapy (IS+), and inaccurately staged with no receipt of adjuvant therapy (IS-). Logistic regression using stepwise selection was utilized to assess the impact of factors on CS accuracy and receipt of adjuvant therapies. Kaplan-Meier and Cox Proportional Hazard methods were used to compare survival outcomes. Results: Approximately 39% of patients (2841/7199) were understaged. T2 tumors, non-well differentiated tumors, and diffuse type histology were associated with increased likelihood of inaccurate CS. Age >60, female sex, Asian/Black race, and non-cardia tumor location were associated with decreased likelihood of inaccurate CS. Only 44% of patients who were inaccurately staged received adjuvant chemotherapy/radiation. Age >75 and fundus/body tumor location were associated with decreased likelihood of receiving adjuvant therapies, while more advanced pT and pN stage were associated with increased likelihood. Treatment facility type (community vs. academic) had no impact on likelihood of accurate CS or receipt of adjuvant treatment after inaccurate CS. 5-year overall survival was significantly different between groups (71.7% AS, 48.3% IS+, 51.1% AS-; p<0.001). Conclusions: CS is inadequate, and understaging has detrimental effects on patient survival outcomes. Novel strategies for improved CS are needed to improve patient care. Research Sponsor: None.
Correlation of heart dose with lymphopenia in esophageal cancer patients treated with chemoradiation.

Amber Post, Stephen R. Bowen, Bao-Ngoc Nguyen, William Logan, Jing Zeng, Smith Apisarnthanarax; University of Washington, Seattle, WA; Seattle Proton Therapy Center, Seattle, WA; Johns Hopkins University School of Medicine, Seattle, WA

Background: Lymphopenia has been associated with survival and disease progression in esophageal cancer patients treated with chemoradiation (cRT). We previously published on our posterior-only proton therapy approach that maximally spares the heart and lungs, but at the cost of increased dose to the bone marrow in the vertebral bodies (VBs). We assessed hematologic toxicity in proton (PT) and IMRT treated patients and studied dosimetric parameters associated with hematologic toxicity. Methods: 35 patients treated with PT and 46 patients treated with IMRT for esophageal cancer between 2011-2018 were analyzed. Most patients were treated concurrently with carboplatin/paclitaxel to a median dose of 50.4 Gy. Lymphocyte, neutrophil and total leukocyte values while under treatment were recorded and graded per the CTCAE v4.03 toxicity scale, and the neutrophil-to-lymphocyte ratio (NLR) was computed. Mean dose and volumes (cc) receiving 5-50 Gy were calculated for the heart and VBs. A receiver-operator characteristic analysis was performed for univariate correlation between incidence of grade ≥3 hematotoxicity and dose-volume parameters. Results: Median follow-up was 36.1 months for all patients and the overall survival at 3 years was 57.5%. The rates of grade 3 or 4 hematologic toxicity in the PT group were 37.1% (leukopenia), 22.9% (neutropenia), and 80.0% (lymphopenia) versus 41.3%, 15.2% and 87.2%, respectively, for IMRT patients. There was a significant correlation between grade 4 lymphopenia and the heart V5, V10 and V20, but no significant correlation between VB doses with any hematotoxicity. Median NLR values and heart dose were higher in the IMRT group (9.17 vs 3.86 with PT, p = 0.0048; 10.5 vs 23.5Gy, p< 0.0001, respectively). There was a correlation between survival and NLR with a hazard ratio of 1.025 (CI 1.006 - 1.044). Conclusions: Low doses to the heart mediate severe lymphopenia in esophageal cancer patients treated with cRT. These data confirm the safety of the posterior-only proton approach without concern for increased hematologic toxicity despite higher vertebral body doses compared to IMRT. They also suggest that the blood pool is more important as a source of severe lymphopenia. Research Sponsor: None.
Prognostic impact of immune-related adverse events with nivolumab in patients with advanced gastric cancer: A multicenter retrospective analysis.

Yuno Ohya, Takayuki Ando, Akira Ueda, Kohei Ogawa, Iori Motoo, Shinya Kajiura, Kenichiro Tsukada, Takuo Hara, Nobuhiro Suzuki, Naokatsu Nakada, Shunsuke Takatori, Naoki Horikawa, Tsutomu Fujii, Ichiro Yasuda; University of Toyama, Toyama, Japan; Third Department of Internal Medicine, University of Toyama, Toyama, Japan; Toyama Red Cross Hospital, Toyama, Japan; Toyama Prefectural Central Hospital, Toyama, Japan; Kouseiren Takaoka Hospital, Takaoka, Japan; Kouseiren Takaoka Hosp, Takaoka, Japan; Itoigawa Sogo Hospital, Itoigawa, Japan; Saiseikai Toyama Hospital, Toyama, Japan; Takaoka City Hospital, Takaoka, Japan; Department of Surgery and Science, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama, Japan

Background: Nivolumab was established as one of the standard treatments for previously treated advanced gastric cancer (AGC). The aim of this study is to evaluate the frequency of immune-related adverse events (irAEs) with Nivolumab and its impact on treatment efficacy in clinical practice. **Methods:** We performed multicenter retrospective analysis, which included 90 patients with advanced gastric cancer who received Nivolumab treatment between October 2017 and September 2019. The frequency of irAEs and its treatment outcome were evaluated, and survival was compared during Nivolumab treatment. **Results:** The characteristics of 90 patients in this analysis were as follows: median age (range), 68 (36-85); male/female, 56/34; ECOG PS 0-1/2, 62/28; number of metastatic sites 1/2, 36/56; treatment line 3/4, 63/27. Median treatment cycle of nivolumab treatment was 3 (range 1-26). The overall response in 68 patients with target lesions was 6.3% (4/68), and the median PFS and OS was 1.5 and 4.3 months, respectively. IrAEs were observed in 8 patients (8.8%), including grade 4 pneumonitis, grade 2 or 3 adrenal insufficiency, and grade 2 hypothyroidism, encephalitis, and immune thrombocytopenia. Median time to onset of irAEs was 1.3 (range 0.6-10.5) months. Six were treated with systemic corticosteroid therapy, and all irAEs were relieved. The median PFS and OS were 4.7 months (95%CI, 1.2-9.3) and 12.2 months (95% CI, 3.2-not reached) in patient with irAEs, and 1.4 months (95%CI, 1.1-1.9) and 4.1 months (95%CI, 2.6-6.6) in those without, respectively. There was significant difference in the PFS (p=0.005) and OS (p=0.03). **Conclusions:** Nivolumab was effective and well tolerated even in clinical practice. Development of irAEs may be associated with better outcome of Nivolumab in patients with AGC. Research Sponsor: None.

Analysis of weight loss as a prognostic factor in patients (pts) with advanced gastric cancer from REGARD, RAINBOW and RAINFALL phase III studies.

Wasat Mansoor, Eric Roeland, Aafia Chaudhry, Ran Wei, Anindya Chatterjee, Holly Knoderer, Paolo Abada, Samuel J. Klemper; Christie NHS, Manchester, United Kingdom; Massachusetts General Hospital Cancer Center, Boston, MA; Novocure, New York, NY; Eli Lilly and Company, Indianapolis, IN; The Angeles Clinic and Research Institute, Los Angeles, CA

Background: Maintaining weight (wt) and adequate nutrition during systemic treatment in advanced gastric cancer (G/GEJ) therapy remains a challenge. We investigated the impact of early wt-loss on survival in three phase 3 studies of ramucirumab (R); REGARD (RG), RAINBOW (RB), and RAINFALL (RF) in G/GEJ. Methods: ITT pts were categorized into 2 groups based on their body wt change from start to end of cycle 1 (C1; C = 28 days in RG, RB; C = 21 days in RF): wt-loss < 3% vs ≥3%. Univariate Cox PH models were performed in each individual study to evaluate the effects of body wt change from the start to end of C1 on OS. A pooled meta-analysis stratified by study and a sensitivity analysis of the subgroup of responders was also performed. Results: A total of 311 (RG: 212 in R+BSC; 99 in Placebo (PB)+BSC), 591 (RB: 306 in the R+Paclitaxel (P); 285 PB+P), and 562 (RF: 279 in R+Cape/Cis (CC); 283 in PB+CC) pts with body wt data during C1 were evaluated. The number of pts with wt-loss of ≥3% and < 3% are shown in Table. Pts with wt-loss < 3% during C1 experienced longer OS compared to those with wt-loss ≥3%, irrespective of treatment arms across studies (Table). In pooled treatment arms within each study, the HR for wt-loss group ( < 3% vs ≥3%) was 0.359 (95% CI = 0.254, 0.507), 0.632 (0.497, 0.804), 0.752 (0.608, 0.930) in RG, RB, RF, respectively. In the meta-analysis that combined the 3-studies, univariate Cox PH model stratified by study showed consistent effect of early wt-loss on OS regardless of treatment arm, HR ( < 3% vs ≥3%) = 0.632 (0.546, 0.732). Conclusions: Analysis from three phase 3 studies demonstrates early wt-loss ≥3% during C1 is an important negative prognostic factor for survival in gastric/GEJ cancer. Prospective studies of the relationship of weight preserving nutritional interventions on OS are warranted. Clinical trial information: NCT00917384, NCT01170663, NCT02314117. Research Sponsor: Eli Lilly and Company.
Perioperative docetaxel, oxaliplatin, and capecitabine (DOX) in resectable adenocarcinomas of lower esophagus, esophagogastric junction, and stomach.

Shaunak Valame, Dipanjn Panda, Shuaib Zaidi, Praveen Garg, Syed Asim Razvi, Manish Kumar Singhal, Pratap K. Das, Pankaj Baweja, Jayanta Patowary; Indraprastha Apollo Hospital, New Delhi, India; Apollo Hospital, Delhi, India

**Background:** In a real-world scenario, Fluorouracil-based triplet combination chemotherapies have limited feasibility with regards to toxicity, need for central venous access, and hospitalization. The primary objective of this study was to assess pathological tumor regression to Capecitabine-based triplet regimes, with the additional possible benefit of overcoming the aforementioned barriers. **Methods:** This Single-Arm, Prospective study investigated the primary outcome of histopathologic regression to perioperative Docetaxel, Oxaliplatin, and Capecitabine (DOX) combination regime in histologically confirmed resectable Esophageal, Esophagogastric Junction, and Gastric Adenocarcinomas. Three preoperative and 3 postoperative cycles of Docetaxel 60mg/m² plus Oxaliplatin 100mg/m² on Day 1, with Capecitabine 500mg/m² twice daily from Day 1 to Day 21 were administered, with cycles repeating every 21 days. Histopathologic regression was assessed by Modified Ryan’s Schema on surgical specimen. The study had an 80% power (two-sided significance of 0.05) to detect a 20% pathological complete response. Secondary endpoints were Overall Survival, Progression-Free Survival, and Toxicity analysis. **Results:** Between June 2017 to May 2019, 28 patients (median age 54.5 years [Range 33 - 82]; Male 78.6%; ECOG PS 1/2 = 42.9%/57.1%) were enrolled in the study of which 92.9% completed preoperative chemotherapy. Of the 20 patients operated upon, 100% were R0 resections. Pathological complete response was observed in 20% (4/20). Ninety percent of the operated patients completed the postoperative treatment. The most common grade ≥3 toxicities were Palmar-Plantar Erythrodysesthesia (10.7%), Fatigue (10.7%), and Diarrhoea (7.1%). **Conclusions:** Perioperative DOX met its primary endpoint of 20% pathologic complete regression with a favourable toxicity profile and was feasible to administer in resectable Esophageal, Esophagogastric Junction, and Gastric Adenocarcinomas. This regimen deserves further evaluation in larger phase III trials. Research Sponsor: None.
A phase II trial of low-dose nab-paclitaxel for patients with previously treated or recurrent advanced gastric cancer (OGSG1302).

Masashi Hirota, Shigeyuki Tamura, Hirokazu Taniguchi, Atsushi Takeno, Hiroshi Imamura, Junya Fujita, Jin Matsuyama, Yutaka Kimura, Junji Kawada, Motohiro Hirao, Kazuhiro Nishikawa, Kazumasa Fujitani, Yukinori Kurokawa, Daizuke Sakai, Hisato Kawakami, Yoshio Shimokawa, Taroh Satoh; Department of Surgery, Toyonaka Municipal Hospital, Toyonaka City, Osaka, Japan; Yao Municipal Hospital, Yao City, Osaka, Japan; Minoh City Hospital, Osaka, Japan; Department of Surgery, Kansai Rosai Hospital, Amagasaki, Japan; Department of Surgery, Toyonaka Municipal Hospital, Toyonaka, Japan; Department of Surgery, Sakai City Medical Center, Sakai, Japan; Department of Gastroenterological Surgery, Higashiosaka City Medical Center, Higashi Osaka City, Japan; Sakai City Medical Center, Sakai, Japan; Department of Surgery, Kaizuka City Hospital, Kaizuka, Japan; National Hospital Organization, Osaka National Hospital, Osaka, Japan; Department of Surgery, Osaka General Medical Center, Osaka, Japan; Department of Gastroenterological Surgery, Osaka University, Graduate School of Medicine, Suita City, Osaka, Japan; Osaka University Graduate School of Medicine, Suita, Japan; Department of Medical Oncology, Kindai University Faculty of Medicine, Osaka, Japan; Osaka Gastrointestinal Cancer Chemotherapy Study Group (OGSG), Osaka, Japan; Osaka University, Osaka, Japan

Background: Paclitaxel is a key drug in second-line chemotherapy for advanced or recurrent gastric cancer (AGC) and nanoparticle albumin-bound paclitaxel (nab-PTX) is also widely used in Japan. A previous phase II trial in Japan showed the effectiveness of nab-PTX (260 mg/m²) administered every 3 weeks (q3w) in patients with AGC with a response rate (RR) of 27.8%; however, toxicity was major concern with grade ≥3 neutropenia (49.1%) and peripheral neuropathy (23.6%). To solve this problem, we investigated the efficacy and safety of low-dose q3w nab-PTX regimen in AGC.

Methods: Eligibility requirements included: aged ≥20 years, HER2-negative, histologically confirmed, unresectable or recurrent gastric adenocarcinoma, one or more prior chemotherapy containing fluoropyrimidine regimens, presence of measurable lesion(s) according to RECIST ver. 1.1, ECOG PS of 0–2, and adequate organ function. Nab-PTX was administered at a dose of 220 mg/m² every 3 weeks. The primary endpoint was the RR. Secondary endpoints were overall survival (OS), progression-free survival (PFS), disease-control rate (DCR), incidence of adverse events, relative dose intensity and proportion of patients who received subsequent chemotherapy. Results: Thirty-three patients were enrolled from 10 institutions in Japan. Of the 32 patients treated with protocol therapy, RR (CR, PR) was 3.1% (95% CI, 0–16.2%), which was not reached the protocol-specified threshold (p = 0.966). DCR (CR, PR, SD) was 37.5% (95% CI, 21.1–56.3%), median OS and PFS were 6.3 months (95% CI, 4.4–14.2) and 2.2 months (95% CI, 1.8–3.1). Relative dose intensity was 97.8% (215 mg/m²). 62.5% of patients received subsequent chemotherapy. Most common grade ≥3 adverse events were neutropenia (38%), anemia (13%), fatigue (19%), anorexia (16%), and peripheral neuropathy (13%). Conclusions: Low-dose regimen of q3w nab-PTX was slightly less toxic, although it did not demonstrate the same effect as the original regimen in response rate. Therefore, it is not recommended for AGC in second or later line setting. Clinical trial information: UMIN 000012701. Research Sponsor: TAIHO PHARMACEUTICAL CO., LTD.
Feasibility and pathological response of TAS-118 + oxaliplatin as perioperative chemotherapy for patients with locally advanced gastric cancer (APOLLO-11).

Daisuke Takahari, Atsuo Takashima, Takako Eguchi Nakajima, Naoki Ishizuka, Manabu Ohashi, Hitoshi Katai, Shinya Mikami, Keishe Chin, Souya Nunobe, Miki Ito, Takeyuki Wada, Takashi Ogura, Takeshi Sano, Narikazu Boku, Kensei Yamaguchi; Department of Gastroenterology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; Gastrointestinal Medical Oncology Division, National Cancer Center Hospital, Tokyo, Japan; Department of Clinical Oncology, St. Marianna University School of Medicine, Kawasaki, Japan; Department of Clinical Trial Planning and Management, The Cancer Institute Hospital of the Japanese Foundation for Cancer Research, Tokyo, Japan; Cancer Institute Hospital of the Japanese Foundation for Cancer Research, Tokyo, Japan; National Cancer Center Hospital, Tokyo, Japan; Department of Gastrointestinal and General Surgery, St. Marianna University School of Medicine, Kawasaki, Japan; Department of Gastroenterological surgery, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; Department of Gastrointestinal and General Surgery, National Cancer Center Hospital, Tokyo, Japan; St. Marianna University School of Medicine, Kawasaki, Japan; Japanese Foundation for Cancer Research Cancer Institute Hospital, Tokyo, Japan; Department of Gastric Surgery, National Cancer Center Hospital, Tokyo, Japan; St. Marianna University School of Medicine, Kawasaki, Japan; Japanese Foundation for Cancer Research Cancer Institute Hospital, Tokyo, Japan; Department of Gastroenterology, The Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: TAS-118 is a novel oral agent, containing S-1 and leucovorin. In the SOLAR study (NCT02322593), TAS-118 + oxaliplatin (OHP) significantly improved overall survival compared to S-1 + cisplatin for patients (pts) with advanced gastric cancer (GC). We conducted this open-label study to assess feasibility of perioperative adjuvant chemotherapy with TAS-118 + OHP in pts with locally advanced resectable GC with lymph node metastasis. (Clinical trial information: UMIN000024688).

Methods: Eligible pts who had histopathologically confirmed GC with clinical T3-4N1-3M0 on image findings (14th Japanese classification of gastric carcinoma), age 20 to 79 years, were enrolled in this study. The protocol treatment consisted of preoperative 4 courses of TAS-118 (80-120 mg/body, days 1-7) + OHP (85 mg/m², day 1) every 2 weeks, and gastrectomy with D2 lymphadenectomy, followed by postoperative 12 courses of TAS-118 alone (step1) or 8 cycles of TAS-118 + OHP (step2). The primary endpoints were tolerability of preoperative chemotherapy, gastrectomy and postoperative chemotherapy with TAS-118 plus OHP. Here, we report the feasibility of preoperative chemotherapy and gastrectomy, and pathological response.

Results: Between December 2016 and April 2018, 45 pts with a median age of 61 years were enrolled. The numbers of pts with T stage (cT3/4a) and those with N stage (cN1/2/3) were 13/32 and 25/17/3, respectively. The completion rate of preoperative chemotherapy and gastrectomy was 88.9% (95% CI 78.0-95.5) and 95.6% (95% CI 86.7-99.2). The relative dose intensity of TAS-118 and OHP was 86.0% and 90.6%. During the 4 cycles of preoperative TAS-118 + OHP, 2 pts discontinued the treatment due to adverse event (AE). Major grade 3-4 AEs were diarrhea (17.8%) and neutropenia (8.9%). R0 resection rate was as high as 95.6%. One pts experienced grade 4 postoperative bleeding, but no treatment-related death was reported. pCR was achieved in 6/45 pts (13.3%) and other 7 pts (28.9%) showed near complete regression (<10 % residual tumor cells).

Conclusions: Preoperative TAS-118 + OHP followed by D2 gastrectomy was well tolerated and showed promising efficacy. Clinical trial information: 000024688. Research Sponsor: Taiho.
A phase I/II study of nivolumab, paclitaxel, and ramucirumab as second-line in advanced gastric cancer.

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Background: Synergistic anti-tumor effect induced by simultaneous blockade of PD-1 and taxanes, and PD-1 and VEGFR-2 has been reported. A phase I/II study was conducted to investigate the safety and efficacy of nivolumab (Nivo) with paclitaxel (PTX) plus ramucirumab (Ram), which is the standard treatment as the second-line treatment for advanced gastric cancer (AGC).

Methods: AGC patients (pts) with measurable lesions, ECOG PS 0-1, and disease progression on the first-line chemotherapy with fluoropyrimidine and platinum were eligible. Pts received Nivo (3 mg/kg on days 1 and 15) combined with PTX (80 mg/m² on days 1, 8 and 15) and Ram (8 mg/kg on days 1 and 15) (Level 1), every 4 weeks. After feasibility was evaluated in 6 pts (phase I part), additional 37 pts were enrolled in a phase II part with the primary endpoint of 6-month progression-free survival (PFS) rate. The combined positive score (CPS) is defined as the number of PD-L1 positive cells (tumor cells, macrophages, and lymphocytes) divided by the total number of viable tumor cells.

Results: Forty-three AGC pts were enrolled: median age, 66 years; ECOG PS 1, 48.8%; and CPS ≥1, 60.5%. Dose limiting toxicities were observed in 2 pts in the phase I part and recommended dose was determined as Level 1. ORR was 37.2% (95% CI, 23.0-53.5%); 46.2% (95% CI, 26.6-66.6%) in CPS≥1 pts and 30.8% (95% CI, 9.1-61.4%) in CPS < 1 pts. With a median follow-up time of 16.8 months, 6-month PFS rate was 46.4% (80% CI, 36.4-55.8%) (P = 0.067); 57.7% (95% CI, 36.8-73.9%) in CPS≥1 pts and 38.5% (95% CI, 14.1-62.9%) in CPS < 1 pts. Median PFS was 5.1 months (95% CI, 4.5-6.5 months). Median survival time was 13.1 months (95% CI, 8.0-16.6 months); 13.8 months (95% CI, 8.0-19.5 months) in CPS≥1 pts and 8.0 months (95% CI, 4.8-24.1 months) in CPS < 1 pts, and 18-months survival rate was 32.1% (95% CI, 18.2-46.8%). Conclusions: Nivo with PTX plus Ram demonstrated promising antitumor activity as the 2nd-line treatment for AGC pts with manageable toxicities. Clinical trial information: UMIN000025947. Research Sponsor: ONO PHARMACEUTICAL CO., LTD.
Low-grade gastric mucosa-associated lymphoid tissue lymphoma: Clinicopathological factors associated with Helicobacter pylori eradication and tumor regression.

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Background: Eradication of Helicobacter pylori is widely accepted as the initial therapy for low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma. The aim of this study was to assess the remission and relapse rates of low-grade gastric MALT lymphoma after H. pylori eradication and to identify the clinical factors affecting remission. Methods: We retrospectively analyzed 151 patients diagnosed with gastric MALT lymphoma from May 2003 to December 2018. Results: Of the 151 patients, 112 (74.2%) had an H. pylori infection. Total regression rates with eradication was 90.2% (101/112) in H. pylori-positive patients and 55% (11/20) in H. pylori-negative patients. Age, sex, tumor location, endoscopic findings, and the severity of mononuclear lymphocytes were not related to achieving successful initial H. pylori eradication and remission. However, patients with a smaller H. pylori burden (p=0.030) and less neutrophil infiltration (p=0.003) were more likely to achieve a successful initial H. pylori eradication. H. pylori (p<0.001) and the burden (p=0.020) were significantly related to remission of MALT lymphoma. Conclusions: The results show that H. pylori burden and neutrophil infiltration were inversely related to the success of the initial H. pylori eradication procedure and that the H. pylori burden was inversely related to the remission of MALT lymphoma. Research Sponsor: None.
Survival benefit of conversion therapy after intensive chemotherapy for unresectable metastatic gastric cancer: A propensity score-matched analysis.

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Background: The significance of conversion therapy (CT), whereby patients (pts) with unresectable disease respond to chemotherapy and subsequently receive surgery with curative intent (adjuvant surgery: AS), has been specifically established for metastatic colorectal cancer. However, such a strategy for advanced or recurrent gastric cancer (AGC) remains controversial. This study aims to clarify the clinical significance of CT for AGC.

Methods: In this retrospective multi-institution observational study, we analyzed 168 AGC pts who received chemotherapy consisting of docetaxel, cisplatin or oxaliplatin, and S-1 and trastuzumab between 2003 and 2019. We divided pts into two groups: those who underwent CT (group CT) or chemotherapy only (group C). Propensity score analysis with 1:1 matching minimized confounding bias when comparing efficacy and safety between groups.

Results: A tumor response to chemotherapy was observed in 82.4% of all cases, while 34.5% (58/168) underwent AS. Fifty-one of the 58 pts underwent an R0 resection, and 79.3% were deemed histological responders. After matching, 44 pairs of C and CT pts were selected; significant differences in baseline characteristics were not observed. Incidences of adverse events during chemotherapy were similar between groups, with neutropenia and febrile neutropenia as common grade 3–4 events. Compared with group C, group CT had a significantly better median overall survival (OS) (15.5 vs. 46.0 months; hazard ratio [HR] 0.32; 95% confidence interval [CI] 0.18–0.58; p < .001), and a prolonged progression-free survival (6.5 vs. 22.6 months; HR 0.33; 95% CI 0.19–0.56; p < .001). Subgroup analysis of OS showed a favorable trend for CT for almost all parameters. In a multivariate analysis, ECOG performance status (HR 0.10; 95% CI 0.03–0.31) and AS (HR 0.20; 95% CI 0.10–0.40) correlated with favorable OS. In the CT group, pathological response was an independent prognostic factor (HR 0.16; 95% CI 0.06–0.39).

Conclusions: CT was associated with better outcomes in AGC pts, even after baseline adjustment. Our data warrants further large-scale studies to establish a conversion therapeutic strategy. Research Sponsor: None.
Gefitinib along with methotrexate as palliative therapy in PS 3 and above in metastatic esophagus squamous cell carcinoma with focus on Q-TWIST.

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**Background:** Metronomic therapy is proven method for treatment of terminally ill patients with malignancy, who are not fit for chemotherapy. The median PFS was significantly superior in responders in previous Indian experiences. However most of them were done in head and neck cancers. The prognosis of patients with metastatic esophageal cancer remains poor with only option being symptomatic care. As the previous experiences show metronomic therapy is safe among various options and there is no study focusing on Quality-Adjusted Time Without Symptoms or Toxicity (Q-TWIST) in southern Indian population, we thought of evaluating the same.

**Methods:** Details of 42 subjects with refractory or progressive metastatic squamous cell carcinoma esophagus having PS ≥ 2 were evaluated. Case records between 2017 September and 2018 September were analyzed for TWIST and QOL. Patients received Gefitinib (250 mg/day), Methotrexate 15 mg IM weekly or in combination. Patients were stratified into those with improved PS and those without. The subjects without PS improvement were continued on the single agent and those with improvement were offered additional chemotherapy based on physician/patient preference. Metronomic therapy could be continued beyond disease progression if there is TWIST/QOL improvement.

**Results:** Out of 42 subjects, 29 had improvement in the PS and were continued later. 9 had stable PS and disease. 4 had worsening of PS. 34 subjects have clinically meaningful response (stable disease + complete + partial responses) and had symptomatic improvement. The median number of cycles was 6 (4–11). The median PFS was 198 days (95% CI, 174 to 214), and the median improvement in QOL was 6 points on a scale of 25. Grade II/IV toxicities were observed in 21 (50%) cases predominantly skin rash, stomatitis and diarrhea.

**Conclusions:** Metronomic therapy is well tolerated and may have a role in the treatment of advanced cancers with poor performance status. 67% of the patients who are otherwise not eligible for any active therapy became eligible and had better QOL and longer PFS, which re-emphasizes role of metronomic therapy in advanced squamous cell carcinoma of esophagus. Research Sponsor: None.
**Personalized ANtibodies for GastroEsophageal Adenocarcinoma (PANGEA): Primary efficacy analysis of the phase II platform trial (NCT02213289).**

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**Background:** 1-yr OS is ~40% for HER2- & ~55% for HER2+ advanced (aGEA). Targeted therapies (tx) have had limited benefit due to molecular heterogeneity. **Methods:** This phase 2a study of a personalized tx strategy (PTS) enrolled newly diagnosed aGEA pts who then received up to 3 cytotoxic (cx) lines: first line (1L) 5FU + oxaliplatin, 2L 5FU + irinotecan & 3L 5FU + docetaxel. Baseline biomarker profiling (BP) was mandated on primary & metastatic tumors (PT/MT) & progressive disease points (PDI, PD2). Assigned antibody (AN) was added to cx by a predefined prioritized tx algorithm (PTA) (Table) based on the MT BP. At PDI, pts went to 2L cx + initial AN. Upon results of PDI BP, pts changed AN only if BP evolved per PTA. The same was done at PD2. If AN was unavailable (MET/FGFR2), these pts were tx'd with cx alone (not ITT). The 1L endpt was 1-yr OS of the PTS. Assuming historical 50% 1-yr OS for all aGEA pts, 68 pts tx’d per protocol PTS provided 80% power to detect an HR=0.67, corresponding to a 1-yr OS rate of 63% (under exponential survival), using a 1-sided test at the 0.10 alpha level. 2 endpts: safety, feasibility, PT/MT BP discordance at baseline & over tx line, & OS/PFS/ORR by tx line & BP group. **Results:** Between 6/2015-5/2019, 80 consecutive pts enrolled at 3 sites: ECOG PS 0-2 40/33/7; Male 80%; median age 60, range 28-81, peritoneal disease 36%. AN assigned by PTA at 1L & 1-yr OS are shown (Table). PT/MT discordance was 37%. Of 68 pts treated by PTS ITT, the 1-yr OS was 69.4% (p<0.001). The mOS was 16.4m [95%CI 13.8-20.8]. Any grade 3 tox thru all 3 tx lines was seen in 32% of pts. 20 analyses will be presented. **Conclusions:** PANGEA was feasible & met its 1st efficacy objective with observed 1-yr OS of 69.4%, meriting a randomized study. Clinical trial information: NCT02213289. U.S. National Institutes of Health.

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1 MT priority over PT
2 priority over HER2 only 2L+
3 priority to higher gene copy
4 excluded from ITT 5 evaluable

DKN-01 in combination with pembrolizumab in patients with advanced gastroesophageal adenocarcinoma (GEA): Tumoral DKK1 expression as a predictor of response and survival.

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Background: Dickkopf-1 (DKK1) modulates Wnt signaling and contributes to an immune suppressive tumor microenvironment. DKN-01 (D), a neutralizing DKK1 antibody + pembrolizumab (P) has demonstrated safety and clinical activity in advanced GEA. We report response and survival outcomes in anti-PD-1/anti-PD-L1 naïve GEA patients by high/low tumoral DKK1 expression.

Methods: We enrolled advanced anti-PD-1/PD-L1 naïve GEA patients (pts) in a Phase 1b/2a study of D + P (NCT02013154). Tumoral DKK1 mRNA expression was assessed by an in situ hybridization RNAscope assay. Objective response rate (ORR), disease control rate (DCR), progression free survival (PFS) and overall survival (OS) were compared between DKK1 high and low groups. Kaplan-Meier method and Cox-PH model was used for survival analysis and logistic regression was used for clinical benefit/response outcome.

Results: 34 GEA pts were enrolled to receive 300 mg D + P. 31 GEA pts had DKK1 expression available (25 response-evaluable/RE) and 27 had both DKK1 and PD-L1 expression available (22 RE). In RE pts, DKK1 high (H-score ≥ upper-tertile [≥ 35]) had an ORR of 50% (5 PR/10), DCR of 80% (8/10) while DKK1 low (< upper-tertile) had an ORR of 0% (0/15) and DCR of 20% (3/15); DKK1 high (vs. low) had an OR of 16 (95%CI: 2.2, 118.3; n = 25) and adjusted (for PD-L1 CPS ≥10 vs. < 10) OR of 17.6 (95%CI: 1.6, 194.4; n = 22) for clinical benefit/response (PR/SD vs. PD). Median PFS was 22.1 weeks in DKK1 high (n = 11) vs. 5.9 weeks in DKK1 low (n = 20); HR of 0.23 (95%CI: 0.081, 0.66; n = 27). Adjusted (for PD-L1 expression) HR for DKK1 high was 0.20 (95%CI: 0.061, 0.68; n = 27) for PFS. DKK1 high (n = 11) had a median OS of 31.6 weeks vs. 17.4 weeks in DKK1 low (n = 20); HR of 0.45 (95%CI: 0.16, 1.3; n = 31) and adjusted HR of 0.62 (95%CI: 0.2, 1.9; n = 27).

Conclusions: High levels of tumoral DKK1 expression identify advanced anti-PD-1/PD-L1 naïve GEA pts with the greatest benefit from D + P. Improvements in response/clincial benefit and PFS were observed independent of PD-L1 expression. Tumoral DKK1 as a potential predictive biomarker for DKN-01 treated GEA pts will be evaluated in future studies. Overall survival follow-up is ongoing. Clinical trial information: NCT02013154. Research Sponsor: Leap Therapeutics.
Postoperative adjuvant chemotherapy with S-1 versus SOX/XELOX regimens for pStage III gastric cancer: A cohort study.

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**Background:** Adjuvant chemotherapy following curative gastrectomy is recommended for patients with pStage II or III, except pT3 (ss), NO gastric cancer in Japan. This study aimed to compare the efficacy of postoperative adjuvant chemotherapy with S-1 versus SOX/XELOX for pStage III gastric cancer. **Methods:** Between January 2015 and December 2018, 51 patients with pStage III gastric cancer underwent curative gastrectomy. The combination therapy group received a combined SOX and XELOX regimen as follows: (1) SOX regimen: 130 mg/m² of oxaliplatin on day 1 every 3 weeks combined with 40 mg/m² of S-1 twice daily on days 1-14 every 3 weeks; (2) XELOX regimen: 130 mg/m² of oxaliplatin on day 1 every 3 weeks combined with 1000 mg/m² of capecitabine twice daily on days 1-14 every 3 weeks. We evaluated their hospital records retrospectively. The indication of SOX/XELOX regimens was based on PS and intent of patients. **Results:** The S-1 group comprised 28 cases (pStage III A/B/C: 12/8/8), while the SOX/XELOX group comprised 23 cases (pStage III A/B/C: 4/10/9). There was no difference in age, sex, comorbidity, prognostic nutritional index and stage between two groups. The 2-year DFS of the S-1 group and the SOX/XELOX group were 58.6% and 71.7%, respectively (p = 0.367). Subgroup analysis showed that the 2-year DFS of patients with pStage IIIC gastric cancer in the S-1 group was significantly lower than the SOX/XELOX group (S-1 vs. SOX/XELOX: 25.9% vs. 78.7%, p = 0.041). As concerns adverse effects (CTCAE ver 4.0), peripheral sensory neuropathy was significantly higher in the SOX/XELOX group than in the S-1 group (S-1: grade I/II 3.6%/0% vs. SOX/XELOX: grade I/II 21.7%/34.8%, p < 0.001), although the other adverse effects did not differ between the two groups. **Conclusions:** SOX/XELOX therapy may be more useful than S-1 therapy for more advanced tumors among pStage III gastric cancers. Research Sponsor: None.
Is splenectomy for dissecting splenic hilar lymph nodes justified in scirrhous type of gastric cancer?

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**Background:** Splenectomy for dissecting splenic hilar nodes (#10) should be avoided for most gastric cancer considering high morbidity and no survival benefit, while that is often selected in scirrhous type of gastric cancer because this special type frequently invades the whole stomach and the #10 nodes. Splenectomy is necessary for dissecting #10, however, survival benefit of dissecting #10 is unclear. **Methods:** Patients who had scirrhous gastric cancer and underwent D2 total gastrectomy with splenectomy in National Cancer Center Hospital, Japan, between 2000 to 2011 were retrospectively analyzed. The therapeutic value index was calculated by multiplying the metastatic rate of each nodal station and the 5-year survival of patients who had metastasis to each node. **Results:** In total, 144 patients were eligible for the present study. The most frequent metastatic site was the nodes along the lesser curvature (#3, 57%), followed by the nodes along the right gastro-epiploic artery (#4d, 45%), the right nodes located at the cardia (#1, 34%), the nodes along the left gastro-epiploic artery (#4sb, 23%), the inferior nodes at the pyloric ring (#6, 22%), the nodes along the left gastric artery (#7, 21%), the nodes along the short gastric artery (#4sa, 18%), the nodes along the cardiac branched artery (#2, 15%), the nodes around the spleen (#10, 15%), the distal nodes along the splenic artery (#1ld, 15%), the proximal nodes along the splenic artery (#1lp, 13%), the nodes around the celiac artery (#9, 13%), and the nodes along the common hepatic artery (#8a, 10%). These lymph nodes had a metastatic rate of more than 10%. The node with the highest index was #3(18), followed by #4d(13.4), #1(9.59), #4sa(5.85), #4sb(5.75), #10(4.86), #7(4.16), #1ld(4.16), #1lp(3.87), #2(3.07), #8a(2.08), and #9(1.39). The index of #10 was exceeded that of #2, #7, #8a, and #9 which are the key nodes dissected in D2. **Conclusions:** The metastatic rate of splenic hilar nodes was relatively high, and the therapeutic index was the sixth highest in the fifteen regional lymph nodes included in D2 dissection. Splenectomy for dissecting splenic hilar nodes would be justified in scirrhous type of gastric cancer considering its survival benefit. Research Sponsor: None.
Safety and tolerability of oxaliplatin based pressurized intraperitoneal aerosol chemotherapy (PIPAC) for patients with peritoneal carcinomatosis: A phase I dose-finding study in Asian patients.

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Background: PIPAC is a novel, laparoscopic intraperitoneal chemotherapy delivery technique which aims to improve on hyperthermic intraperitoneal chemotherapy (HIPEC), ameliorating drug distribution and tissue penetration. Thus far, PIPAC has been conducted with oxaliplatin chemotherapy in Europe, at an arbitrary dose of 92mg/m²; 150mg/m² was found to be intolerable. We conducted a dose-escalation phase 1 study to establish the safety, tolerability and recommended phase 2 dose (RP2D) for PIPAC in Asian patients. Methods: This phase 1 study of oxaliplatin administered via PIPAC was designed as a traditional 3+3 dose escalation study for patients with predominant peritoneal metastasis from a gastrointestinal primary tumor, after failure of standard therapies. Dose levels were planned at 45, 60, 90 and 120mg/m². Repeat doses of PIPAC were permitted, 6 weeks apart. Dose limiting toxicities (DLT) were defined as any clinically relevant grade 3 adverse events occurring within 28 days after PIPAC. Results: This study included 16 patients (25 PIPAC procedures; 8 gastric, 4 colorectal and 1 gallbladder, pancreas and appendix cancer each). Median age was 62 years, with a median peritoneal carcinomatosis index (PCI) score of 17 (range 1 - 39). Two patients developed pancreatitis (grade 2 and 3) on day 6 and day 9 after PIPAC administration at the dose cohort of 45mg/m², necessitating cohort expansion to 6 patients. One patient was noted to have asymptomatic grade 3 hyperamylasemia (90mg/m² cohort). There were no other DLTs and all 3 patients in the highest dose cohort (120mg/m²) tolerated PIPAC well. Nine patients who underwent a 2nd PIPAC procedure had a decrease in PCI score from 18.4 to 15.5; one patient at 120mg/m² had an improvement in PCI from 30 to 12. Conclusions: The RP2D of PIPAC with oxaliplatin is 120mg/m². Single agent PIPAC is well tolerated, and future studies with PIPAC must consider a bi-directional approach with the incorporation of systemic therapy, with either chemotherapy or immunotherapy to improve efficacy. Clinical trial information: NCT03172416. Research Sponsor: National Medical Research Council Singapore.
A phase II trial of cytoreduction, gastrectomy, and hyperthermic intraperitoneal perfusion with chemotherapy for patients with gastric cancer and stage IV peritoneal disease.

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Background: Current national guidelines do not include hyperthermic intraperitoneal chemotherapy (HIPEC) as treatment for gastric cancer, and there are no completed clinical trials of cytoreduction, gastrectomy, and HIPEC from the US. However, recent international studies report long-term survival rates of approximately 20% with cytoreduction/gastrectomy/HIPEC. Methods: Patients with gastric adenocarcinoma and positive peritoneal cytology or carcinomatosis who had completed systemic chemotherapy and laparoscopic HIPEC underwent cytoreduction, gastrectomy, and HIPEC with 30 mg mitomycin C and 200 mg cisplatin. The primary end point was overall survival (OS), with secondary end points of safety and postoperative complications. Results: We enrolled 20 patients from 9/2016 to 3/2019, with a median age of 58 years (range, 20-75 years). Six patients had positive cytology only at diagnosis of stage IV disease, whereas 14 had carcinomatosis. All patients were treated with systemic chemotherapy with a median of 8 cycles (range, 5-11 cycles) and at least one laparoscopic HIPEC. The median peritoneal carcinomatosis index at cytoreduction/gastrectomy/HIPEC was 2 (range, 0-13). After surgery, the 90-day morbidity and mortality rates were 70% and 0%, respectively. Median length of hospital stay was 13 days (range, 7-23 days). Median follow-up was 1.8 years. Median OS from the date of diagnosis of metastatic disease was 2.1 years. Median OS from the date of cytoreduction, gastrectomy, and HIPEC was 1.4 years. One, 2, and 3-year OS rates from the diagnosis of metastatic disease are 90%, 54%, and 29%. Conclusions: Survival rates for patients with gastric adenocarcinoma and peritoneal disease treated with cytoreduction, gastrectomy, and HIPEC are encouraging; our early results are similar to those of recent prospective registry studies. Cooperative group trials should be supported and will be required to confirm survival and safety outcomes. Clinical trial information: NCT02891447. Research Sponsor: No Stomach for Cancer Foundation, Holly Clegg Gastric Cancer Fund.
Enhanced efficacy of anti-VEGFR2/taxane therapy after progression on immune checkpoint inhibition (ICI) in patients (pts) with metastatic gastroesophageal adenocarcinoma (mGEA).

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Background: Most pts with mGEA do not respond to ICI or ramucirumab/paclitaxel (RAM/TAX). Emerging data suggest that ICI may potentiate subsequent therapy (Tx). In KN059 we unexpectedly observed durable responses in 2 pts on RAM/TAX after ICI (PMID 29674442). We examined if ICI impacts efficacy of subsequent RAM/TAX in a larger cohort and explored alterations in the tumor microenvironment. Methods: All pts with mGEA at Mayo Clinic (MN, AZ, FL) who received RAM/TAX (2014-19) were included. We compared best objective response rate (ORR: complete [CR] or partial response [PR]) per RECIST1.1 and overall survival (OS) in pts who received RAM/TAX with (Group A) vs without (Group B) immediately preceding PD-1 blockade. Chi square and multivariate logistic and Cox regression were used. We adjusted for total lines of Tx received and the line of Tx in which RAM/TAX was given, to control for potential differences in the biology of heavily treated pts or those receiving RAM/TAX as 2nd vs 3rd line Tx. We also adjusted for age and ECOG PS. Results: In total 87 pts met inclusion criteria. In the 19 pts (Group A) who received RAM/TAX (usually as 3rd line Tx) after progression on ICI, there was a 77% relative risk reduction of death after initiation of RAM/TAX compared to the 68 pts (Group B) who received RAM/TAX (usually as 2nd line) without preceding ICI (median OS 15.0 vs 7.6 mo; HR 0.23; P = .001). The ORR was also significantly higher (58% vs 18%; P < .001) including the CR rate (16% vs 1%; P = .006). Two CRs in Group A are ongoing (10 - 34 mo). Of note, 95% of Group A pts did not respond to ICI, and all had irRECIST progression on ICI. Immunofluorescent analysis from a responder showed 65-fold reduction (post vs pre-Tx) in intratumoral density of immunosuppressive FOXP3+ Tregs, with preserved density of antitumor CD8+ T cells. Conclusions: Higher than expected efficacy was observed on RAM/TAX when immediately preceded by ICI, suggesting ICI may enhance efficacy of subsequent anti-VEGFR/taxane therapy. This serial immunotherapy combination may be a novel option for pts with primary resistance to ICI and will be tested prospectively in a new randomized phase 2 trial (NCT04069273). Research Sponsor: None.
The real-world practice of surgery in patients with metastatic gastric cancer (mGC).

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Background: According to recent studies the results of treatment patients with initially mGC are still not sufficient: median overall survival varies between 6.1 and 12.4 months. The triplet-chemotherapy regimens demonstrate high efficacy and allow to downstage the disease and perform surgical treatment. Conversion treatment in stage IV GC is a modern trend and still an area of ongoing research. Methods: We analyzed the efficacy of first line chemotherapy (6-9 courses) for patients with mGC (n = 55) including the following regimens: 1) mFOLFIRINOX; 2) douplet: oxaliplatin/irinotecan + fluoropyrimidine; 3) triplet variations: docetaxel, platinum and fluoropyrimidine. 27/55 patients had > 2 metastatic sites, 2/55 patient - 5 metastatic sites. The most common localizations of metastases were peritoneum (n = 34) and retroperitoneal lymph nodes (n = 11). Unlike in REGATTA trial all patients underwent surgical treatment with curative intent followed by complete response of distant metastases after chemotherapy. For patients with ovarian metastases ovariectomy was also perfomed. Results: Median progression-free survival and median overall survival were 18.5 and 33.27 months, respectively and the 3-year survival rate was 43.5%. Multivariate analysis showed that clinically determined ascites (p = 0.023), linitis plastica (p = 0.022), tumor grade 3 (p = 0.014), present of lymphovascular invasion (p = 0.037), absence of grade III-IV pathomorphosis (p = 0.037) and treatment free interval before surgery < 3.4 month (p = 0.046) were poor independent prognostic factors. Conclusions: Surgery after effective combination chemotherapy may have significant clinical efficacy for selected patients with initially unresectable gastric cancer. According to our data the optimal time for surgery is a 3.4 and more months treatment-free interval in the absence of disease progression. Research Sponsor: None.
Refusal of surgery results in inferior survival in esophageal cancer.

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Background: Trimodality therapy with chemoradiation followed by surgery is the standard of care for non-metastatic esophageal cancer. Some patients refuse surgery and this information is captured in the National Cancer Database (NCDB). We sought to understand factors associated with refusal of surgery in these patients and to compare their survival rates with those who undergo surgery. Methods: Data from the NCDB for patients with pathologically proven non-metastatic esophageal cancer from 2006 to 2013 were pooled and screened. Patients with T1N0M0 disease were excluded. Pearson’s chi-squared test and multivariate logistic regression analyses were used to assess the distribution of demographic, clinical, and treatment factors. After propensity-score matching with inverse probability of treatment weighting, overall survival (OS) was compared between patients who refused surgery and those who had surgery using Kaplan Meier analyses and doubly-robust estimation with multivariate Cox proportional hazards modeling. Results: We found 890 of 18,942 patients (4.6%) refused surgery. Older patients, females, those with squamous histology, patients insured by Medicare and those who received radiation therapy (RT) were more likely to refuse. Patients who had N1 disease, high incomes, those who received chemotherapy and those who lived farther from care were more likely to have surgery. The initial 6 month OS was not significantly different between patients who refused surgery and those who had surgery (93.5% vs 95.1% P = 0.064). However, five-year OS was significantly lower in patients who refused (16.4% vs. 38.4% P< .01). This survival decrement was observed uniquely in patients with both adenocarcinoma and squamous cell carcinoma histology. Among those who refused surgery, the OS decrement was mitigated by increasing RT doses. In those who received over 54 Gy of RT, there was no statistical difference in OS between the groups (HR = 0.84, 95% CI 0.65-1.09). Conclusions: We identified a number of patient characteristics that are related to the refusal of surgery in esophageal cancer. Refusal of surgery was related to a decrease in OS in propensity weighted cohorts. This survival decrement may be mitigated by RT in a dose dependent fashion. Research Sponsor: None.
A phase II study of nab-paclitaxel plus ramucirumab for the second-line treatment of patients with metastatic gastroesophageal cancer.

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Background: Nab-paclitaxel (NP) is a protein-stabilized formulation of paclitaxel, US FDA approved for treatment of metastatic breast cancer, advanced/metastatic non-small cell lung cancer and metastatic adenocarcinoma of the pancreas. Ramucirumab (R) is an antibody targeting vascular epithelial growth factor receptor 2 (VEGFR-2) approved for treatment of gastric or gastroesophageal (GE) adenocarcinoma in combination with paclitaxel as 2nd line treatment. This phase II study evaluated the efficacy of NP and R for pts with metastatic GE cancer. Methods: Pts with metastatic GE adenocarcinoma were treated with 125 mg/m² NP on days 1, 8, and 15, and 8 mg/kg R on days 1 and 15 of each 28-day cycle. Pts continued study treatment (tx) until intolerable toxicity, disease progression (PD), or withdrawal of consent. Restaging occurred every 2 cycles. The primary objective was progression-free survival (PFS); secondary objectives were response rate (RR), time to progression (TTP), overall survival (OS) and toxicity. Results: 65 pts were enrolled between 05/15 and 12/18: median age 63 yrs (35-86), 75% male, 71% ECOG 1. Primary tumor sites were stomach (37%), GE junction (35%), and esophagus (28%). 83% were stage IV at initial diagnosis. 29% were HER2+ at study entry. 57% had 1st line chemo, 40% chemo + targeted agent and 3% chemo + immunotherapy. Median tx duration was 13 weeks (.1-55) for NP and 12 weeks (.1-54) for R; at data cutoff 2 pts remained on tx. 60% discontinued due to PD; 17% due to AE. 43% and 23% had AE-related dose reductions of NP and R, respectively; 8% and 6% were on day 15. 58% had dose interruptions of R due to AE; 42% on day 15. Median PFS was 3.8 months (CI 95% 3.4, 4.8); median TTP 4.5 months (CI 95% 3.5, 6.3); and median OS 8.8 months (CI 95% 6.1, 11.3). RR was 15% (CI 95% 6.6, 24.2); disease control rate was 68% (CI 95% 56.3, 79.1). Most common tx related AEs were neutropenia (55%), fatigue (40%), peripheral neuropathy (37%), anorexia and mucositis (26% each). Conclusions: There were no unexpected toxicity findings with NP and R in pts with GE cancers. Compared to historical controls, outcomes in this study were similar to those seen in the Western population of pts who received paclitaxel plus R. Clinical trial information: NCT02317991. Research Sponsor: Celgene.
A phase II study of neoadjuvant chemotherapy with DCS for resectable advanced esophageal cancer.

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**Background:** The current standard treatment for clinical stage II/III esophageal cancer is neoadjuvant chemotherapy (NAC) with CDDP/5-FU (CF) regimen followed by surgery. However, to improve the survival of patients with advanced ESCC, more effective regimens are urgently needed. Triplet regimens containing docetaxel have been one of the next candidates for advanced ESCC. **Methods:** The DCS regimen (Docetaxel 40mg/m2/day Day 1 div, CDDP 60mg/m2/day Day 1 div, S-1 80mg/m2/day Day 1~14 civ) was repeated every 4 weeks until toxicity became unacceptable, the patient refused treatment, or disease progression was observed to a maximum of 3 cycles. In this phase II trial of DCS, the primary endpoint was pathological response rate. **Results:** 40 patients were enrolled in this study and finally 39 patients underwent surgery and one patient performed chemoradiotherapy because of patient refusal. cT3 was 85%, cStage III and IV were 90%. Far advanced cases were in this study. Surgical complication was not increased compared to the historical data. R0 resection rate was achieved in 85%. The clinical response rate was 76%. Pathological response rate was 33%, which was the primary endpoint. 2-year recurrence-free survival rate was 56% and 2-year overall survival rate was 71%. The rate of Grade 3 or 4 Neutropenia was 69%, and FN was 18%. NAC-DCS was a high toxic regimen, but manageable regimen. The median time of onset with Grade 3/4 neutropenia was day 11 from start of each cycle. **Conclusions:** NAC with DCS regimen was feasible and good response for advanced ESCC and became a promising candidate. Further, the survival benefit of triplet regimen including S-1 should be verified by the randomized controlled trial. Clinical trial information: UMIN000017153. Research Sponsor: None.
Apatinib combined with SOX neoadjuvant therapy for locally advanced gastric cancer: A multicenter, single-armed, prospective study.

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Background: Molecular targeted therapy has made great progress in the treatment of gastric cancer. In some previous studies, apatinib, an oral small molecular of VEGFR-2 TKI, had been confirmed can improve OS and PFS with an acceptable safety profile in patients with advanced gastric cancer refractory to two or more lines of prior chemotherapy. However, there is limited evidence about the safety and feasibility of apatinib combined with SOX regimen as neoadjuvant therapy for locally advanced gastric cancer (AGC).

Methods: This is a multicenter, single-armed, prospective study. Patients with AGC (cT2-4N+M0) without prior anti-cancer strategies were included. Patients were received 2 to 5 cycles (21 days a cycle) of neoadjuvant therapy using S-1 (po, 40-60 mg bid, day1-day14), oxaliplatin (iv, 130 mg/m², day1), and apatinib (po, 500 mg qd). Apatinib was prohibited in the last cycle. The operation should be performed 2 to 4 weeks later of the neoadjuvant therapy. The primary endpoint was R0 resection rate. The secondary endpoint included safety, ORR, and DCR.

Results: A total of 56 patients from 10 centers in China were recruited. There were 43 males and 13 females. The median age was 63.04 years (range 41-75 years). There were 43 patients with tumor response evaluation, 29 patients (67.4%) had partial response (PR), 12 patients (27.9%) had stable disease (SD), and 2 patient (4.6%) had progressive disease (PD). The ORR and DCR were 67.4% (29/43) and 95.3% (41/43), respectively. 36 patients received gastric surgery, the R0 resection rate was 97.2%, 3 patients had postoperative complication: one had intestinal obstruction and 2 had pneumonia (all Clavien-Dindo classification less than grade II). 46 patients were included for safety analysis. The incidence of adverse events (AEs) and grade 3/4 AEs were 84.8% (39/46) and 17.4% (8/46), respectively. The most common AEs were neutropenia (40%), low platelet count (40%), leucopenia (32.6%), vomit (13%).

Conclusions: This prospective study shows that neoadjuvant therapy using apatinib plus SOX brings clinical benefit to AGC with a high disease control rate and tolerable adverse reactions. Clinical trial information: NCT 03192735. Research Sponsor: Jiangsu Hengrui Pharmaceutical.
Endoscopic versus surgical resection for mucosal esophageal squamous cell carcinoma: Treatment outcomes and factors affecting survival.

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Background: Mucosal esophageal squamous cell carcinoma (T1a EC) is treated with endoscopic (ER) or surgical resection (SR). The data regarding prognosis of T1a EC and the associated factors are still lacking. This study aimed to compare the treatment outcomes of T1a EC in ER and SR groups, and to investigate the factors affecting long-term survival. Methods: We retrieved data for 263 patients with T1a EC who underwent ER (n = 200) or SR (n = 63). Relevant clinical and tumor-specific parameters were reviewed. Underlying comorbidity was scored using Charlson co-morbidity index (CCI). Significant factors affecting survival were determined by Cox regression analysis. Results: The mean age of the patients was 64.5±8.0 years. During a mean follow-up of 54.4±20.4 months, the 5-year overall survival (OS) of all T1a EC patients was 85.7% (86.8% in ER and 82.4% in SR group; p = 0.631). In multivariate analysis, CCI was a significant factor affecting survival (p < 0.001). The 5-year OS was 60.2% in patients with CCI > 2 and 88.2% in patients with CCI ≤2 (p < 0.001). The 5-year cumulative incidence of primary EC recurrence was 1.9% and metachronous EC recurrence was 15.1% in ER group (0% in SR group). Incidence of subsequent second primary cancers was 9% in ER and 9.5% in SR. The 5-year cumulative incidences of all cases of cancer recurrence in ER and SR groups were 27.5% and 10.8%, respectively (p = 0.037). The procedure-related adverse events occurred in 10.0% in ER and 41.3% in SR (p < 0.001). Among the 24 (12.0%) and 10 (15.9%) deaths in ER and SR group, respectively, primary EC-specific death was not reported. The major causes of death were second primary cancers in ER group (75%), and post-operative complications or organ failure in SR group (70%). Conclusions: Long-term survival was excellent in patients undergoing ER or SR for T1a EC. The prognosis of T1a EC was significantly associated with underlying comorbidity. Attention should be paid to metachronous cancer recurrence in ER group and operation-related adverse events in SR group. Research Sponsor: None.
Short- and long-term outcomes following laparoscopic gastrectomy for advanced gastric cancer compared with open gastrectomy.

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Background: To investigate the oncological feasibility and technical safety of laparoscopic gastrectomy with D2 lymphadenectomy for advanced gastric cancer. Methods: 186 advanced gastric cancer patients treated by gastrectomy with D2 lymphadenectomy were eligible for inclusion including those with invasion into the muscularis propria, subserosa, and serosa without involvement of other organs, and stages N0–2 and M0. We retrospectively compared the short- and-long term outcomes between laparoscopic gastrectomy and open gastrectomy. Results: We analyzed short-term outcomes by comparing distal- with total gastrectomy results. We found no significant difference for distal gastrectomy for postoperative morbidity (laparoscopic vs. open: n = 4 (4.6%) vs. n = 1 (3.6%); p = 1.00). We also found no significant difference in postoperative morbidity for total gastrectomy (laparoscopic vs. open: n = 2 (4.0%) vs. n = 1 (4.0%); p = 1.00). No deaths occurred in any group. The entire cohort analysis revealed no statistically significant differences in overall- or recurrence-free survival between the laparoscopic and open groups. For overall survival, there were no significant differences between open and laparoscopic groups for clinical stage II or III (p = 0.29 and 0.27, respectively), and for pathological stage II or III (p = 0.88 and 0.86, respectively). For recurrence-free survival, there were no significant differences between open and laparoscopic groups for clinical stage II or III (p = 0.63 and 0.60, respectively), and for pathological stage II or III (p = 0.98 and 0.72, respectively). Conclusions: Laparoscopic gastrectomy for advanced gastric cancer compared favorably with open gastrectomy regarding short- and long-term outcomes. Clinical trial information: 160907. Research Sponsor: None.
Association between postoperative pneumonia and prognosis of patients with esophageal cancer.

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Background: We examined the association between postoperative pneumonia and prognosis of patients with esophageal cancer after curative surgery. Methods: We enrolled 122 patients who underwent curative resection for esophageal cancer between 2008 and 2018. The patients who had postoperative pneumonia were categorized into the pneumonia group, while those without postoperative pneumonia were classified into the non-pneumonia group. We identified the risk factors for the recurrence-free survival (RFS) and the overall survival (OS). Postoperative pneumonia was defined using the revised Uniform Pneumonia Score. Results: Thirty-four of the 122 patients (27.9%) had postoperative pneumonia. The 5-year OS rate after surgery in the pneumonia group was significantly lower than that in the non-pneumonia group (28.2% versus 55.1%, p = 0.006). Although not significant, the 5-year RFS rate after surgery in the pneumonia group tended to be lower than that in the non-pneumonia group (18.9% versus 49.2%, p = 0.061). A multivariate analysis identified postoperative pneumonia as a significant independent risk factor for the OS (hazard ratio = 2.15; 95% confidence interval, 1.25 to 3.68; P = 0.006). Conclusions: Our analysis showed postoperative pneumonia was an independent risk factor for worse overall survival in patients who underwent curative resection for esophageal cancer. This finding suggests that we should plan the surgical procedure, perioperative care and surgical strategy to prevent postoperative pneumonia. Research Sponsor: None.
Loss of body weight during neoadjuvant chemotherapy with docetaxel, cisplatin, and fluorouracil as predictive of poor survival of patients with esophageal squamous cell carcinoma.

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Background: Though neoadjuvant chemotherapy with docetaxel/cisplatin/5-fluorouracil (DCF) showed a promising efficacy in patients (pts) with resectable esophageal squamous cell carcinoma (ESCC), grade 3 anorexia during the course and body weight loss (BWL) were frequently experienced. BWL is considered as a factor for poor survival in operable cancer pts, however, there is rarely reported of the relationship of BWL during neoadjuvant therapy and survival. Methods: We retrospectively evaluated pts of ESCC with clinical stage II or III, excluding T4, who had received neoadjuvant DCF and esophagectomy (R0 resection) at our institution between April 2010 and December 2018. We define the cut-off level at more than 3% weight reduction (BWL3 group) between before and after of first cycle of DCF. Results: Among the 77 pts who were selected for this analysis, 13 patients showed BWL3% (BWL3 group), and other 64 pts did not (no-BWL group). The median age, proportions of performance status of 0, cT3 stage, cN2-3 stage and serum albumin lower than normal level in no-BWL and BWL3 group were 65 and 67y.o, 59 and 77%, 88 and 54%, 75 and 69%, 34 and 31%, respectively. There was no significant difference in histological therapeutic effect (grade 2-3) with 50% in no-BWL and 62% in BWL3 group (P = 0.549). The incidence of postoperative grade 2 or higher pneumoniawas same in both group (23% vs 17%, P = 0.695). The median overall survival (OS) was not reached in non-BWL group and 39.5 m in BWL3 group (P = 0.048), respectively. The median progression free survival (PFS) was not reached in non-BWL group and 39.5 m in BWL3 group (P = 0.382), respectively. In multivariate analysis, BWL is independent prognostic factor for OS (hazard ratio [HR] = 11.5, 95%CI: 2.45-53.8, P = 0.002).

Conclusions: Our exploratory study demonstrated that body weight loss during first course of neoadjuvant DCF therapy for ESCC patients may be a prognostic factor for survival. Research Sponsor: None.
A phase I/II multisite study of nivolumab and carboplatin/paclitaxel with radiation therapy (RT) in patients with locally advanced esophageal squamous cell carcinoma (ESCC).

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Background: Preoperative chemoRT is a standard-of-care as shown in the CROSS trial (N Engl J Med 2012;366:2074-2084), Surgery is sometimes deferred in pts with clinical CR (cCR) based on lack of overall survival benefit (J Clin Oncol 2005;23:2310-2317, J Clin Oncol 2007;25:1160-1168). Nivolumab has activity in advanced ESCC (Lancet Oncol 2017;18:631-639), and adding it to chemoRT may improve outcomes. Methods: This phase I/II study was designed to assess the safety and tolerability and efficacy of nivolumab added to chemoRT (6 weekly carboplatin AUC 2, paclitaxel 50mg/m2, RT 50.4 Gy in 1.8 Gy fractions 5/7 days) for pts with TanyN1-3 or T3-4N0M0 ESCC. The phase I primary endpoint is “unacceptable toxicity” at 28 days after the last dose of chemotherapy. The phase II primary endpoints are cCR (endoscopy + PET/CT) and pCR rates for pts undergoing surgery. Nivolumab is given q2W x3, then concurrent chemoRT with nivolumab q2W x3. If no cCR, pt proceeds to esophagectomy, then adjuvant nivolumab q2W x3; if cCR, pt has an option of no surgery but receives nivolumab q2W x3. Results: From 7/20/17 to 12/27/18, 6 pts were enrolled. No unacceptable or grade 5 toxicities were observed. The most common grade 1/2 AEs in 1 pt were anorexia, myelosuppression, elevated AST and nausea. Grade 3/4 AEs in 1 pt were lymphopenia and leukocytopenia. 2 pts required hospitalizations (dyspnea 1, colitis 1). All pts completed therapy; 1 pt had dose delay due to grade 2 esophagitis; 2 pts progressed, 4 achieved cCR. Of 4 pts with cCR, 2 pts chose surgery and both achieved pCR. None of the 4 pts recurred. Conclusions: ChemoRT with nivolumab is tolerable with manageable toxicities in locally advanced ESCC. Enrollment to the phase II portion ended because of slow accrual. Adverse Events. Grade 1 & 2 in 1 pt: 4/6: Anorexia & Anemia 3/6: Leukocytopenia Neutropenia Thrombocytopenia Nausea & Elevated AST 2/6: Hypomagnesemia Hypokalemia Grade 3 & 4 in 1 pt: 5/6: Lymphopenia, 2/6: Leukocytopenia Research Sponsor: Rosanna Caroleo.
Induction oxaliplatin capecitabine followed by switch to carboplatin-paclitaxel based RT versus continuing oxaliplatin capecitabine RT in operable esophageal adenocarcinoma: Survival analysis of the randomized phase II neoscope trial.

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Background: Initial results of the NEOSCOPE trial comparing pre-operative CarPac vs OxCap based chemoradiotherapy (CRT) in patients with adenocarcinoma of the oesophagus or oesophago-gastric junction showed comparable toxicity and improvement in pathological complete response (pCR) in favour of the CarPacRT. Here we report survival after a median follow-up of 40.7 months (95% CI: 45.1-53.6). Methods: NEOSCOPE was an open, randomised, 'pick a winner’ phase II trial. Patients with resectable oesophageal adenocarcinoma ≥ cT3 and/or ≥ cN1 were randomised to OxCapRT (oxaliplatin 85 mg/m² day 1, 15, 29; capecitabine 625 mg/m² bd on days of RT) or CarPacRT (carboplatin AUC2; paclitaxel 50 mg/m² day 1, 8, 15, 22, 29). RT dose was 45 Gy/25 fractions/5 weeks. Induction OxCap (2 cycles) was given prior to CRT. Surgery was performed 6–8 weeks after CRT. The primary endpoint was pCR, secondary endpoints were toxicity, PFS and OS.

Results: Between Oct 2013 and Feb 2015, 85 patients were recruited from 17 UK centres. Median OS was not reached in the CarPacRT group and was 41.72 months (95% CI 19.58-). In the OxCap group (HR 0.56[95% CI 0.29-1.07]; p=0.079), 3-year and 5-year OS rates were 74% (95% CI 58%-85%) and 54% (95% CI 34%-71%) (CarPacRT), and 52% (95% CI 35%-67%) and 39% (95% CI 21%-56%) (OxCapRT). Median PFS (not reached vs 35.3 months, HR=0.61 [95% CI 0.33-1.12]; p=0.111) and metastatic PFS (not reached vs 39.0 months, HR=0.61 [95% CI 0.32-1.14], p=0.118) both favoured the CarPacRT arm. Local recurrence rate was low (OxCapRT= 10% ; CarPacRT= 7%). The OS benefit for CarPacRT was consistent across subgroups but not statistically significant.

Conclusions: In this longer term analysis there was some evidence that induction OxCap followed by switch to CarPacRT was superior to continuing OxCapRT, with efficacy similar to that seen in other published studies such as 'CROSS' and 'FLOT'. Taken together with the previously published pCR results CarPacRT rather than OxCapRT warrants inclusion in future trials. Funding: Cancer Research UK (C44694/A14614). Clinical trial information: NCT01843829. Research Sponsor: NEOSCOPE.

An open-label phase II study of lenvatinib plus pembrolizumab in patients with advanced gastric cancer (EPOC1706).

Akihito Kawazoe, Shota Fukuoka, Yoshiaki Nakamura, Yasutoshi Kuboki, Yuichi Mikamoto, Hikari Shima, Noriko Fujishiro, Tsukiko Higuchi, Masashi Wakabayashi, Shogo Nomura, Akihiro Sato, Kohei Shitara; National Cancer Center Hospital East, Kashiwa, Japan; Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan; National Cancer Center Hospital East, Kashiwa, Japan; Clinical Research Support Office, National Cancer Center Hospital East, Kashiwa, Japan; Clinical Research Support Office, National Cancer Center Hospital East, Kashiwa, Japan; Chiba, Japan; Chiba, Japan; JCOG Data Center/Operation Office, National Cancer Center Hospital East, Tokyo, Japan; National Cancer Center Hospital East, Chiba, Japan

Background: Pembrolizumab, anti-PD-1 antibody, provides response rates of around 15% in patients (pts) with PD-L1-positive advanced gastric cancer (AGC). Lenvatinib, a multikinase inhibitor of VEGF receptors and other receptor tyrosine kinases, substantially decreased the tumor-associated macrophages and increased infiltration of CD8-positive T cells and enhanced antitumor activity of PD-1 inhibitors in vivo model. This phase 2 study has been conducted to evaluate efficacy and safety of the combination of lenvatinib plus pembrolizumab in pts with AGC. Methods: Eligible pts were with AGC having measurable lesions according to RECIST ver. 1.1. Pts could be enrolled regardless of PD-L1 status. Pts received 20 mg oral lenvatinib daily plus 200 mg intravenous pembrolizumab every 3 weeks. Primary endpoint was objective response rate (ORR). Planned sample size was 29 pts based on Simon's optimal two-stage design with one-sided $\alpha = 5\%$ and power = 80%. The threshold and expected ORRs were 10% and 30%. PD-L1 combined positive score (CPS) was assessed using the anti-PD-L1 22C3 antibody. Results: From October 2018 to March 2019, 29 pts (27 MSS and 2 MSI-H) were enrolled and assessed for anti-tumor response. Fourteen pts received the study treatment as first-line and 15 pts as second-line. ORR was 69% (95% CI 49 to 85). The disease control rate was 100%. ORR in MSS pts was 70%. ORR was numerically higher in pts with CPS $\geq$ 1 (n=19, ORR 84%) than that of pts with CPS < 1 (n = 10, ORR 40%). Median progression-free survival was 6.9 months (95% CI, 4.4-9.4 months) with 14 pts with ongoing treatment at the data cut off in August 2019. Grade 3 treatment related adverse events occurred in 13 pts (45%) including hypertension (34%), proteinuria (17%), and platelet count decreased (7%). Conclusions: Lenvatinib with pembrolizumab showed a promising antitumor activity with acceptable safety profiles for pts with AGC, which warrants further investigations in a larger cohort. Clinical trial information: NCT03609359. Research Sponsor: MSD.
Continuous fluropyrimidine (FP) with platinum (P) based chemotherapy (CT) versus maintenance FP after induction therapy in advanced gastric (G) and gastroesophageal (GE) cancer.

Daniel Walden, Mohamad Bassam Sonbol, Skye Buckner Petty, Mitesh J. Borad, Tanios S. Bekaii-Saab, Daniel H. Ahn; Mayo Clinic Arizona, Phoenix, AZ; Mayo Clinic, Phoenix, AZ

Background: Combination FP with P CT have become the standard of care for advanced G/GEJ cancer. Clinical trials in conjunction with practice, have adopted induction FP and P CT for 3-4 months (mos). In other GI malignancies, induction CT followed by maintenance CT (MTC) has been shown to improve patient (pt) outcomes compared to observation, with a decrease in treatment (trmt) related toxicities with induction therapy. However a maintenance approach in G/GEJ cancer has not been investigated in clinical trials. We investigated pt outcomes with metastatic G/GEJ cancer who received continuous induction (CTX) versus induction followed by MTC. Methods: A retrospective analysis of pts with metastatic G/GEJ adenocarcinoma treated with (FP+ P)-based CT between 2007 to 2017 from three centers of a single institution was performed. Metastatic G/GEJ cancer pts who achieved at least stable disease after initial induction trmt were included. Pts were categorized into the CTX group if they received greater than 16 weeks or 8 cycles of combined CT and assigned to the MTC group if they received maintenance FP monotherapy after 8 or less cycles of combined induction CT. Data was extracted from the medical record to determine progression free survival (PFS), overall survival (OS), and toxicities. Results: Sixty-four pts that met criteria and were evaluated, thirty-four received CTX and thirty received MTC. No significant difference in PFS (12.1 vs 8.0 mos p = .72, HR=1.10 95%CI .66-1.83) was observed between the CTX and MTC groups, additionally there was no significant difference in OS. A significant decrease in trmt related toxicities were observed, with a higher proportion of thrombocytopenia (84.8% vs 50.0% p = .004), and grade 3 neuropathy (39.4% vs 13.8% p =.024) in CTX pts (Table). Conclusions: MTC following induction FP/P CT is associated with an improved toxicity profile and appears to be effective compared to CTX in metastatic G/GEJ cancer. Prospective randomized studies confirming its potential benefits compared with continuous induction CT are warranted. Research Sponsor: None.

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Economic evaluation of trifluridine/tipiracil (TT) versus nivolumab (N) in patients with advanced/metastatic gastric cancer (GC) or gastro-esophageal junction cancer (GEJC) in Canada.

Kiran Virik, Robert B. Wilson; Department of Medical Oncology, Queen’s University, Kingston, ON, Canada; Department of Surgery, University of NSW, Sydney, NSW, Australia

**Background:** Systemic treatment options in pre-treated patients with advanced/metastatic GC and GEJC have historically been limited especially in the third line or more. Recent potential advances in the therapeutic landscape of this patient population include TT (TAGS study) and immune checkpoint inhibitors (ICI) such as N (ATTRACTION-2 study). There is an anticipated budgetary impact on healthcare systems within the context of these potentially funded options. An economic evaluation can be instrumental in choosing a regimen if survival and quality of life are felt to be comparable.

**Methods:** A cost minimization analysis was performed in Canadian dollars ($) comparing TT and N respectively in advanced de novo and relapsed GC/GEJC cases diagnosed in 2017 and subsequently treated in the third line in Canada. Direct costs including drug acquisition costs, supportive medications, transfusions, laboratory tests, physician visits, pharmacy and nursing time (health resource utilization-HRU) costs were calculated utilizing Ontario data. Direct costs for treatable adverse events G3/4 > 5% were incorporated. The analysis assumed complete drug delivery and the number of target patients was derived from constructed schema. **Results:** Compared to TT, the use of N was associated with a higher direct cost by a difference of $2.63 million (M) in the third line for GC and GEJC in Canada, principally reflecting a greater drug acquisition cost. The direct costs ranged (IQR) from 3.65M - 10.62M for TT to 3.3M - 15.69 M for N. N also had a greater HRU cost at 2.7 times that of TT and this was 64% of the direct costs for N excluding drug cost versus 42% of the direct non drug costs for TT. Supportive care (GCSF and transfusions) were 34% of the direct cost for TT excluding drug cost. A sensitivity analysis was performed. **Conclusions:** N generated a higher direct cost both for drug acquisition cost and other direct costs especially in HRU. Despite the increased cost of supportive care for adverse events related to TT, the direct non drug costs were less for this option. The use of biomarkers predictive of response may reduce the potential cost burden of the use of ICIs. Research Sponsor: None.
Hyperprogressive disease during nivolumab chemotherapy in metastatic gastric cancer: Multicenter retrospective study in Japan.

Takeshi Suzuki, Masahiko Aoki, Hiromichi Shirasu, Naoki Takahashi, Rie Nakatsu, Takayuki Ando, Yosuke Kito, Yoshiyuki Yamamoto, Kentaro Kawakami, Toshihiko Matsumoto, Keitaro Shimozaki, Michitaka Nagase, Yoshiyuki Yamaguchi, Yuji Negoro, Takao Tamura, Yusuke Amanuma, Taito Esaki, Yuji Miura, Kenji Nagashima, Narikazu Boku; Department of Gastroenterology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; National Cancer Center Hospital, Tokyo, Japan; Division of Clinical Oncology, Shizuoka Cancer Center, Shizuoka, Japan; Saitama Cancer Center, Saitama, Japan; Department of Surgery, Osaka General Medical Center, Osaka, Japan; Third Department of Internal Medicine, University of Toyama, Toyama, Japan; Department of Medical Oncology, Ishikawa Prefectural Central Hospital, Ishikawa, Japan; University of Tsukuba, Tsukuba, Japan; Department of Medical Oncology, Keiyukai Sapporo Hospital, Sapporo, Japan; Himeji Red Cross Hospital, Himeji, Japan; Keio University, Tokyo, Japan; Department of Clinical Oncology, Jichi Medical University, Shimotsuke, Japan; Department of Cancer Chemotherapy Center, Osaka Medical College Hospital, Osaka, Japan; Department of Gastroenterology, Kochi Health Sciences Center, Kochi, Japan; Department of Medical Oncology, Kindai University Nara Hospital, Ikoma, Japan; Clinical Trial Promotion Department, Chiba Cancer Center, Chiba, Japan; National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan; Department of Medical Oncology, Toranomon Hospital, Tokyo, Japan; Research Center for Medical and Health Data Science, The Institute of Statistical Mathematics, Tokyo, Japan

Background: Nivolumab has demonstrated a survival benefit for advanced gastric cancer (AGC). However, hyperprogressive disease (HPD) has been reported in various cancers. Methods: The subjects of this retrospective study were AGC patients with measurable disease who received nivolumab, and their tumors were assessed at least 3 times (during prior therapy, before and after nivolumab) in 24 institutions. Tumor growth rates (TGR) during nivolumab were compared to those during prior therapy as reported (Champiat S, 2017). HPD was defined as an increase in TGR > 2-fold. Results: 218 patients were identified as the subjects. While 33 (15.1%) partial response (PR) were achieved, 130 patients (59.6%) showed progression disease (PD), 38 of whom were classified as HPD (17.4%) and 2 patients showed pseudo progression (1.0%). The median progression-free survival (PFS) was 1.9 months (95% CI: 1.5 - 2.4) and the median overall survival (OS) was 8.5 months (95% CI: 7.1 - 9.6) in all patients. While patients with PD showed shorter prognosis compared with non-PD patients (median PFS: 1.5 months vs 6.4 months, hazard ratio: 6.0 [95% CI: 4.3 - 8.4]; p < 0.0001; median OS: 4.7 months vs not reached, hazard ratio: 4.1 [95% CI: 2.8 - 6.3]; p < 0.0001), there were no differences either in PFS or OS between patients with HPD and those with PD other than HPD (median PFS: 1.5 months vs 1.6 months, hazard ratio: 1.3 [95% CI: 0.9 - 2.0]; p = 0.119; median OS: 5.0 months vs 4.6 months, hazard ratio: 1.0 [95% CI: 0.6 - 1.5]; p = 0.8695). Histological type, liver metastases, carbohydrate antigen 19-9 (CA19-9) level were associated with HPD. Conclusions: HPD was observed 17.4% in AGC patients treated with nivolumab. There were no differences either in PFS or OS between patients with HPD and those with PD other than HPD. Clinicopathological characteristics might be a predict factor for HPD. Research Sponsor: None.
Laparoscopic versus open total gastrectomy for clinical stage I gastric cancer: Morbidity and mortality results from a prospective randomized multicenter controlled trial (CLASS02).

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Background: The safety of laparoscopic total gastrectomy (LTG) for the treatment of gastric cancer remains lack of clinical evidence. The aim of this study was to compare the safety of LTG for clinical stage I gastric cancer with the conventional open total gastrectomy (OTG).

Methods: From January 2017 to September 2018, a total of 227 patients with clinical stage T1N0-1M0/T2N0M0 gastric cancer were enrolled in this clinical trial and randomly assigned to Laparoscopic Gastrectomy group (LG, n=113) or Open Gastrectomy group (OG, n=114). The morbidity and mortality within 30 days following surgery, the recovery course, and the postoperative hospital stay between LG group (n=105) and OG group (n=109) were compared. Clavien-Dindo classification system was used to stratify surgical complications.

Results: The overall morbidity rate was not significantly different in each group (LG group: 19.05%; OG group: 20.18%; Rate difference [RD]: -1.14%, 95%CI, -11.75%-9.58%). Intraoperative complications occurred in 3 (2.86%) patients in LG group and 4 (3.67%) patients in OG group (RD: -0.81%, 95%CI, -6.52%-4.85%). In addition, there was no significant difference in the overall postoperative complication rate of 18.10% in LG group and 17.43% in OG group (RD: 0.66%, 95%CI, -9.61%-11.01%). Each subtype of postoperative complication were not significantly different between groups. One patient in LG group died of intra-abdominal bleeding from splenic artery, and there was no significant difference in mortality between LG group and OG group (RD: 0.95%, 95%CI, -2.54%-5.20%). The distribution of severity was similar between the two groups.

Comparing five-weekly S-1 plus cisplatin with tri-weekly capecitabine plus cisplatin in patients with HER2-negative recurrent gastric cancer after S-1 adjuvant therapy or chemotherapy naive advanced gastric cancer: A pooled analysis of HERBIS-2 (OGSG 1103) and HERBIS-4A (OGSG 1105) trials.

Jin Matsuyama, Hisato Kawakami, Kazumasa Fujitani, Yusuke Akamaru, Shigeyuki Tamura, Shunji Endo, Yutaka Kimura, Youichi Makari, Takao Tamura, Naotoshi Sugimoto, Daisuke Sakai, Toshimasa Tsujinaka, Masahiro Goto, Yukinori Kurokawa, Toshio Shimokawa, Taroh Satoh; Department of Gastroenterological Surgery, Higashiosaka City Medical Center, Higashiosaka, Japan; Department of Medical Oncology, Kindai University Faculty of Medicine, Osaka-shi, Japan; Osaka Prefectural General Medical Center, Osaka-shi, Japan; Department of Surgery, Ikeda Municipal Hospital, Ikeda, Japan; Yao Municipal Hospital, Yao City, Osaka, Japan; Sakai City Medical Center, Sakai, Japan; Department of Medical Oncology, Kindai University Nara Hospital, Ikoma, Japan; Osaka International Cancer Institute, Osaka, Japan; Osaka University Hospital, Osaka, Japan; Department of Cancer Chemotherapy Center, Osaka Medical College Hospital, Osaka, Japan; Department of Gastroenterological Surgery, Osaka University, Graduate School of Medicine, Suita City, Osaka, Japan; Osaka Gastrointestinal Cancer Chemotherapy Study Group (OGSG), Osaka, Japan; Osaka University, Osaka, Japan

Background: HERBIS-2 trial was a phase II trial where S-1 plus cisplatin (SP) and capecitabine plus cisplatin (XP) were compared in recurrent HER2 negative gastric cancer (GC) patients with recurrence free interval (RFI) by S-1 containing adjuvant of ≥ 6 months. We performed pooled analyses of HERBIS-2 and HERBIS-4A trial where SP and XP were compared in chemotherapy-naive HER2 negative gastric cancer (GC) patients as these trials being identical. Methods: Both HERBIS-2 and 4A trials, patients were randomly assigned to receive either SP (S-1 at 40–60 mg twice daily for 21 days plus cisplatin at 60 mg/ m² on day 8, every 5 weeks) or XP (capecitabine 1,000 mg/m² twice daily for 14 days plus cisplatin 80 mg/m² on day 1, every 3 weeks). Results: In HERBIS-2 which was closed early due to poor accrual, SP (N = 10) tended to confer a better overall survival (OS) compared with XP (N = 9) [18.7 (95%CI, 2.8 – NR) months vs. 13.4 (95% CI, 5.2 – 31.3) months; hazard ratio (HR), 0.443 (95% CI, 0.156 – 1.258); P = .117]. In pooled analyses with HERBIS-2 and 4A, SP (N = 50) vs. XP (N = 51) showed longer progression free survival (6.4 vs. 5.1 months; HR, 0.666; P = .62), OS (14.8 vs. 10.6 months; HR, 0.695; P = .999), time to treatment failure (4.6 vs. 3.6 months; HR, 0.668; P = .045), and higher disease control rate (86.4% vs. 68.1%, P = .149). Subgroup analysis revealed that OS benefit in SP arm compared to XP arm was significantly larger if the patient having PS of 0 [HR, 0.554 (95% CI, 0.309 to 0.959); interaction P = .035], or the tumor arising from upper area of stomach [HR, 0.266 (95% CI, 0.070 to 0.731); interaction P = .013] or harboring differentiated type cancer [HR, 0.433 (95% CI, 0.228 to 0.822); interaction P = .011], respectively. Conclusions: Our data suggest the use of SP in the 1st line setting in HER2 negative advanced or recurrent GC with RFI by S-1 adjuvant of ≥ 6 months. Pooled analyses further suggest SP as the standard 1st line chemotherapy for HER2 negative AGC irrespective of S-1 adjuvant in Japan. Clinical trial information: UMIN000006755/UMIN000006105. Research Sponsor: None.
Palliative systemic chemotherapy with or without pressurized intraperitoneal aerosol chemotherapy with cisplatin and doxorubicin (PIPAC C/D) for gastric cancer with peritoneal metastasis: A propensity score analysis.

Vladimir Khomiakov, Christoph Meisner, Andrey Ryabov, Larisa Bolotina, Anna Utkina, Ilia Kolobaev, Dmitry Sobolev, Anna Chayka; P.A. Hertsen Moscow Research Oncological Institute–National Medical Research Centre of Radiology, Moscow, Russian Federation; Institute for Clinical Epidemiology and Applied Biometrics, University Hospital Tübingen, Tübingen, Germany

Background: Gastric cancer (GC) with peritoneal metastasis (PM) has a dismal prognosis. Palliative systemic chemotherapy (SC), usually doublet combinations of platinum and fluoropyrimidines, is the standard of care. Pressurized IntraPeritoneal Aerosol Chemotherapy with Cisplatin and Doxorubicin (PIPAC C/D) yields promising results. Here we aimed to compare overall survival (OS) between SC + PIPAC C/D vs. SC alone in patients with PM from GC.

Methods: Prospective cohort of 95 consecutive patients with PM from GC treated in palliative intent at our institution from 2010 to 2018. Of these patients, 69 received SC + PIPAC C/D (“PIPAC”), 26 SC alone (“control”). Choice of treatment was not dictated by medical criteria, but by (non-) availability of the single-use medical devices needed for PIPAC in Russia. All patients received doublet or triplet chemotherapy with platinum together with fluoropyrimidines or capecitabin. A Cox proportional hazard model based on propensity score (PS) was used to assess the effect of PIPAC on OS and account for confounding factors.

Results: The HR adjusted for PS for PIPAC vs. control was 0.396 (CI 5-95% = 0.224-0.700, p-value 0.001). In the simple (unadjusted) Kaplan-Meier, median survival in the control group was 7.0 months (CI: 4.51 - 9.49) and in the PIPAC group 14.0 months (CI: 11.46-16.54). In the control group, all 26 patients died after 1-25 months. In the PIPAC group, 36 of 69 patients died after 4 to 20 months. The longest observed survival time in the PIPAC group was 27 months. Significance for the log-rank test after Mantel-Cox (not adjusted) was p < 0.0001.

Conclusions: Compared with SC alone, intensified chemotherapy combining PIPAC C/D and SC doubled OS. These promising results need to be confirmed in a randomized trial. Research Sponsor: None.
Surrogate indicators of survival in patients who received neoadjuvant chemotherapy for type 4 and large type 3 gastric cancer in JCOG0501.

Masanori Terashima, Junki Mizusawa, Hiroshi Katayama, Yoshiaki Iwasaki, Yoshiyuki Kawashima, Takahiro Kinoshita, Souya Nunobe, Hideki Nakatsuka, Takeshi Omori, Mikihiro Nakamori, Yuki Akiyama, Hironori Tsujimoto, Seiji Ito, Yukinori Kurokawa, Takaki Yoshikawa, Narikazu Boku, Takeshi Sano, Mitsuhiro Sasaki, Tsuneaki Fujiiya, Stomach Cancer Study Group, Japan Clinical Oncology Group; Division of Gastric Surgery, Shizuoka Cancer Center, Shizuoka, Japan; Japan Clinical Oncology Group Data Center/Operations Office, National Cancer Center Hospital, Tokyo, Japan; Department of Surgery, IMS Tokyo-Katsushika General Hospital, Tokyo, Japan; Saitama Cancer Center, Saitama, Japan; Gastric Surgery Division, National Cancer Center Hospital East, Kashiwa, Japan; Department of Gastroenterological Surgery, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; Department of Surgery, Tsukuba Rosai Hospital, Tsurumai, Japan; Osaka International Cancer Institute, Osaka, Japan; Second Department of Surgery, Wakanayama Medical University, School of Medicine, Wakanayama, Japan; Department of Surgery, Iwate Medical University, Morioka, Japan; National Defense Medical College, Tokorozawa, Japan; Aichi Cancer Center Hospital, Aichi, Japan; Department of Gastroenterological Surgery, Osaka University, Graduate School of Medicine, Suita City, Osaka, Japan; Kanagawa Cancer Center, Kanagawa, Japan; National Cancer Center Hospital, Tokyo, Japan; Japanese Foundation for Cancer Research Cancer Institute Hospital, Tokyo, Japan; Division of Upper Gastrointestinal Surgery, Department of Surgery, Hyogo College of Medicine, Nishinomiya, Japan; Department of Gastrointestinal Surgery, Miyagi Cancer Center, Sendai, Japan

Background: Pathological response rate (pRR) is a common endpoint for assessing the efficacy of neo-adjuvant chemotherapy (NAC) in patients with advanced gastric cancer (GC). We performed supplementary analysis to investigate if pRR can be a surrogate endpoint using data from JCOG0501.

Methods: Patients with type 4 and large type 3 resectable GC were randomized either surgery plus adjuvant S-1 (arm A) or NAC (S-1 plus cisplatin) plus surgery plus S-1 (arm B) in JCOG0501. Histological type (sig vs non-sig) was evaluated using preoperative biopsy specimen. Cox proportional hazards model was utilized to assess the effects of covariates for overall survival (OS). Pathological response was defined as Grade1b-3 according to the Japanese Gastric Cancer Association grading. Results: Among 286 (147 in arm A and 139 in arm B) patients who underwent surgery, 132 patients with complete pathological data in arm B were evaluated. Macroscopic tumor response (PR) was observed in 47 patients (36%) and pathological response (Grade 0/1a/1b/2/3) was 15/40/30/44/3, respectively. As shown in the table, pathological response was significantly better OS after adjusting other factors (HR, 0.51 [95% CI 0.30-0.87], p = 0.014). Conclusions: pRR may be used as a surrogate endpoint for future clinical trials in type 4 and large type 3 GC. Clinical trial information: C000000279. Research Sponsor: National Cancer Center Research and Development Funds. Grant-in-Aid for Clinical Cancer Research from the Ministry of Health, Labour and Welfare of Japan.

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S-1+oxaliplatin with pembrolizumab for advanced gastric cancer: The cohort 1 in a phase IIb KEYNOTE-659 study.

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Background: The KEYNOTE-059 study showed the preliminary antitumor activity and tolerability of chemotherapy with pembrolizumab (P) for advanced gastric cancer (AGC). In Japan, S-1 + platinum regimen is a standard chemotherapy for AGC. The KEYNOTE-659 study (NCT03382600) investigated the efficacy and safety of S-1 + oxaliplatin (SOX; cohort 1) or cisplatin (SP; cohort 2) with P as the first line treatment in patients (pts) with human epidermal growth factor receptor 2 (HER2)-negative, programmed death-ligand 1 (PD-L1)-positive AGC. Here, we report the results of cohort 1.

Methods: The key inclusion criteria were as follows: age 18 to 75 years; an ECOG performance status of 0 or 1; and chemotherapy-naïve, HER2-negative and PD-L1-positive AGC. PD-L1 positivity was defined as a combined positive score of 1 using the IHC 22C3 PharmDx assay. An S-1 dose of 40-60 mg per dose was orally administered, twice daily, for the first 2 weeks of a 3-week cycle. P (200 mg) and oxaliplatin (OX; 130 mg/m²) were administered on day 1 of each cycle. The primary endpoint was overall response rate (ORR) that was assessed by a blinded independent central review (BICR). The secondary endpoints were progression-free survival (PFS), overall survival (OS), disease control rate (DCR), duration of response (DOR), and safety.

Results: From April to September 2018, 54 pts were enrolled at 25 sites in Japan. The median follow-up time was 10.1 months. The median number of P doses and cycles in SOX were 9 (range, 2-18) and 6 (range, 2-13), respectively. The relative dose intensities of S-1 and OX were 73% and 60%, respectively. The ORR and DCR assessed by BICR were 72.2% (95% CI 58.4-83.5) and 96.3% (95% CI 87.3-99.5), respectively. The median PFS was 9.4 months (95% CI 6.6-NR). Median DOR and OS were not reached. Grade ≥3 adverse events (AEs) were reported in 31 pts (57.4%). The most common treatment-related AEs of grade ≥3 were thrombocytopenia (14.8%), neutropenia (13.0%), colitis (7.4%), and adrenal insufficiency (5.6%). There were no treatment-related deaths. Conclusions: This study showed the encouraging efficacy and manageable safety of SOX with P therapy as a first line in pts with HER2-negative, PD-L1-positive AGC. Clinical trial information: NCT03382600. Research Sponsor: Merck Sharp & Dohme Corp. Pharmaceutical/Biotech Company.
A phase III study of nivolumab (Nivo) in previously treated advanced gastric or gastric esophageal junction (G/GEJ) cancer (ATTRACTION-2): Three-year update data.

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Background: Nivo is the first immune checkpoint inhibitor (ICI) to show efficacy and tolerability in G/GEJ cancer patients refractory to or intolerant of standard chemotherapy. Although Nivo has demonstrated durable efficacy in several cancer types, no long-term efficacy data in G/GEJ cancer has been reported to date. Here, we report the 3-year survival data of Nivo in G/GEJ cancer.

Methods: A total of 493 patients with unresectable advanced or recurrent G/GEJ cancer after the failure of two or more chemotherapy regimens were randomized in a 2:1 ratio to receive 3 mg/kg Nivo (N = 330) or placebo (N = 163) until disease progression or unacceptable toxicity. The primary endpoint was overall survival (OS). Updated results of the efficacy and safety were based on ≥ 3 years of follow-up after last patient enrollment. In subgroup analysis, we evaluated OS by BOR and incidence of select treatment-related adverse events (TRAEs). Results: As of data cut-off in February 2019, 3 years after last patient enrollment, the hazard ratios of OS and PFS in the Nivo group compared with the placebo group remained 0.62 and 0.60, respectively. The 36-month OS rates of Nivo and placebo were 5.6% and 1.2% and the 36-month PFS rates were 2.4% and 0%, respectively. In the OS subgroup analysis by BOR, the median OS and 3-year OS rate in CR/PR patients with Nivo were 26.7 months and 35.5%, respectively. The incidence rate and severity of TRAEs were comparable with those of the 2-year cut-off. In the OS subgroup analysis based on the presence or absence of select TRAEs, the hazard ratio in patients with select TRAEs was 0.46 compared to those without select TRAEs. We are analyzing the baseline characteristics that are associated with long-term survival with Nivo. Conclusions: Nivo showed durable efficacy and a good safety profile on long-term follow-up in heavily pretreated G/GEJ cancer patients. Clinical trial information: NCT02267343. Research Sponsor: ONO Pharmaceutical and Bristol-Myers Squibb.
Comparison of efficacy of aspirin plus epirubicin, oxaliplatin, and capecitabine versus epirubicin, oxaliplatin, and capecitabine alone in patients with locally advanced and metastatic gastric cancer: A randomized clinical trial.

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**Background:** Aspirin was long known to prevent cancer, the last decade revealed its therapeutic role via varied mechanisms like inhibition of platelet activation, COX and PI3K pathway. Since PI3K/AKT/mTOR is one of the pathways activated in gastric cancer and Giampieri et al (2016) showed improved response rates, PFS and OS with addition of aspirin to capecitabine in heavily pretreated metastatic colorectal cancer, a cancer in which efficacy of aspirin is related to presence of PI3K mutations, we aimed to compare the efficacy of aspirin added to a standard regime EOX with EOX alone in locally advanced and metastatic gastric cancer. **Methods:** All patients with advanced gastric cancer coming to JIPMER, Department of Medical oncology between March 2017 to May 2019 were screened for eligibility in the trial. Those eligible were randomly assigned to standard EOX or standard EOX plus 150 mg of daily aspirin. Tumor measurements were performed at baseline, then after 3-4 cycles (interim response) and the response to treatment was assessed by the radiologist who was blinded to treatment arms according to RECIST1.1 criteria. Toxicity profiles were recorded as per CTCAE v 4.03. In per protocol analysis, response rates, PFS (progression free survival) and OS (overall analysis) were analysed for patients who received ≥3 cycles and had an evaluable interim response. **Results:** 95 patients were randomised. In per protocol analysis, 70 patients were included. The results are shown in table. **Conclusions:** No statistically significant difference was seen with respect to response rates, PFS, OS and toxicity, although there was a higher ORR (overall response rate = complete response, CR + partial response, PR) and OS seen in EOX plus aspirin arm. Clinical trial information: CTRI/2017/11/010651. JIPMER, Puducherry, India.

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<thead>
<tr>
<th></th>
<th>EOX arm</th>
<th>EOX plus aspirin arm</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>ORR (CR+PR)</td>
<td>27 %</td>
<td>42.46 %</td>
<td>0.176</td>
</tr>
<tr>
<td>DCR (CR+PR+SD)</td>
<td>75.69%</td>
<td>72.72%</td>
<td>0.778</td>
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<tr>
<td>Median OS</td>
<td>12 months</td>
<td>15 months</td>
<td>0.696</td>
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<tr>
<td></td>
<td>(10.18-13.8)</td>
<td>(4.8-25)</td>
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<tr>
<td>Median PFS</td>
<td>9 months</td>
<td>8 months</td>
<td>0.467</td>
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<td></td>
<td>(4.2-13.7)</td>
<td>(6.66-13.39)</td>
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DCR (disease control rate), SD (stable disease)
Immune-related adverse events and neutrophil-to-lymphocyte ratio are possible predictive factors for gastric cancer treated with nivolumab.

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Background: The Immune-related adverse events (irAEs) and neutrophil-to-lymphocyte ratio (NLR) are effective as a predictive factor for lung cancer treated with nivolumab. The objective of this study was to determine the effectiveness of irAEs and NLR for patients with advanced gastric cancer (AGC) treated with nivolumab. Methods: This was a retrospective study of patients with AGC treated with nivolumab from October 2017 to August 2019. The NLRs were calculated before the first cycle. Results: Forty patients were enrolled (males 29, females 11) with a median age of 65 years. The overall response rate was 12.5%. The median PFS was 4.2 months (range, 0.5 - 21). Stratified with high NLR (≥5) and low NLR (< 5), the median PFS was shorter in the high NLR arm (1.1 vs. 5.1 months; p = 0.0003). irAEs were observed in 5 of the 40 study patients (12.5%), including 1 patients (20%) with such events of grade 3 or 4, and 1 patient requiring systemic corticosteroid therapy. Median PFS was 6.5 months (95% CI, 4.4 to not reached [NR]) and 3.9 months (95% CI, 3.0 to 7.5) (P = .09) for patients with or without irAEs, respectively. Conclusions: NLR may be an effective prognostic factor in patients with AGC treated with nivolumab. Development of irAEs was associated with survival outcome of nivolumab treatment in patients with AGC. Further studies are needed to confirm our findings. Research Sponsor: None.
Magnetic marking clip for easier laparoscopic localization of small gastrointestinal tumors.

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Background: Laparoscopic surgery for gastrointestinal tumors requires fast and precise tumor localization. As tumor palpation is not possible during laparoscopic surgery, tumor identification is often difficult for some cases. Despite various methods, such as tattooing or endo-clipping, have been introduced for the localization of tumors, these methods own clear limitations. To overcome the drawbacks of these conventional marking methods, we designed a magnetic marking device linked to an endo-clip (MMC, Magnetic Marking Clip) for endoscopy. We performed preoperative endoscopic clipping with MMC and analyzed the intraoperative localization efficacy and safety during laparoscopic surgery. Methods: Study enrolled 30 patients with gastric and colorectal neoplasms scheduled to undergo endoscopic clipping before laparoscopic surgery at the Korea University Medical Center, Korea, between August 2017 and June 2019. A silicone-coated high-power neodymium marking device (ring or rod type) was fixed together with an endo-clip and applied on the center of the lesion during preoperative endoscopy. During laparoscopic surgery, a detecting magnetic body was inserted through a laparoscopic trocar and was used to localize the tumor that is marked with MMC. The time needed for endoscopists to place MMC at the lesion, laparoscopic clip detection time and success rate were studied. Results: Endoscopists placed MMC within 30 seconds. It was possible to find MMC in all cases of laparoscopic surgery. Time needed to find the MMC laparoscopically was relatively shorter than the time conventionally taken just with an endo-clip itself. There was no reported dislodgement of the clip before the surgery or any other adverse events associated with the MMC procedure. Conclusions: The MMC method enabled simple and fast tumor localization and showed excellent outcomes in efficacy of tumor localization. The MMC method may help surgeons localize GI tumor lesions easily and safely during laparoscopic surgery. Research Sponsor: None.
Cost-effectiveness analysis of pressurized intraperitoneal aerosol chemotherapy (PIPAC C/D) in patients with gastric cancer and peritoneal metastasis.

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Background: The efficacy of systemic chemotherapy is still highly unsatisfactory for patients with gastric cancer and peritoneal metastases (PM). The aim of this study was to assess the costs effectiveness of pressurized intraperitoneal aerosol chemotherapy with low-dose cisplatin and doxorubicin (PIPAC C/D) for advanced gastric cancer. Methods: We developed a state transition Markov Model to estimate the costs and effectiveness of the use of PIPAC C/D versus palliative chemotherapy. Intervention was assessed in two different levels including upfront therapy (PIPAC C/D plus XELOX chemotherapy versus first-line chemotherapy alone) and second line therapy (PIPAC C/D only versus second-line chemotherapy (ramucirumab monotherapy)). Data from multiple sources such as published literature and UK-based databases were used to inform the economic model. Deterministic and probabilistic sensitivity analyses were conducted to explore the impact of key parameter variation on the results. Results: For the upfront therapy the estimated total costs in the intervention and comparator arms were £33,587 (SD: £2,394) and £17,477 (£927) respectively. PIPAC C/D plus XELOX led to an increase of 0.56 in QALYs. Estimated incremental cost per quality adjusted life years (QALYs) was £28,879. Result from probabilistic sensitivity analysis showed that PIPAC C/D plus XELOX is cost effective in more than 50% of Monte Carlo simulations at £30,000 threshold. For the second-line therapy, the total costs for PIPAC C/D was £15,985 (£1,391) and for the second-line palliative chemotherapy was £36,319 (£3,673). PIPAC C/D led to an increase of 0.21 in QALYs and £20,222 reduction in costs, meaning the intervention is dominant strategy in the second line therapy as it is less costly and more effective. Conclusions: The cost effectiveness results for the upfront therapy indicate that PIPAC C/D plus chemotherapy intervention is more costly and more effective and a cost effective intervention. PIPAC C/D only intervention has the potential to reduce costs and improve clinical outcomes for patients with advanced gastric cancer with peritoneal metastasis and therefore a dominant strategy. Research Sponsor: Capnomed GmbH, Zimmern, Germany.
Real-world efficacy and biomarker of nivolumab for advanced gastric cancer.

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**Background:** Although nivolumab demonstrated survival benefit and a manageable safety profile in previously-treated advanced gastric cancer in a phase III trial (ATTRACTION-2), the efficacy of nivolumab in real-world and predictive factors of responses to nivolumab for advanced gastric cancer remain unclear. We evaluated the efficacy of nivolumab and compared clinicopathological characteristics with responses to nivolumab and long-term survivals in patients with gastric cancer. **Methods:** 205 patients with unresectable or recurrent gastric cancer who were treated with nivolumab as 3rd or more line treatment were enrolled from 23 institutions. Tissue specimens were collected in 199 patients. PD-L1 expression of tumor specimens defined as tumor positive score (TPS) and combined positive score (CPS) and mismatch repair (MMR) were analyzed by immunohistochemistry. Tumor responses were assessed according to RECIST version 1.1. Hyper progressive disease (HPD) was defined as $\geq$ two folds increase in tumor growth rate. **Results:** 138 out of 205 enrolled patients had measurable lesions. Response rate and HPD rate were 16.7% (23/138) and 22.0% (29/132), respectively. Response rate was significantly higher in patients with performance status (PS) 0-1, non-peritoneal diseases, CPS $\geq$10, and MMR deficient patients. On the other hand, PS 2-3 and liver metastases were predictive factors of HPD. Patients with CPS $\geq$10 and MMR deficiency showed significantly better progression-free (P = 0.005, P = 0.001) and overall survivals (P = 0.005, P = 0.002). TPS showed no significant association with any outcomes. **Conclusions:** Real-world efficacy of nivolumab was shown in previously-treated advanced gastric cancer. CPS and MMR could be the useful biomarkers for the efficacy of nivolumab treatment as well as PS and metastasis site. Clinical trial information: UMIN000032164. Research Sponsor: None.
Treatment efficacy of ramucirumab-based chemotherapy in patients with alpha-fetoprotein producing gastric cancer (AFPGC).

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**Background:** AFPGC is an aggressive subgroup of gastric cancer and is associated with a worsened survival because of a high incidence of liver metastasis. Ramucirumab-based chemotherapy is the standard treatment as a second line in advanced gastric cancer. Recently ramucirumab has showed survival benefit in hepatocellular carcinoma, but only those with higher AFP levels. However, the efficacy of ramucirumab in AFPGC is unknown. **Methods:** We retrospectively assessed 283 patients who received paclitaxel or nab-paclitaxel combined with ramucirumab between July 2015 and December 2018. AFPGC was defined when serum AFP levels were elevated and correlated with the disease state during treatment. Non-AFPGC was defined when serum AFP levels were normal when diagnosed. Other patients were excluded. Patients’ demographics, progression-free survival (PFS), overall survival (OS) and objective response rates (ORR) were compared between the two groups. **Results:** Among the 283 patients, 24 patients were AFPGC and 189 patients were non-AFPGC. AFPGC was associated with high incidences of intestinal histology (46%) and liver metastasis (63%), while AFPGC was associated with a low incidence of peritoneal metastasis (21%), compared with non-AFPGC. There was no significant difference in PFS and OS between the two groups. Median PFS were 5.4 (95%CI 3.6-6.7) months in AFPGC and 4.1 (3.7-5.1) months in non-AFPGC (HR 0.93 95%CI 0.60-1.46, p = 0.788), respectively. Median OS were 19.0 (95%CI 13.2-NA) months in AFPGC and 19.3 (17.9-20.1) months in non-AFPGC (HR 1.21 95%CI 0.70-2.10, p = 0.494), respectively. Regarding with ORR, AFPGC showed higher ORR with 52.6% (95%CI 30.2-75.1), while 37.3% (95%CI 26.4-48.3) in non-AFPGC (p = 0.296), although this was not statistically significant. **Conclusions:** Ramucirumab showed comparable survival and higher ORR in AFPGC than in non-AFPGC. Considering the generally poor prognosis of AFPGC, it is speculated that ramucirumab may have compensated for disadvantage in survival. Research Sponsor: None.

Long-term survival in patients with peritoneal metastasized gastric cancer treated with cytoreductive surgery and HIPEC: A multi-institutional cohort from PSOGI.

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Background: Peritoneal metastasis of gastric cancer is relatively common (17%) and is associated with poor survival. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is still controversially discussed, as it has proven an increase in median survival in selected patients, but only a small subgroup reached long-term survival. The aim of this study was to collect and analyze a worldwide cohort of patients treated with CRS and HIPEC with long-term survival in order to explore relevant patient characteristics. Methods: We conducted a questionnaire, which was distributed to all collaborators of the Peritoneal Surface Oncology Group International (PSOGI). Inclusion criteria were: histopathologic proven peritoneal metastasis of gastric cancer, treated with CRS and HIPEC, and overall survival > 5 years. Patient, tumor, and therapeutic details were collected and analyzed. Results: A total of 29 patients with a mean age of 52.5 years and a mean PCI of 3.2 were included. The overall median survival was 11.0 years (min 5.0; max 27.9). The predictors completeness of cytoreduction (CC-0) and low PCI (PCI < 6) were present in 23/29 patients. 13/29 patients developed at a median of 82.2 months tumor recurrence. Tumor recurrence was associated with inferior median overall survival compared to patients without tumor recurrence (8.8 years vs. not reached; p = 0.002). Conclusions: Long-term survival and even cure are possible in patients with peritoneal metastasis of gastric cancer treated with CRS and HIPEC. Completeness of cytoreduction (CC-0) and low PCI seemed to be crucial. Further studies are needed in order to improve existing selection criteria. Research Sponsor: None.
Prognostic factor of nivolumab for advanced gastric cancer patients with poor performance status patients.

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**Background:** Nivolumab has changed the treatment of advanced gastric cancer (AGC). Nivolumab shows better outcome compared to best supportive care in AGC patients who received at least two prior regimen. Although there is not reliable data of poor performance status (PS) AGC patients who received nivolumab. We investigated efficacy and safety of nivolumab for AGC patients with poor PS. **Methods:** We retrospectively collected clinicopathologic data from patients with AGC who received nivolumab monotherapy in Himeji Red Cross Hospital from October 2017 to June 2019. **Results:** 49 AGC patients who received nivolumab were analyzed. 27 patients were PS 0 or 1 (Good Group), and 22 patients were PS 2 or 3 (Poor Group). Median progression free survival and overall survival was 61 days and 180 days in Good Group and 36 days and 85 days in Poor Group. Overall survival (OS) was significantly shorter in Poor group (180 days vs 85 days, p = 0.0255). Disease control rate was 23% in Good group and 9% in Poor group. 33% patients were experienced immune related adverse event (iRAE) in Good Group, and 18% in Poor Group. We investigated prognostic factor of OS in Poor Group such as Royal Marsden Hospital Score (RMH score), modified Glasgow prognostic score (mGPS), and Japan Clinical Oncology Group (JCOG) prognostic index. RMH score and JCOG prognostic index good or moderate group was significantly longer overall survival than poor group (93 days vs 35 days (p = 0.0214)). JCOG prognostic index was most correlated with OS among these tools. **Conclusions:** This study suggested that nivolumab has a modest effect and is feasible as third line or later line for AGC patients. JCOG prognostic index was suggested to be effective in predicting prognosis in AGC patients who received nivolumab. Research Sponsor: None.
Retrospective analysis for efficacy and safety of nivolumab in advanced gastric cancer patients (pts) with malignant ascites.

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**Background:** Nivolumab is a standard of care as the later-line therapy for advanced gastric cancer. However, there are few data about efficacy and safety of nivolumab for pts with malignant ascites. **Methods:** We conducted a multicenter retrospective study for pts with advanced gastric cancer who received nivolumab alone from Oct. 2017 to Feb. 2019. Pts were divided into two groups; high ascites burden (HAB) with moderate or massive ascites and non-HAB with none or a small amount of localized ascites at pelvis and/or liver surface. **Results:** A total of 72 pts (23 pts with HAB and 49 pts with non-HAB) were evaluable. The HAB group had more pts with young (median 62 vs 70 years), female (35 vs 14 %), no prior gastrectomy (63 vs 35 %) and poor performance status (PS > 1; 26 vs 10 %), compared to the non-HAB group. Disease control rate was 44% (95% CI 23-64%) in the HAB group and 57% (95% CI 43-71%) in the non-HAB group. Ascites decreased in 4 pts (17%) and completely disappeared in 2 pts (8.7%) in the HAB group. These 6 pts were all male and had prior ramucirumab treatment with a mean neutrophil-lymphocyte ratio 2.1 (from 0.85 to 3.7) at the initiation of nivolumab. After 5 months of follow up period, disease progression or death events for progression-free survival (PFS) occurred in 74% of the HAB group and 53% of the non-HAB group. Median PFS was 1.0 (95%CI 0.5-1.5) and 2.6 (95%CI 0.9-7.4) months in pts with HAB and non-HAB, respectively. PFS rates at 6 months were 31% in the HAB group and 33% in the non-HAB group. Immune-related adverse events occurred in 26% of the HAB group and 16% of the non-HAB group including one and two pts with grade 3 or 4 events, respectively. There was no treatment-related death in both groups. **Conclusions:** Although pts with HAB showed trends of worse outcomes compared with those with non-HAB, nivolumab was suggested to provide a survival benefit to some pts with HAB, and was tolerable in the HAB group. Research Sponsor: None.
Preliminary analysis of total neoadjuvant therapy for patients with locally advanced gastric (G) and gastroesophageal (GE) adenocarcinoma.

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Background: Nearly half of patients with G/GE cancer do not receive or complete post-operative chemotherapy and/or chemoradiation (CRT). Total neoadjuvant therapy (TNT) is an emerging alternate treatment strategy. We have previously reported a 28% pCR with FOLFIRINOX followed by CRT. However, TNT outcomes with FLOT or FOLFOX followed by CRT are lacking. Methods: We retrospectively analyzed patients after resection of locally advanced G/GE after receiving TNT. Patient received neoadjuvant FLOT or FOLFOX x 8 cycles, CRT (G 45 Gy, GE 50.4 Gy) with concurrent chemotherapy (5FU, carboplatin/paclitaxel). The primary aim was to explore TNT completion rates. Secondary aims included pCR and toxicity. We performed descriptive statistics, t-test, chi-squared, and Fisher’s exact tests as appropriate. Results: From 12/2015 to 8/2019, 57.1% (40/70) completed TNT and resection (15.7% active treatment, 15.7% progressive disease, 11% treated elsewhere). Median age was 66.0 (range: 27-79) and 73% male. Tumor locations included 57.5% G, 30.0% GE, and 12.5% overlapping. Neoadjuvant chemotherapy included FLOT 22.5% (n = 9) or FOLFOX 77.5% (n = 31). Overall we found a 25% pCR without significant differences between type of neoadjuvant chemotherapy. Conclusions: TNT followed by resection is feasible with acceptable rates of treatment completion and toxicity. Notable limitations include the retrospective analysis, small sample size, and heterogenous treatment. The pCR rate is promising and warrants further prospective study to optimize TNT approaches. None.

<table>
<thead>
<tr>
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<th>FLOT (n = 9)</th>
<th>FOLFOX (n = 31)</th>
<th>P value</th>
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<tr>
<td>Age, years (mean)</td>
<td>6.27 (95% CI 51.4-73.9)</td>
<td>6.15 (95% CI 59.3-67.6)</td>
<td>0.87</td>
</tr>
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<td>Sex, male (n, %)</td>
<td>6 (66.7%)</td>
<td>23 (74.2%)</td>
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<tr>
<td>Pre-TNT weight, kg (mean)</td>
<td>71.9 (61.7-92.1)</td>
<td>82.7 (74.5-90.8)</td>
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</tr>
<tr>
<td>Total chemotherapy received (%)</td>
<td>75.6 (53.8-97.4)</td>
<td>75.5 (65.8-85.2)</td>
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<td>CRT received (%)</td>
<td>96.6 (95.1-102.1)</td>
<td>97.6 (92.0-102.7)</td>
<td>0.81</td>
</tr>
<tr>
<td>Duration of TNT, months (mean)</td>
<td>17.2 (14.2-20.2)</td>
<td>15.7 (14.2-17.3)</td>
<td>0.36</td>
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<tr>
<td>Adverse effects</td>
<td></td>
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<tr>
<td>Weight loss (%)</td>
<td>-5.86 (-12.4-0.66)</td>
<td>-0.01% (-4.48-4.46)</td>
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</tr>
<tr>
<td>Neuropathy (n, %)</td>
<td>7 (78.8)</td>
<td>21 (67.7)</td>
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<td>Onycholysis (n, %)</td>
<td>2 (22.2)</td>
<td>3 (9.6)</td>
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<td>R0 resection (n)</td>
<td>8 (88.9)</td>
<td>30 (96.8)</td>
<td>0.34</td>
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<td>pCR (n, %)</td>
<td>2 (22.2)</td>
<td>8 (25.8)</td>
<td>1.00</td>
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</tbody>
</table>
Durvalumab (D) and PET-directed chemoradiation (CRT) after induction FOLFOX for esophageal adenocarcinoma.

Michele Ly, Daniela Molena, Smita Sihag, Abraham Jing-Ching Wu, Pari M. Shah, Ping Gu, Ryan Sugarman, Steven Brad Maron, Sree Bhavani Chalasani, Marina Shcherba, Randy Yeh, Laura H. Tang, Carly Alterman, Paige Collins, Kendall Cowie, Yelena Yuriy Janjigian, David H. Ilson, Geoffrey Yuyat Ku; Memorial Sloan Kettering Cancer Center, New York, NY; Memorial Sloan-Kettering Cancer Center, New York, NY

Background: We previously presented safety data for the combination of D with carboplatin/paclitaxel (C/P) and RT for locally advanced esophageal cancer (J Clin Oncol 2018;36:172 [abstr]). Based on the positive results of the CALGB 80803 study (J Clin Oncol 2017;35:1 [abstr]), we amended the study to administer induction FOLFOX prior to PET assessment. Here, we present updated results. Methods: Patients (Pts) had TanyN+ or T3-4NanyM0 esophageal and Siewert Type I-III GEJ adenocarcinoma staged by EUS, PET/CT and CT. Pts received mFOLFOX6 x2 prior to repeat PET/CT. PET responders (PETr) received 5-FU or capecitabine and oxaliplatin with RT to 50.4Gy, while PET non-responders (PETnr) received C/P with RT. All Pts received D 1,500 mg q4W x2 starting 2 wks prior to and during CRT. Esophagectomy was planned 6-8 weeks after CRT. Pts who had R0 resections received adjuvant D 1,500 mg q4W x6. Results: 20 Pts have been enrolled: 16 GEJ, 4 esophageal; 3 T1-2N+, 8 T3-4N0, 1 T3Nx, 8 T3-4N+. 13 of 20 Pts (65%) are PETr. Of 13 Pts who have had surgery (8 PETr, all R0), pathologic complete response (pCR) was seen in 3 (23%; 2 PETr); 3 Pts (23%; all PETr) had ypT1bN0 tumors with 99% response and 1 Pt (8%; PETnr) had ypT0N1 (1/30 LN) with profound response in LN. 2 Pts had MSI tumors (1 PETr; 1 pCR, 1 ypT2N0 with 90% response). Notable gd 3/4 adverse events (AEs) observed were lymphopenia in 16 Pts (80%), neutropenia in 4 Pts (20%) and diarrhea and dysphagia in 1 Pt each (5%). Notable gd 1/2 AEs in ≥20%; thrombocytopenia (18 Pts), fatigue (13 Pts), anemia (12 Pts), increased AST (12 Pts), constipation (11 Pts), nausea (11 Pts), diarrhea (7 Pts) and odynophagia (7 Pts). Immune-related AEs noted were gd 3 hepatitis and gd 2 dermatitis in 1 Pt and gd 1 hypothyroidism in 1 Pt. Median length of post-op stay is 8 days, with 18% anastomotic complication rate. Conclusions: The addition of D to induction FOLFOX and PET-directed CRT is safe and feasible. pCR and near-pCR in ½ of Pts is encouraging and compares favorably to our historical pCR rate of 15% in PETr (Cancer 2016;122:2083) and pCR rate of 31% in CALGB 80803 Pts who received induction FOLFOX. Accrual to 36 Pts continues and updated outcomes and immune correlative data will be presented. Clinical trial information: NCT02962063. Research Sponsor: Parker Institute for Cancer Immunotherapy. Pharmaceutical/Biotech Company.
Concurrent versus sequential neoadjuvant chemoradiation therapy for esophageal and gastroesophageal junction adenocarcinoma.

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Background: Neoadjuvant therapy is the standard of care for locally advanced esophageal and gastroesophageal junction (GEJ) adenocarcinoma, with most patients receiving neoadjuvant chemoradiation (CRT). CRT can be delivered concurrently or sequentially after induction chemotherapy. The purpose of this study was to evaluate pathologic complete response (pCR) and overall survival (OS) among patients who received concurrent versus sequential CRT in the National Cancer Database (NCDB). Methods: Patients who received neoadjuvant CRT and underwent curative intent esophagectomy for esophageal or GEJ adenocarcinoma from 2006-2015 were included. Patients with clinical T4 or metastatic disease were excluded. Concurrent CRT was defined as radiation treatment starting within 6 weeks of chemotherapy start. Sequential CRT was defined as radiation treatment starting greater than 6 weeks after chemotherapy start. Propensity weighting was conducted to balance patient, disease, and facility covariates between groups. Results: 12,460 patients met inclusion criteria. 11,880 (95%) patients received concurrent CRT and 580 (5%) patients received sequential CRT. Patients who received sequential CRT were significantly younger (mean age: 60.7 vs 62.2 years), had higher clinical nodal stage (N2-3: 14.7% vs 10.1%), and were more often treated at academic/research hospitals (67.1 vs 55.5) (all p < 0.001). pCR was achieved in 16.2% of patients who received sequential CRT and in 14.0% of patients who received concurrent CRT (p = 0.131). Following propensity weighting, OS was significantly improved among patients who received sequential versus concurrent CRT (HR 0.82; 95% CI 0.74-0.92; p < 0.001) with a median OS for the sequential cohort of 41.4 months versus 29.4 months for those who received concurrent CRT. Conclusions: In this retrospective study from a large national database of patients who received neoadjuvant CRT for esophageal and GEJ adenocarcinoma, sequential CRT is associated with a significant OS benefit. These results merit consideration of a well powered prospective multi-institutional randomized clinical trial to further evaluate this observed difference. Research Sponsor: None.
Efficacy and safety of nivolumab and irinotecan as third-line chemotherapy for advanced gastric cancer: A multi-institutional retrospective study.

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Background: Although nivolumab (NIVO) and irinotecan (IRI) are currently used as third- or later-line therapy for advanced gastric cancer (AGC), few direct comparisons between them have been available. The present study therefore aims to compare the efficacy and safety of NIVO with IRI and explore clinical factors that predict efficacy. Methods: Patients with AGC who underwent NIVO or IRI treatment between November 2016 and June 2018 at three institution were retrospectively examined, subsequently evaluating response rates (RR), progression-free survival (PFS), overall survival (OS), and adverse events (AEs). The main inclusion criteria were patients pretreated with fluoropyrimidines and taxanes, Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0–2, and no previous NIVO or IRI treatment. Results: A total of 71 and 61 patients received NIVO and IRI, respectively, with both groups having similar baseline characteristics, except for gender. Efficacies were as follows (NIVO/IRI): RR, 20%/6% (p = 0.17); median PFS, 1.6 months (m)/1.8 m (HR 0.93, p = 0.67); median OS, 6.4 m/6.4 m (HR 0.91, p = 0.61); 1-year survival rate, 24.9%/19.3% (p = 0.61), respectively. Interaction analysis found no significant interaction between drugs and various factors such as ECOG PS (p = 0.59) and neutrophile/lymphocyte ratio (p = 0.33) related to OS. Subsequent chemotherapy agents were administered to 32 patients (45%) in the NIVO group (17 patients out of them received IRI) and 36 patients (59%) in the IRI group (23 patients out of them received NIVO) (p = 0.12). NIVO tended to have lower grade 3 or more AEs than IRI, especially neutropenia (3% vs. 28%, respectively; p < 0.01) and febrile neutropenia (1% vs. 8%, respectively; p = 0.09), as well as neutropenia, nausea, diarrhea, constipation, fatigue, and anorexia of any grade. Five patients developed immune-related adverse events in the NIVO group: pneumonitis (n = 1) and rash (n = 4). Conclusions: Although no remarkable differences in efficacy were found between NIVO and IRI for AGC, NIVO had a better safety profile compared to IRI. This study found no clinical factors that predicted efficacy. Research Sponsor: None.
Neoadjuvant chemotherapy with docetaxel plus oxaliplatin and S-1 for locally advanced, resectable gastric or gastro-esophageal junction adenocarcinoma: Short-term results from a phase II trial.

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**Background:** In locally advanced, resectable gastric or gastro-oesophageal junction (EGJ) adenocarcinoma, perioperative the docetaxel-based triplet FLOT (fluorouracil plus leucovorin, oxaliplatin and docetaxel) is the standard chemotherapy in Europe. However, there is no evidence of neoadjuvant chemotherapy for resectable gastric cancer in Japan. Therefore, we conducted a phase II trial of neoadjuvant chemotherapy with docetaxel plus oxaliplatin, and S-1 (DOS) for locally advanced, resectable gastric or EGJ adenocarcinoma. **Methods:** Eligible patients had histologically confirmed gastric or EGJ adenocarcinoma of a clinical Stage III according to the 14th Edition of Japanese Classification of Gastric Carcinoma. DOS was administered for two or three preoperative cycles followed by eight postoperative cycles of S-1. Each 3-week cycle of DOS consisted of docetaxel 40 mg/m² and oxaliplatin 100 mg/m² on day 1 plus S-1 80-120 mg/body on days 1 to 14. Primary endpoint was 3-year progression-free survival rate, and secondary endpoints included overall survival, progression-free survival, response rate, histological response rate, R0 resection rate, and adverse events. **Results:** Of 50 enrolled patients, 48 (37 gastric and 11 EGJ) were eligible for the analysis. 42 (88%) patients completed two or three preoperative cycles of DOS. The most common grade 3-4 adverse events of DOS were neutropenia (69%), leukopenia (56%), diarrhea (19%), and febrile neutropenia (13%). Of 45 patients who underwent gastrectomy, postoperative morbidities (Clavien-Dindo ≥ Grade II) occurred in 12 (27%) patients. R0 resection could be achieved in 43 (90%) patients. 12 (27%) and 30 (67%) of 45 patients achieved pathological response rate of Grade2-3 and Grade1b-3, respectively. There was no treatment-related death. **Conclusions:** Neoadjuvant DOS for locally advanced, resectable gastric or EGJ adenocarcinoma might be favorable. Long-term results will be published in two years. Clinical trial information: 000017652. Research Sponsor: Yakult Honsha Co.,Ltd.
Safety of perioperative atezolizumab in combination with FLOT versus FLOT alone in patients with resectable esophagogastric adenocarcinoma: An interim safety analysis of the DANTE, a randomized, open-label phase II trial of the German Gastric Group at the AIO and the SAKK.

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**Background:** The DANTE study evaluates atezolizumab in the perioperative treatment of locally advanced, potentially resectable gastric or GEJ adenocarcinoma in combination with perioperative FLOT. Here, we report the protocol-defined interim safety analysis. **Methods:** DANTE is a large, multinational, prospective, multicenter, randomized, investigator-initiated, open label phase II trial. Patients (pts) with locally advanced, potentially resectable adenocarcinoma of the stomach and GEJ (≥cT2 and/or N-positive) without distant metastases are enrolled. Pts are randomized 1:1 to 4 pre-operative 2-week cycles (8 weeks) of FLOT followed by surgery and 4 additional cycles of FLOT plus atezolizumab at 840 mg every 2 weeks, followed by a total of 8 additional cycles of atezolizumab at 1200 mg every 3 weeks as monotherapy (arm A) or FLOT alone (arm B). Primary endpoint is time to disease progression or relapse after surgery (PFS/DFS). **Results:** Recruitment started in Sept 2018; by September 2019, a total of 122 pts have been randomized. This analysis is based on the first 40 pts (20 pts in each arm). The pts had a median age of 62 y and 75% of pts had an ECOG PS of 0 in both arms. The cohort was well balanced in terms of tumor location and clinical stage. 90% of pts enrolled completed all pre-operative cycles in each arm. Total number of adverse events with relation to study treatment was 154 in arm A and 148 in arm B. Total number of serious adverse events (SAE; related or not) was 16 in Arm A and 14 in arm B. 20% of pts in each arm had an SAE due to perioperative morbidity. No surgical mortality was observed. 18 and 19 pts proceeded to operation in arms A and B, respectively. Premature treatment discontinuation occurred in 2 pts in each arm: disease progression (1) and deterioration of general health condition (1) in arm A; and pts’ wish (1) and death (1) in arm B. Median hospitalization time was 15 days in arm A and 16 days in arm B. **Conclusions:** perioperative atezolizumab plus FLOT is feasible and safe. The study continued recruitment. Clinical trial information: NCT03421288. Research Sponsor: Roche Pharma.
Multicenter phase II study of neoadjuvant chemotherapy with S-1 and oxaliplatin for locally advanced gastric cancer (Neo G-SOX PII).

Masato Kondo, Hironaga Satake, Motoko Mizumoto, Akira Miki, Takanori Watanabe, Norimitsu Tanaka, Kenro Hirata, Hiroaki Tanioka, Yoshihiro Okita, Takahisa Kyogoku, Mitsutoshi Matoba, Shinichi Adachi, Satoshi Kaihara, Hisateru Yasui, Akihito Tsuji; Kobe City Medical Center General Hospital, Kobe, Japan; Department of Medical Oncology, Kobe City Medical Center General Hospital, Kobe, Japan; Department of Surgery, Kobe City Medical Center General Hospital, Kobe, Japan; Department of Surgery, Tooyoka Hospital, Tooyoka, Japan; Department of Surgery, Himeji Red Cross Hospital, Himeji, Japan; Department of General and Gastroenterological Surgery, Kagawa Prefectural Central Hospital, Kagawa, Japan; Division of Gastroenterology and Hepatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan; Medical Oncology, Okayama Rosai Hospital, Okayama, Japan; Nishikobe Medical Center, Kobe, Japan; JCHO Hoshigaoka Medical Center, Hiramata, Japan; Kobe Rosai Hospital, Kobe, Japan; Department of Surgery, Nishinomiya Municipal Central Hospital, Nishinomiya, Japan; Department of Surgery, Kobe City Medical Center General Hospital, Kobe, Japan; Department of Medical Oncology, Kagawa University Hospital, Takamatsu, Japan

Background: Prognosis for locally advanced gastric cancer (LAGC), such as clinical T4 disease, bulky nodal metastases, type 4 and large type 3 gastric cancer, was not satisfactory even by D2 gastrectomy followed by adjuvant chemotherapy. Neoadjuvant chemotherapy is another promising approach, therefore, we have conducted a phase II study to evaluate the efficacy and safety of the neoadjuvant chemotherapy of S-1 and oxaliplatin (G-SOX) followed by gastrectomy with D2/3 lymph node dissection for LAGC, and the primary endpoint of curative resection rate was met [Miki A, ESMO 2019]. We show longer follow-up data from this study.

Methods: Patients with adenocarcinoma of the stomach; clinical T4; clinically resectable gastric cancer of type 4 or large type 3; bulky nodal involvement around major branched arteries to the stomach were enrolled. Patients receive two cycles of neoadjuvant chemotherapy with S-1 (80 mg/m2, p.o., days 1-14 followed by 1 week rest) and oxaliplatin (130 mg/m2 at day 1), followed by D2 or higher surgery with no residual disease. Patients with pathological R0/1 resection received S-1 (80 mg/m2, p.o., days 1-14 followed by 1 week rest) and oxaliplatin (130 mg/m2 at day 1), followed by D2 or higher surgery with no residual disease. Patients with pathological RO/1 resection received S-1 (80 mg/m2, p.o., days 1-28 followed by 2 week rest) for 1 year as adjuvant chemotherapy. Primary endpoint was curative resection rate.

Results: Between August 2015 and March 2017, forty-one patients were in enrolled. Of the patients, 39 patients (95%) completed the two courses of neoadjuvant chemotherapy of G-SOX, 37 (90%) received gastrectomy, and 36 (87.8%) received curative resection (R0/1). Grade 3 or higher toxicities during neoadjuvant chemotherapy of G-SOX were neutropenia (7%), fatigue (7%), diarrhea (5%) and thrombocytopenia (2%). No treatment related deaths were observed. Surgical complications including postoperative complications were observed in 13 patients (35%). Pathological response rate after neoadjuvant G-SOX was 40%. With a median follow-up period of 33.8 months, 3year-relapse free survival and 3year-overall survival was 54.3% and 73.1%, respectively. Conclusions: An update analysis confirmed that neoadjuvant chemotherapy of G-SOX is a feasible and might be one of the promising strategies for patients with LAGC. Clinical trial information: UMIN000018661. Research Sponsor: None.
Efficacy of palliative liquid nitrogen spray cryotherapy in curbing progression of dysphagia in esophageal cancer.

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Background: Progressive dysphagia in locally advanced esophageal cancer worsens quality of life (QOL). Endoscopic cryoablation may effectively palliate dysphagia. Aim: To study the effect of palliative cryoablation with truFreeze Spray Cryotherapy (SCT) in patients with esophageal cancer. Methods: This is an interim analysis of a multi-center prospective study of esophageal cancer patients who are non-surgical candidates, not on active systemic therapy, without esophageal stents, or prior SCT. SCT is an endoscopic ablation modality using liquid nitrogen (LN2) delivered by catheter. SCT occurred at 6 week intervals or as indicated at a dose of 2x30 or 3x30 secs/treatment site. Dysphagia and esophageal symptoms were assessed at baseline and after treatment with a 5-point Dysphagia score and the EORTC-QLQ-OES18 (higher score = more symptoms). Results: 39 subjects (mean age 74.4 ±12.2; 87% men, Table) had 182 treatment sessions over a mean follow-up of 206.9 days, and received a median 3 SCT sessions with an average dose of 90 (3x30) secs/site. There was 1 procedure related SAE (2.6% of patients and 0.5% procedures). Mean follow-up dysphagia score was 1.6 ±0.8 and 90% had same or improved dysphagia score after SCT treatment, p<0.01. On average, treated patients maintained the same or improved levels of dysphagia for 117 days. Esophageal QOL was maintained with improvement in “eating problems” (24.4 before treatment to 18.2 after, p=0.01). Only 4 subjects needed an esophageal stent (n=2) or gastrostomy tube (n=2) for nutrition. Conclusions: SCT for palliation of esophageal cancer was effective in limiting progression of dysphagia, while maintaining esophageal QOL. Only 10% required either esophageal stenting or feeding tube at >6 month follow-up. Clinical trial information: NCT03243734. Research Sponsor: CSA Medical, Inc.

Patient Characteristics.

<table>
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<th>Characteristic</th>
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<td>Age, mean ± SD</td>
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<tr>
<td>Cancer Type</td>
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<tr>
<td>Adenocarcinoma</td>
<td>35 (90)</td>
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<tr>
<td>Squamous</td>
<td>4 (10)</td>
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<tr>
<td>Tumor stage</td>
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<tr>
<td>Stage 1</td>
<td>9 (30)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>3 (10)</td>
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<td>Stage 3</td>
<td>15 (50)</td>
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<tr>
<td>Stage 4</td>
<td>3 (10)</td>
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<tr>
<td>Esophagectomy</td>
<td>8 (21)</td>
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<tr>
<td>Chemoradiation</td>
<td>27 (69)</td>
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<td>Luminal obstruction, n (%)</td>
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<td>None</td>
<td>8 (21)</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>22 (56)</td>
</tr>
<tr>
<td>≥ 50%</td>
<td>9 (23)</td>
</tr>
<tr>
<td>Follow-up time, mean days (SD)</td>
<td>206.9 ± 161.1</td>
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<tr>
<td>SCT sessions, median (IQR)</td>
<td>3 (1-6)</td>
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<tr>
<td>Total freeze time/session, sec, median (IQR)</td>
<td>3x30 secs/site, 90 sec (71-60)</td>
</tr>
</tbody>
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A hybrid of the prone and left lateral decubitus positions for thoracoscopic esophagectomy with extended LN dissection for esophageal squamous cell carcinoma.

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**Background:** We first performed thoracoscopic esophagectomy (TE) as a minimally invasive procedure with the left decubitus position in 1996. In 2009 we developed a hybrid of the prone and left lateral decubitus positions for TE with extended LN dissection (Extensive-TE). The patient is fixed with the semi-prone position and we can easily change patient positions from the left lateral decubitus position to the prone position using rotation system of the operation table. The upper mediastinal procedure including lymphadenectomy along the right and left recurrent laryngeal nerve (RLN) is performed with the patient in the left lateral decubitus position, while the middle and lower mediastinal procedures are performed with the patient in the prone position with artificial pneumothorax. **Methods:** ESCC patients who underwent Extensive-TE between January 2009 and December 2016, were retrospectively reviewed. The patients' background, surgical outcomes, postoperative complications and recurrence-free survival (RFS) were studied. **Results:** Primary tumor was located in Cervical esophagus for 2 (1%), the upper-thoracic esophagus for 28 (15%), the mid-thoracic esophagus for 104 (54%) and the lower-thoracic esophagus for 57 (30%). The number of patients classified with pre-treatment clinical stage of 1/2/3/4 was 94(49%)/42(22%)/46(24%)/9(5%), respectively. Eight patients were evaluated as having cM1 disease due to supraclavicular LN metastasis. The number of patients classified with postoperative pathological stage of 0/1/2/3/4 was 5(3%)/70(37%)/48(26%)/49(27%)/19(7%), respectively. The average total operation time was 542.1 and blood loss was 274.2. The incidence of postoperative pneumonia, anastomotic leakage, chylothorax, and recurrent nerve palsy was 17%, 14%, 2%, and 7% respectively. One patient died postoperatively within 90 days after surgery. Three years RFS with clinical stage of 1/2/3+4 was 91.5%/54.8%/51.9%, respectively. **Conclusions:** The magnifying effect of thoracoscopy enables us to perform more precise surgery and preserve nerve and vessels. Extensive-TE with a hybrid position is thought to be feasible and effective methods. **Research Sponsor:** None.
Surgery for stage IV gastric cancer: An Italian perspective.

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Background: Surgical approach to gastric cancer with hepatic metastases is becoming more and more accepted but few information exist concerning the surgical management of gastric cancer with extra-hepatic metastases. With this retrospective study we evaluated if the prognosis is influenced by different metastatic sites and we looked for the presence of prognostic factors.

Methods: We analysed 282 patients with gastric cancer and synchronous metastases treated at our Institutions from 2010 to January 2017. We investigated survival performances after surgery according to the site of metastases: peritoneal, haematogenous, hepatic, distant lymph nodes and more than one site. Furthermore, we investigated how survival was influenced by patient-, gastric cancer-, metastases- and treatment-related prognostic factors.

Results: Median overall survival was 10.9 months. We found no survival differences according to the site of metastases: median survival was 11.2, 11.6, 9.8, 21.4, 7.0 months for peritoneal, hepatic, lymph-nodal, haematogenous and more than one site of metastases, respectively (p = 0.797). In all subgroups we observed an interesting number of long-term survivors (peritoneal 14.3% ≥36 months, 7.6% ≥60 months; hepatic 13.0% ≥36 months, 2.2% ≥60 months; lymph nodes 12.5% ≥36 months, 3.1% ≥60 months; > 1 site 18.7% ≥36 months, 1.6% ≥60 months). At multivariate analysis the factors that influenced survival were: number of resected lymph-nodes (p = 0.013), extension of lymphadenectomy (p < 0.001), pN (p = 0.003), curativity (p = 0.032) and histology (p = 0.028).

Conclusions: We showed that no differences in overall survival according to site of metastases exist and we suggest that patients in whom a curative resection is possible, should be treated by resection of both gastric cancer and metastases. Research Sponsor: None.
Safety and efficacy of durvalumab following multimodality therapy for locally advanced esophageal and GEJ adenocarcinoma: Two-year follow-up results from Big Ten Cancer Research Consortium study.

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Background: Concurrent chemoradiation (CRT) followed by esophagectomy is a standard of care for locally advanced esophageal (LA-EAC) and GEJ adenocarcinoma. Approximately 50% of patients (pts) experience disease relapse within the 1st yr after treatment (tx) completion. No adjuvant tx has been shown to improve survival in these pts. Immune checkpoint inhibitors have activity in metastatic PD-L1 positive EAC. Preclinical studies have shown radiation +/- chemotherapy upregulate PD-1/PD-L1 pathway. Methods: We conducted a phase II trial evaluating safety and efficacy of durvalumab (durva) in pts with LA-EAC and GEJ adenocarcinoma who have residual disease in surgical specimen after neoadjuvant CRT and R0 resection. Pts received durva 1500mg IV every 4 weeks for up to 1yr. Results: 24 pts were enrolled from 4/2016-1/2018 (median age: 60yrs, range, 43-70). 18 received carbo/paclitaxel and 6 received cis/5-FU concurrently with radiation. Staging at diagnosis: T2N0 (n = 3, 12.5%), T2N2(n = 3, 12.5%), T3N0(n = 6, 25%), T3N1(n = 6, 25%), T3N2(n = 4, 17%), T3N3(n = 1, 4%), T3Nx(n = 1, 4%). 19 pts (79%) had positive lymph nodes (LNs) at the time of surgery following CRT. 12 pts completed 1yr of tx, 12 came off tx because of relapse(6), AEs(5), and consent withdrawal(1). Most common AEs were fatigue(n = 8, 33.3%) and nausea(n = 6, 25%). 3pts (12.5%) developed grade 3 irAEs: pneumonitis(1), hepatitis(1), colitis(1). At median follow up of 21.9mo (range, 1.7-23.9mo), 11 pts have relapsed: 9 distant and 2 locoregional. Two of 3 pts with grade 3 irAEs are alive and disease free at 17 and 23 mo respectively. 1-yr RFS and OS were 79.2% and 95.5%, respectively. RFS at 26 mo was 20.6%. Overall mOS and mOS after relapse were 28.1mo (range, 22.9-28.1) and 11.1 mo (range, 0.1-11.3mo) respectively. The study was expanded to enroll 14 additional pts who are currently undergoing tx. Conclusions: Adjuvant durvalumab following trimodality therapy for LA-EAC and GEJ adenocarcinoma is safe with improvement in 1-yr RFS to 79.2% compared to historical rate of 50%. RFS was 20.6% at 26 months. Evaluation of predictive biomarkers of RFS with durva is underway. Clinical trial information: NCT02639065. Research Sponsor: AstraZeneca.
Propensity score regression analysis of esophageal cancer treatment with surgery alone or neoadjuvant chemotherapy.

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**Background:** The aim of this study was to examine the outcomes of oesophageal adenocarcinoma (OC) treatment with either surgery alone (S), or with neoadjuvant chemotherapy (NAC) followed by surgery (NACS), by means of propensity score (PS) regression analysis, in order to examine whether the benefits reported in the MRC OE02 trial were reproducible in UK cancer network clinical practice. **Methods:** Consecutive patients undergoing potentially curative treatment for OC in a regional cancer network were studied. Multiple regression models, including PS were developed to account for confounding factors and the primary outcome measure was disease-free (DFS) and overall survival (OS). **Results:** A cohort of 440 patients was included in a regression analysis controlling for confounders (176 S, 264 NACS). NACS was associated with positive margin status (NACS vs. S, 42.4% vs. 26.7%, p<0.05), poor 5-year DFS (32.1% vs. 56.9, p<0.001), and poor 5-year OS (27.5% vs. 47.3%, p<0.001). On regression adjustment based on propensity scores, NACS was not associated with DFS (p=0.220) or OS (p=0.431). Mandard tumour regression grade (TRG) was significantly associated with DFS (HR 0.21, 95% CI 0.07-0.70) and OS (HR 0.27 (95% CI 0.13-0.59). Five-year DFS and OS related to TRG was 63.6 and 61.5% vs. 8.0 and 8.6% (p<0.001) for good and poor responders respectively. **Conclusions:** Prescribing NAC to all OC patients risks delay in effective treatment of patients who are relatively chemo-resistant, given the variability in pathological response. Identifying OC patients who derive the most NAC benefit should be the focus. Research Sponsor: None.
Tumor treating fields (TTFields; 150 kHz) and FOLFOX combination treatment effects on gastric cancer in vitro.

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Background: Gastric cancer is the third most common cause of cancer mortality worldwide, yet long-term survival in gastric cancer remains poor despite systemic therapeutic advances. FOLFOX (oxaliplatin, fluorouracil [5-FU], and leucovorin) is an approved chemotherapy regimen for gastric cancer treatment. Tumor Treating Fields (TTFields) are an antimitotic, loco-regional anticancer treatment delivered via non-invasive application of low intensity (1-3V/cm), intermediate frequency (100-500 kHz), alternating electrical fields. TTFields targets rapidly dividing cancer cells by disrupting microtubules leading to mitotic catastrophe, abnormal chromosome segregation, and apoptosis induction. We investigated the potential use of TTFields alone and in combination with FOLFOX for gastric carcinomas. Methods: Gastric cells (AGS and KATO III) were treated for 72 hours with TTFields (1.1 and 1.7 V/cm, respectively) at frequencies of 100-400 kHz using the inovitro system. Efficacy of TTFields and FOLFOX and its individual components was tested by applying TTFields at the optimal frequency in combination with various drug concentrations. Cell counts, apoptosis induction, clonogenic potential, and overall effect were determined. Results: The optimal TTFields frequency that led to the greatest cell count reduction (AGS, 55%; KATO III, 52%) was 150 kHz. The clonogenic potential was reduced by >70% in both cell lines. TTFields combined with each FOLFOX component (oxaliplatin, 5-FU, or leucovorin) led to a significant reduction in AGS and KATO III cell survival (2-way ANOVA, \( P < 0.001 \) for each cell line) versus each treatment alone. In AGS, TTFields plus FOLFOX combination treatment led to a further reduction in the overall effect (cytotoxic and clonogenic; 79%) versus TTFields alone (65%) and FOLFOX alone (34%). Similar results were observed in KATO III cells. Conclusions: These results suggest that TTFields (150 kHz; optimal frequency) are an effective gastric cancer treatment; and combining TTFields with FOLFOX may further enhance efficacy. There is a strong rational to continue exploring the use of TTFields in combination with standard of care for gastric cancer treatment in the clinical settings. Research Sponsor: Novocure.
Neoadjuvant chemotherapy (TPF regimen) followed with robotic surgery and its impact on outcome in management of esophageal cancers: Indian experience.

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**Background:** Neo-adjuvant chemotherapy coupled with robotic three stage esophagectomy have shown promising results in esophageal cancer. **Methods:** 136 patients diagnosed with squamous cell cancer esophagus were included to analyze the benefit of NACT with DCF (docetaxel 75mg/m² day 1, cisplatin 75mg/m² day 1, 5-FU 750mg/m² per day 1-4) regimen 3 cycles followed by three stage robotic esophagectomy. Esophagus, assessed by EUS and PET-CT scan, pre-chemo and post-chemo, in biopsy proven Squamous cell Carcinoma Oesophagus. All the data pertaining to chemotherapy and surgery were prospectively maintained in a data base. **Results:** Median age 62.7 years, male to female 5.9:4.1. T2 4%, T3 90% & T4 6%. N0 10% & N+90%. Post NACT, Partial response of 50.8%, and a complete pathological response of 27.6% was observed with response rate of 66.3%. 20 pts. had mucositis, but none had grade 3 toxicity, neutropenia in 24 pts. and febrile neutropenia in 7 pt., vomiting and fatigue in 35 pts. Mean blood loss 256.5±85.8ml, duration of surgery 322.4±28.4min, ICU stay 1.5±0.8-day, hospital stay 10.5±2.1 day. Proximal and distal margin was negative for all whereas only 2 patients had a positive CRM. Mean Lymph node yield was 22.4±3.5 nodes. All patients had complete robotic surgery with no conversions and major intraoperative complication. Post-operatively Minor complication was noted in 5 patients temporary vocal cord palsy, 10 delayed gastric emptying, wound infection in 3 and minor lung infection 9. Major complication in form of leak (3), stenosis (5), chylous leak (4) was noted. 30-day mortality 4.5%. With the longest follow up of 50 months, 3 year DFS and OS was 75.4% & 68% respectively. **Conclusions:** Neoadjuvant chemotherapy with TPF regimen showed excellent response rates with minimal G3 toxicity and is well tolerated in Indian patients. Combination of NACT with robotic esophagectomy has excellent outcome with low morbidity & mortality. Research Sponsor: None.

Potency of CD8+ T-cell mediated antitumor immunity from intratumoral immunotherapy with STING agonist, ADU-S100, in an esophageal adenocarcinoma model.

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Background: Esophageal adenocarcinoma (EAC) is a deadly disease with poor prognosis due to limited treatment options. STING is a transmembrane protein that activates the transcription of type I IFN genes, resulting in the stimulation of APCs and enhanced CD8+ T-cell infiltration. Recently, STING agonists have demonstrated durable anticancer activity in solid tumors when used alone and in combination with either chemotherapy, radiation or immunotherapy. In this study we evaluated the efficacy and immunomodulatory effects of STING agonist +/- radiation in an established EAC model.

Methods: Esophagojejunostomy was performed on rats to induce reflux leading to the development EAC. At 32 weeks post operatively, rats received either STING (ADU-S100) or placebo (PBS), +/- 16Gy radiation. Drug efficacy was evaluated by pre- and post- treatment MRI, serial biopsies, histology and RT-PCR. Additionally, immunofluorescence was performed using CD8 and PD-L1 antibodies. Results: A comparison of MRIs in the study groups between 32 and 40 weeks demonstrated a mean increase in percentage tumor volume of 76.7 % and 152.4% in the P and P+R arms and a decrease of 30.1 % and 50.8% in the S and S+R arms, respectively (ANOVA test p< 0.0001) Overall, the S+R group demonstrated the best results with maximum mean volume reduction with all cases responding. Downstream gene expression, pre, on, and post- treatment demonstrated significant upregulation of IFNβ, TNFα, IL-6 and CCL-2 in the treatment groups compared with placebo. On and post treatment, radiation alone, ADU-S100 alone and ADU-S100 + radiation groups demonstrated enhanced PD-L1 expression, induced by higher densities of IFNy producing CD8+ T-cells (p < 0.01). Conclusions: ADU-S100 +/- radiation exhibits potent anti-tumor efficacy and a promising immunomodulatory profile in a de novo EAC model providing the rationale for clinical testing, likely concurrently in combination with immune checkpoint inhibitors. Research Sponsor: None.
Cytoreductive surgery in selected patients with metastatic gastric cancer treated with systemic chemotherapy.

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Background: Cytoreductive surgery (CRS – gastrectomy combined with metastasectomy) for non-palliative indications is controversial for patients with metastatic gastric adenocarcinoma (MGA). We hypothesized that CRS in addition to systemic chemotherapy is associated with an improved survival when compared to patients with MGA receiving chemotherapy alone. Methods: Patients with MGA who received systemic chemotherapy between 2004-2016 were identified using the National Cancer Database (NCDB). Nearest neighbor 1:1 propensity score matching of demographic, tumor-related and treatment-related factors was used to create comparable groups. Overall survival (OS) was compared between subgroups using Kaplan-Meier analyses. Immortal bias analysis was performed among those that survived at least 90 days. Results: We identified 29,728 chemotherapy-treated patients who were divided into 4 subgroups: No surgery (NS, n = 25,690), metastasectomy alone (n = 1170), gastrectomy alone (n = 2248) and CRS (n = 620) with a median OS of 8.6, 10.9, 14.8 and 16.3 months, respectively (p < 0.001). Compared to patients who underwent no surgery, patients who underwent CRS were younger (58.9 ± 13.4 vs. 62.0 ± 13.1 years), had lower proportion of disease involving multiple sites (5.0% vs. 26.2%), and were more likely to have clinically occult disease (cM0 58.9% vs. 7.3%) - all p < 0.001. OS for propensity matched patients who underwent CRS (n = 490) was longer than NS (16.3 vs. 8.8 months, p < 0.001), including those with clinical M1 stage (n = 203) in both unmatched and propensity matched (median OS 19.7 vs. 8.6 months, p < 0.001) cohorts. On Cox regression model using the matched data, the hazard ratio for CRS vs. NS was 0.80 (95%CI 0.76-0.84). In the immortal matched cohort, the corresponding median OS was 16.7 vs. 9.7 months, p < 0.001. Conclusions: CRS in addition to systemic chemotherapy may be associated with an OS benefit in a selected group of patients with metastatic gastric adenocarcinoma. Suboptimal matching for tumor burden is our major limitation. In contrast to studies that focus on gastrectomy alone in the setting of MGA, this study highlights the role of CRS among patients receiving systemic chemotherapy. Research Sponsor: None.

Regulation of gastric carcinoma development in gastric adenoma/dysplasia by crebfz inhibition via miRNA-421.

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Background: In our previous study, we identified three miRNAs (hsa-miR-421, hsa-miR-29b-1-5p, and hsa-miR-27b-5p) with two mRNAs (FBXO11 and CREBZF) that might play an important role in the development of gastric adenocarcinoma (GAC) from premalignant adenomas. However, the expression and function of these miRNAs have not been well characterized. Methods: We investigated the roles of CREBZF and miRNAs as potential biomarkers for the progression of gastric cancer (GC) in low-/high-grade dysplasia and early gastric cancer patients using immunohistochemical staining and miRNA in situ hybridization. Considering that targets can modulate in GC, we analyzed the CREBZF expression in gastric cancer cell lines by RT-PCR and western blot analysis. Results: We observed lower expression of CREBZF with increasing miRNAs in the MKN-74 gastric cancer cells compared to that in SNU-NCC-19. Next, the role of CREBZF in MKN-74 gastric cancer cells was investigated via cell viability and migration assays by miRNA/anti-miRNA modulation. Furthermore, we found that hsa-miR-421/hsa-miR-29b-1-5p target CREBZF and might play an important role in the migration of MKN-74 cells. Conclusions: This study suggests that increased CREBZF by hsa-miR-421/hsa-miR-29b-1-5p inhibition may be important to prevent the progression of gastric cancer in its early stage. Research Sponsor: National Research Foundation of Korea (NRF-20141A1A3050247).
LINE-1 hypo-methylation as a distinct phenotype in non-EBV/non-MSI-H esophagogastric junction adenocarcinoma.

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Background: Most esophagogastric junction (EGJ) adenocarcinoma exhibits chromosomal instability (CIN) type with wide range of CpG site methylation. However, it is still uncertain if epigenetic alteration is clinically useful. LINE-1 methylation level is representative of genome-wide methylation status. The aim of this is to examine clinicopathological and molecular characteristics of LINE-1 methylation, and its prognostic role, in non-EBV/non-MSI-H EGJ adenocarcinoma. Methods: After removing EBV-associated or MSI-H tumors, which are the distinct molecular subtype with hyper methylation, a total 335 case of chemo-naive non-EBV/non-MSI-H EGJ adenocarcinoma from four academic institutions in Japan, were eligible. LINE-1 methylation was examined by Pyrosequencing. Results: LINE-1 methylation level was successfully sequenced in 319 cases (92.5%). LINE-1 methylation level was associate with tumor differentiation. Intestinal type was frequently observed in the lowest quartile Q1 cases (P = 0.0006). Of note, TP53 mutation rate was significantly frequent in Q1-2 cases (P < 0.0001). Ki-67 index was also higher in Q1-2 cases. Tumor PD-L1 expression, or CD8+ cell infiltration was not associated with LINE-1 methylation level. In survival analysis, the patients with the lowest LINE-1 methylation level (Q1), experienced the worst outcome in disease-specific survival, relapse-free survival, and overall survival rates. Conclusions: Tumor with LINE-1 hypomethylation harbors significantly higher TP53 mutation and higher Ki-67 index, resulting in worse outcome in EGJ adenocarcinoma patients. Research Sponsor: KAKEN Japan Society for the Promotion of Science.
Significance of intratumoral tertiary lymphoid structure (TLS) as predictive factors of nivolumab therapy after conversion surgery for unresectable gastric cancer: A retrospective study.

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**Background:** Conversion surgery for unresectable advanced gastric cancer has been increasing with the development of chemotherapy. Adjuvant chemotherapy regimens after conversion surgery have not been standardized. The main mechanism of nivolumab is augmentation of antitumor immune response of tumor infiltrating cytotoxic T cells (CTL) to cancer cells, and it has recently been reported that nivolumab therapy before and after chemotherapy is effective in other carcinomas. We previously reported that tertiary lymphoid architecture (TLS) correlates with tumor-infiltrating T cells and is associated with a better prognosis in untreated patients. The purpose of this study was to investigate the relationship between the presence of TLS in the primary tumor and prognosis in patients with gastric cancer who underwent conversion therapy.

**Methods:** We evaluated 52 patients with advanced gastric cancer including 17 patients underwent conversion surgery and 35 patients underwent palliative surgery without prior chemotherapy in our department from 2009 to 2017. The local immune environment and presence of TLS was evaluated by immunohistochemical staining. **Results:** Intratumoral TLS occurred in 20% of patients with advanced cancer who did not receive chemotherapy before surgery and in 52% of patients who received conversion surgery. And the prognosis of patients with the presence of TLS was better than no TLS. Intratumoral CD8 T-cell infiltration was slightly associated presence of TLS. We had a case in which nivolumab was highly effective and converted to conversion surgery, and a case in which nivolumab was highly effective in patients with recurrence after conversion surgery. TLS was observed in the vicinity of the tumor in these patients. **Conclusions:** The prognosis was good in the case in which intratumoral TLS was present after conversion surgery. These results suggest that the adjuvant nivolumab therapy may improve the outcome of patients underwent conversion surgery for advanced gastric cancer. These results suggest that peri-tumor TLS is a predictor of nivolumab efficacy in adjuvant therapy after conversion surgery. Research Sponsor: None.
Correlation of tumor mutation with efficacy in patients with gastric cancer who received nivolumab and ramucirumab combination therapy.

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Background: Nivolumab (Nivo) plus ramucirumab (Ram) showed promising efficacy in the second-line chemotherapy for advanced gastric cancer (AGC) in NIVORAM study with the 44% of objective response rate (ORR) and 38.6% of 6-month progression free survival (PFS) rate. We investigated the correlation of tumor mutation load and efficacy. Methods: Patients received Nivo (3mg/kg, Q2W) in combination with Ram (8mg/kg, Q2W) until unacceptable toxicity or disease progression. Tissue samples were collected before the treatment, and analyzed for tumor mutation load using Oncomine Tumor Mutation Load Assay. Efficacy included ORR, overall survival (OS), PFS and duration of response. OS and PFS curves were estimated using the Kaplan-Meier method. Hazard ratio (HR) was estimated using the Cox proportional hazards model. Results: By the data cut off of December 15, 2018, the median follow duration on therapy was 13.7 month. Thirty AGC pts who obtained tissue sample were analyzed. Median tumor mutation load (TML) was 6.755 mutation/Mb (range 0.84-19.67). Higher TML (cut-off median) related to better tendency of efficacy with ORR (40.0% vs 20.0%), PFS (5.32 vs 2.33 months) and OS (18.1 vs 10.6 months). 6-month PFS rate was better in TML higher group (48%) compared to TML lower group (18%). In multivariate analysis, higher TML showed 2.030 of hazard ratio (95% CI; 0.849-4.855, p=0.112) for PFS, and 1.915 (95% CI; 0.578-6.343, p=0.287) for OS. Conclusions: The patients with higher tumor mutation load have a better tendency for OS and PFS, among AGC patients who received Nivo and Ram combination therapy. Clinical trial information: NCT02999295. Research Sponsor: Ono Pharmaceutical Co. Ltd.
Molecular characterization of a gastric cancer transmitted from an organ donor to four transplant recipients.

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Background: Donor-derived malignancy may occur even when not suspected based on donor or recipient factors, including age and time to cancer diagnosis. Early recognition of donor-derived malignancy has treatment implications. We describe the molecular characterization of a gastric cancer transmitted from an organ donor to heart, liver (LR), left kidney (LKR), and right kidney-pancreas (KPR) recipients. Methods: IRB approval for chart review was obtained; LR, LKR, and KPR also provided research consent for molecular profiling. Short Tandem Repeat (STR) genotyping was performed by polymerase chain reaction and gel electrophoresis. Tumor and germline DNA from patients and the organ donor were subjected to next generation sequencing (NGS) of 479 genes. Fluorescence in situ hybridization (FISH) was used to confirm MET amplification. Results: Donor origin was established by STR analysis, with the tumors showing high levels of donor alleles. Pathology revealed a poorly differentiated adenocarcinoma with signet ring features. Immunohistochemical staining and CA-19-9 elevation were most consistent with gastric or pancreas origin. Tumor sequencing was notable for somatic mutation of CDH1, MET amplification and wild-type KRAS genes. Tumors from LR and KPR were nearly identical based on pathogenic variants, allele frequency, and copy number variation. Insufficient tumor cellularity in all LKR specimens precluded NGS profiling, but clinical testing found that the cancer was mismatch repair proficient; ERBB2 equivocal; and PDL-1 positive. A circulating tumor DNA test did not uncover any genomic alterations; however, MET amplification was confirmed in this tumor using FISH probes. Conclusions: STR analysis and reporting should be standard immediately following diagnosis of cancer in an organ transplant recipient to ascertain donor derivation. Further molecular characterization, including NGS, may aid in defining primary tumor origin. Here, diagnosis with PDL1-positive gastric cancer enabled use of pembrolizumab. One patient remains alive and without evidence of cancer following prompt organ explant after cancer was reported in other recipients. Research Sponsor: None.

A retrospective multicenter study evaluating the efficacy and safety of irinotecan in patients with advanced gastric cancer: Analysis of albumin-bilirubin (ALBI) grade.

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**Background:** It is important to predict prognosis and risk of adverse events in patients with advanced gastric cancer receiving chemotherapy. Albumin-bilirubin (ALBI) grade is recently used as liver function assessment and prognosticator in hepatocellular carcinoma. Irinotecan is metabolized in the liver, so ALBI score may be useful for predicting irinotecan efficacy and safety.

**Methods:** We conducted a retrospective multicenter study and investigated association between efficacy and ALBI grade in patients who received irinotecan monotherapy between January 2010 and December 2017. All patients had to receive fluoropyrimidine and platinum as prior therapy. The ALBI score is calculated by the equation: ALBI score = (log_{10} bilirubin [μmol/L] × 0.66) + (albumin [g/L] × −0.0852). As a result, ALBI grades 1, 2, and 3 were developed as follows: ALBI score ≥ 2.60 (ALBI grade 1), > −2.60 to ≤ −1.39 (ALBI grade 2), and > −1.39 (ALBI grade 3). **Results:** The number of patients with ALBI grade 1/2/3 is 100/68/5. In ALBI 1/2-3 patients, performance status 0/1/2 were 37/57/6 and 17/43/14, treatment line 2nd/3rd or later was 58/42 and 21/53, HER2 positive/negative 14/86 and 16/58, respectively. In ALBI 1/2-3 patients, median PFS was 3.3 and 2.3 months (HR = 0.684, P = 0.018) and median OS was 11.7 and 6.7 months (HR = 0.492, P < 0.001), respectively. In ALBI 1/2-3 patients, median treatment cycle which was 6 and 4 (P = 0.09) and RDI were significantly different was, and RDI was 0.80 vs 0.70 (P = 0.027), respectively. Hematological AEs were observed in 88% and 87% (P = 1.000), severe hematological AEs (≥G3) were 41% and 58% (P = 0.040). Non-hematological AEs were 87% and 86% (P = 1.000), severe non-hematological AEs (≥G3) were 11% and 18% (P = 0.257), respectively. Severe AEs in more than 5% patients were leukopenia (12% and 18%), neutropenia (23% and 28%), anemia (16% and 31%), and anorexia (2% and 10%). In multivariate analysis, ALBI grade was associated with shorter OS (ALBI 1 and 2-3: HR 1.773 95%C.I. 1.184-2.654, P = 0.005). **Conclusions:** ALBI grade might be both prognostic factor and risk factor in treatment with irinotecan monotherapy for patients with AGC. Research Sponsor: None.
Transcriptional profile of immune microenvironment and their prediction role for the prognosis of esophageal squamous cell carcinoma.

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**Background:** Esophageal squamous cell carcinoma (ESCC) is one of the most common cancer in China. The genetic characterizations have already been described in many studies, but the immune microenvironment features were seldom reported. Our study was aimed to explore the relationship between the immune profile in stage IIIa ESCC and patients’ prognosis. **Methods:** 20 eligible stage IIIa ESCC patients with received surgery and radiotherapy (19 with and 1 without radiotherapy). RNA targeted sequencing was performed on 20 primary tumor specimens. Transcripts of 395 immune-related genes expressed in tumor were analyzed. The univariate and multivariate Cox proportional hazards analyses were examined the relations of 395 genes’ expression and the prognosis. **Results:** Patients were divided into two groups based on the median expression values of 395 genes. The univariate analyses showed 20 genes were significantly associated with overall survival (OS). Unsupervised hierarchical clustering analysis using 20 gene expression data revealed two distinct clusters (cluster 1 and 2). The cluster1 patients had high level expression of AXL, ADGRE5, CD40, CXCR6, MPO, etc., which were associated with tumor proliferation and migration. However, the cluster2 patients expressed higher NOS2, IL15, IKZF2, TNFRSF18 which were related with T lymphocyte activated. Therefore, the cluster2 patients had significantly longer OS than cluster 1. Moreover, the combined expression of 10 genes (CD40, ADGRE5, CSF1R, CCR1, IGSF6, MPO, MRC1, SRGN, CD63, LRP1) which had high correlation among 20 genes were significantly related to OS and DFS (disease free survival) in univariate analysis. The multivariate analyses demonstrated that 10 genes signature expression was the independent high risk factor for OS, and the low signature value was associated with better prognosis. **Conclusions:** In IIIa ESCC, the 20 genes can profile the tumor immune microenvironment, and were independently associated with the patients’ OS. The 10 genes’ signature which represents the malignancy and immune activation of tumor was an independent predictive factor for OS, which can identify the patients with favorable or poor prognosis. Research Sponsor: Guangxi medical and health appropriate technology development and extension application project (S2019012).
Gastric Immune Prognostic Index (GIPI) in metastatic (m) gastro-oesophageal junction (GOJ)/gastric cancer (GC) patients (pts) treated with PD-1/PD-L1 immune checkpoint inhibitors (ICIs).

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Background: ICIs demonstrated improved overall survival (OS) in heavily pre-treated mGOJ/GC pts. Pts selection exclusively based on PD-L1 tissue expression appears to be suboptimal, despite data from subgroup analyses of KEYNOTE trials. Strong rationale suggests a potential predictive role of inflammatory biomarkers in ICIs treated mGOJ/GC pts. Methods: 11 systemic inflammatory markers [platelets, monocytes, neutrophil/lymphocyte ratio (NLR), platelets-lymphocyte ratio, lymphocytes, sum of mononuclear cells, albumin, lactate dehydrogenase, alkaline phosphatase (ALP), c-reactive protein (CRP) and serum globulin] were retrospectively analyzed at baseline in 57 mGOJ/GC pts with unknown PD-L1 status treated in second-line with ICIs, and correlated with OS. Least Absolute Shrinkage and Selection Operator (LASSO) method was used to select variables (preliminarily subject to optimal coding using HR smoothed curves for OS) with the highest prognostic value. Selected variables were then analysed in a multivariate Cox Regression Model and used to build a GIPI nomogram. Results: NLR and CRP taken as continuous variables and ALP categorized as < vs > 150 IU/L were found as the most meaningful independent predictors of OS [(HR 1.30 (95%CI 1.02-1.65), 2.00 (95%CI 1.09-3.66), 2.82 (95%CI 1.29-6.20) and p values 0.04, 0.01, 0.02, respectively)] and used to build the GIPI nomogram. Nomogram-based lowest(l), mid and highest(h) risk tertiles were associated with median(m)OS of 14.5, 10.6 and 2.4 months(mos), respectively [HR of l vs h 0.26 (95%CI 0.12-0.53), p 0.0002]. By optimally dichotomizing CRP and NLR, pts with one or more of the following risk factors: NLR > 6, CRP > 15 mg/L, ALP > 150 IU/L (n: 31) had a mOS of 3.9mos vs 14.5mos of pts with no risk factor (n: 26) (HR 2.72, p 0.0005). Conclusions: GIPI, combining NLR, CRP and ALP, is the first inflammatory index with a significant prognostic value in mOGJ/GC pts receiving second line ICIs. Its implementation with analysis of PD-L1 expression in the present cohort is ongoing. GIPI merits validation in external cohorts and prospective clinical trials. Research Sponsor: None.
Molecular landscape of gastric cancer (GC) harboring mutations of histone methyltransferases.

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Background: Alteration of histone modifications participating in transcription and genomic instability, has been recognized as an important role in tumorigenesis. Aberrant expression of histone-lysine N-methyltransferase 2 (KMT2) family, which methylate histone H3 on lysine 4, is significantly correlated with poor survival in GC. Understanding how gene mutations of KMT2 family interact to affect cancer progression could lead to new treatment strategies. Methods: A total of 1,245 GC were analyzed using next-generation sequencing (NGS) and immunohistochemistry (IHC; Caris Life Sciences, Phoenix, AZ). Tumor mutational burden (TMB) was calculated based on somatic nonsynonymous mutations, and MSI status was evaluated by a combination of IHC, fragment analysis and NGS. PD-L1 status was analyzed by IHC (SP142). Gene fusions were detected by Archer (N = 59) or whole-transcriptome sequencing (N = 129). Results: The overall mutation rate of genes in KMT2 family was 10.6% (KMT2A: 1.7%, KMT2C: 4.7%, KMT2D: 7.1%). Overall, the mutation rates were significantly higher in KMT2-mutated (MT) GC than KMT2-wild type (WT) GC, except for TP53 (43% vs 63%, p < .0001). Interestingly, among the genes with significant higher mutation rates in KMT2-MT GC, 28% (21/76) of them were related to DNA damage repair (including BRCA1/2, RAD50) and 33% (25/76) of them were related to chromatin remodeling (including ARID1A/2, SMARCA4). Overexpression of HER2, amplifications of KRAS, CDK6 and HER2 were significant lower, while PCM1 and BCL3 amplifications were significant higher in KMT2-MT, compared to KMT2-WT GC (p < .05). Significantly higher prevalence of TMB-high (>17mut/MB) (49% vs 3%), MSI-H (53% vs 2%), and PD-L1 overexpression (20% vs 7%) were present in KMT2-MT GC, compared to KMT2-WT GC (p < .001). The rates of fusions involving ARHGAP26 (19% vs 3%, p < .01) and RELA (29% vs 0%, p < .001) were significantly higher in KMT2-MT than those in KMT2-WT GC. Conclusions: This is the largest study to investigate the distinct genomic landscape between KMT2-MT and WT GC. Our data indicates that KMT2-MT GC patients could potentially benefit from agents targeting DNA damage repair and immunotherapy, which warrants further in-vitro and in-vivo investigation. Research Sponsor: None.
Background: 18F-FDG PET is widely used in clinical cancer diagnostics. However, 18F-FDG PET scan in gastric cancer (GC) is still controversial because of its lower sensitivity in diagnosis and staging compared to other imaging modalities. The purpose of this study was to establish a gene panel for 18F-FDG PET positivity in GC by using patient-derived xenografts (PDXs).

Methods: BALB/c nude mice were subcutaneously implanted with 30 cases of GC PDX tissues and underwent a simultaneous PET/MRI scanner. Using RNA-seq data of the 30 GC PDXs for training set, we constructed a gene co-expression network which was correlated with the maximal standardized uptake values (SUVmax). The least absolute shrinkage and selection operator (LASSO) was used for identification of genomic signature for the PET positivity and a prediction model was established. By using qRT-PCR, a gene panel (PredictionScore) based on the gene signature was developed.

Results: We found that the PDXs could recapitulate FDG avidity of those parental tumors between 15 Patient-PDX pairs (Spearman r = 0.54, p-value = 0.04). The prediction model with the identified five genes (PLS1, PYY, HBQ1, SLC6A5, NAT16) provided excellent prediction values compared with actual SUVmax for 15 patients as a validation set (Spearman r = 0.56, p-value = 0.03) and for 8 patients as a test set (Spearman r = 0.90, p-value = 0.005). The PredictionScore showed significant positive correlation with the actual SUVmax for 7 patients as an external validation set (Spearman r = 0.82, p-value = 0.03).

Conclusions: PDX can be used to develop a gene panel for the PET positivity prediction in GC. Our results showed that the scoring system can be clinically applicable for developing a predicted stratification model. Future studies will aim to evaluate the panel for a higher number of PET-scanned GC patients to establish a rational patient selection for PET scan in clinical settings. Research Sponsor: Development of standard personalized medicine platform integrating clinical genomics with PDX models.
The FGFR-inhibitor derazantinib (DZB) is active in PDX-models of GI-cancer with specific aberrations in FGFR.

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Background: DZB is an oral small-molecule Fibroblast Growth Factor Receptor 1/2/3 inhibitor (FGFRi) with clinical activity in FGFR2-fusion-positive cholangiocarcinoma. DZB was screened for activity in gastrointestinal cancer (GIC), by using a panel of GIC cell-lines, human tumor xenografts and 30 GIC patient-derived xenograft (PDX) models. Methods: DZB anti-proliferative potency was determined in 26 GIC cell lines to determine the GI50. The GIC cell-line, SNU-16 was grown s.c. in nude mice and treated daily for 3-weeks with DZB at the MTD of 75 mg/kg, p.o. Plasma and tumor were removed and analyzed for drug-levels and PD biomarkers to assess pathway inhibition. DZB (@MTD) was tested in the PDX-screen (15 biliary, 13 gastric and 2 colorectal cancer; n=3/group) using models with FGFR-fusions, FGFR-mutations and/or differing FGFR copy-number (CN)/RNA-seq expression levels. Efficacy and tolerability were quantified as a dT/C (treated/control).

Results: Cellular GI50s ranged from 0.02-20 μM; the most sensitive (GI50=0.5 μM) had FGFR-fusions or high-expression. In mice, DZB induced stasis of SNU-16 tumors (dT/C=0.0) and was well tolerated (dT/C > 1.0); the plasma PK was dose-dependent with a Cmax of 2 μM (4 hr), a Cmin of 0.5 μM. DZB induced dose- and time-dependent changes in the MAPK-pathway and expression of downstream genes, consistent with its mode of action. In PDX-models, efficacy varied from no-response to 100% regression. Known driver-mutations were associated with partial-responses (best dT/C = 0.42), but models with FGFR-fusions, especially FGFR2-fusions, were very sensitive leading to stasis or strong-regression, particularly in gastric cancer. High-expression of FGFR2 was also associated with strong responses. There was no direct correlation between CN and high RNA-seq values suggesting amplification was not always a predictor of high expression. Endpoint PD-analyses of the PDX-models is ongoing to identify other potential stratifiers and PD-markers of response. Conclusions: DZB showed convincing activity in GIC-models with FGFR-fusions and/or high expression. A clinical trial is planned in patients with gastric cancer to investigate DZB as mono- and combination-therapy. Research Sponsor: Basilea Pharmaceutica International Ltd.
Comparison of immune-related gene expression between primary and metastatic site in advanced gastric cancer patients with peritoneal dissemination.

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Background: Immune checkpoints inhibitor (ICI) is effective and approved in some solid tumors including advanced gastric cancer (GC). Peritoneal dissemination is known as a poor prognostic factor and was reported to be associated with the resistance to ICI according to the previous reports. The aim of our study is to compare the immune-related gene expression between primary site and peritoneal lesion in advanced GC patients. Methods: Among advanced GC patients, we selected those who underwent surgical resection for both primary and peritoneal lesions simultaneously. Formalin-fixed paraffin-embedded (FFPE) tumor tissues of primary and peritoneal lesions were prepared and RNA was extracted by Maxwell RSC RNA FFPE kit (Promega). Immune-related gene expression was evaluated by using nCounter Max Analysis System (NanoString). We used nCounter PanCancer Immune Profiling Panel Kit which includes 770 immune-related genes. Results: Immune-related gene expression was evaluated by using twenty-four FFPE tumor tissues in twelve GC patients. Scatter plot and hierarchical clustering analyses showed that the pattern of immune-related gene expression was not much different between primary and peritoneal lesions beyond the individual differences. Regarding the T cell function, high expression of Immune-related genes was widely detected in patients with EB virus-positive (n = 2) and HER2-positive (n = 1). Gene expressions such as CD70, FAS, MAF and IL-3 were higher in peritoneal lesion compared with primary lesion (p < 0.05). Whereas, expressions of F2RL1 and IL-11 were lower in peritoneal lesion compared with primary lesion (p < 0.05). Conclusions: Our study indicated that there was not much difference of Immune-related gene expression between primary and peritoneal lesion in advanced GC patients. Positive status of EB virus and HER2 may be associated with high expression of immune-related genes. Further analysis to evaluate immune-related gene expression between primary and metastatic site may contribute the further understanding of cancer immunity in advanced GC. Research Sponsor: Grant-in-Aid for Scientific Research.
Gene mutations distinguishing gastric from colorectal and esophageal adenocarcinomas.

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Background: Genetic analysis of gastrointestinal malignancies shows a great number of mutations. Most mutations found in gastric tumors are found in colorectal and esophageal tumors, and vice versa. The challenge remains to identify mutations that distinguish gastric from colorectal and esophageal cancers. Using open-access cancer genomics data, we sought to identify mutations that accounted for the unique phenotypic features of gastric tumors. Methods: Thirteen cancer genomics datasets with demographic, clinical, and genetic variables were analyzed. Each subject was flagged with or without a mutated gene. For each anatomical location, pathologic stage and histology were compared between subjects with and without a specific mutated gene, using two-sample t tests, adjusted for multiple gene testing. Results: Analysis included 1,915 subjects with valid pathologic stage and histology. Mean age was 68 years (SD=10). About 54% were female. The most common race was Caucasian (37%) while minorities were rare with high rate of missing data (44%). Pathologic stage: 20% stage I, 35% stage II, 31% stage III, and 14% stage IV. Anatomical location: 29.5% gastric, 59.5% colorectal, and 11.0% esophageal. Histology of gastric cancer: 61.4% intestinal, 23.2% diffuse, 14.9% others, and 0.5% missing. One gene—HEATR7B2—though rarely mutated, occurred only in stage IV of gastric tumors. Two mutated genes—CDH1, RHOA—distinguished diffuse from intestinal gastric histology. One mutated gene—CDH1—distinguished gastric from colorectal and esophageal tumors. Conclusions: This study confirmed the genes involved in the pathogenesis of gastric malignancies (CDH1, RHOA) and linked one novel gene to stage IV of gastric tumors (HEATR7B2). Future animal and human epidemiologic studies are needed to elucidate how this novel gene contributes to gastric malignancies. Research Sponsor: None.
Tumor microenvironment evaluation to predict pembrolizumab benefit of metastatic gastric cancer: Results from phase II clinical trial.

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Background: Clinical studies support the efficacy of immune checkpoint blockades (ICBs) in a subset of patients with metastatic gastric cancer (mGC). With the aim of identifying determinants of response to ICBs, we performed molecular characterization of tissues from 61 patients with mGC who were treated with pembrolizumab as salvage treatment in a prospective phase 2 clinical trial (NCT#02589496).

Methods: Of 61 patients, 60 patients underwent pretreatment biopsy and 45 specimens were of sufficiently high quality for RNA sequencing. TMEscore, which was previously established to quantify the tumor microenvironment (TME), was used to estimated TME of pretreatment specimens. The predictive value and correlation of integrative molecular characterization were systematically explored. Results: We established a methodology (TMEscore) to evaluated the TME of GC patients, which was previously found to be a robust prognostic and predictive biomarker for patients treated with ICBs. By applying ROC curve analysis, the TMEscore was found to be a best predictive biomarker (TMEscore: AUC = 0.891; CPS: AUC = 0.830; TMB: AUC = 0.672; MSI status: AUC = 0.708; EBV status: AUC = 0.727; respectively). Moreover, TMEscore was the most significant gene signature that correlated with tumor response (TMEscore: P = 1.7 x 10^-5; GEPs: P = 0.00035; ImmunoScore: P = 0.29106; CD8+ T cell fraction: P = 0.00011; Immune checkpoint score: P = 0.00149; respectively). TMB was not correlated with TMEscore (Kruskal-Wallis test, P = 0.14). A higher TMEscore was significantly associated with EBV+ and high-MSI TCGA molecular subtypes (Kruskal-Wallis test, P = 0.002) which were reported to benefit from ICBs of GC.

Conclusions: These findings indicate that the assessment of TMEscore via high throughput-sequencing and PCA algorithm provides a robust biomarker for the selection of GC patients who may derive greater benefit from pembrolizumab. Our data also suggest that TMEscore may be a more accurate predictive biomarker than TMB, MSI and EBV status, and this resource may help facilitate the development of precision immunotherapy. Clinical trial information: NCT#02589496. Research Sponsor: Merck Sharp & Dohme Corp., USA. Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea (HI16C1990).
**Slug overexpression and association with clinicopathological features in gastric cancer.**

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**Background:** Slug is a suppressive transcriptional factor of E-cadherin, acting as an activator of epithelial-mesenchymal transition (EMT). Its clinical relevance in gastric cancer (GC) is not fully known. **Methods:** Our study evaluated the expression patterns of EMT and cancer stem cell markers in GC patients who had clinical stage 2-3, underwent gastrectomy, D2 lymph node dissection (LND), adjuvant chemotherapy. Immunohistochemistry of E-cadherin, vimentin, CD133, ABCG2, NEDD9, SMAD4, XB130, Slug, Snail were investigated from 210 gastric cancer samples using tissue microarrays. The correlation between each markers expressed and the association with clinicopathological factors were analyzed. **Results:** Slug expression was more frequent in stage 3 than stage 2 (p=0.000), advanced T (p=0.007) and N stage (p=0.001), while histologic type did not make difference. Slug expression correlated with the expression of cancer stem cell marker CD133 (r=0.180, p=0.015) and CD133 expression was also related with ABCG2 (r=0.412, p=0.000). High Slug group showed shorter overall survival, compared to low Slug group (median OS 134 vs 124 months, p=0.044). The 2-year and 5-year disease-free (DF) rate for patients with high Slug and low Slug was 87.1% and 79.8%, 68.1% and 79.8%, respectively (p=0.038). The DFS curve reached an earlier plateau at 11-month in low Slug group, while in high Slug group took as long as 99 months. A multivariate analysis using the Cox proportional hazards regression model demonstrated Slug to be an independent prognostic factor for overall survival; hazard ratio 0.504 [95% CI 0.278-0.916] (p=0.025). **Conclusions:** In stage 2-3 GC patients who underwent gastrectomy with D2 LND and adjuvant chemotherapy, high Slug expression is associated with better disease-free and overall survival. Patients may benefit by testing Slug immunohistochemistry to predict prognosis after gastrectomy. Research Sponsor: None.
Efficacy of pembrolizumab (pembro) monotherapy versus chemotherapy for PD-L1-positive (CPS ≥10) advanced G/GEJ cancer in the phase II KEYNOTE-059 (cohort 1) and phase III KEYNOTE-061 and KEYNOTE-062 studies.

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Background: Pts with advanced gastric/gastroesophageal junction (G/GEJ) cancer received pembro monotherapy (200 mg Q3W) 3L+ in cohort 1 of KEYNOTE-059 (NCT02335411), 2L in KEYNOTE-061 (NCT02370498), or 1L in KEYNOTE-062 (NCT02494583). We present efficacy data for patients with PD-L1 combined positive score (CPS) ≥10 tumors in these trials. Methods: In study 059, 46 pts in cohort 1 with PD-L1 CPS ≥10 received pembro. In study 061, 108 pts with PD-L1 CPS ≥10 received pembro (n=53) or chemotherapy (chemo; n=55). In study 062, 182 pts with CPS ≥10 received pembro (n=92) or placebo + chemo (n=90). Efficacy end points included overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and duration of response (DOR). Results: Median follow-up in study 059 was 5.6 mo. Median OS with pembro was 7.9 mo (95% CI, 5.8-11.1), and 12-mo OS was 32.6%. PFS at 6 mo was 17.4%, ORR was 17.4%, and median DOR was 20.9 mo (2.8+ to 34.9+). In study 061, after a median follow-up of 8.8 mo, pembro prolonged OS vs chemo (median 10.4 vs 8.0 mo; HR, 0.64; 95% CI, 0.41-1.02); 12-mo OS was 45.3% for pembro and 23.6% for chemo. Median PFS was 2.7 mo for pembro and 3.4 mo for chemo (HR, 0.86; 95% CI, 0.56-1.33). ORR was 24.5% vs 9.1%, and median DOR was NR (4.1 to 26.0+) and 6.9 mo (2.6-6.9) for pembro vs chemo. In study 062, median follow-up was 17.4 mo for pembro and 10.8 mo for chemo. Pembro prolonged OS vs chemo (median 17.4 vs 10.8 mo; HR, 0.69; 95% CI, 0.49-0.97); 12-mo OS was 56.5% vs 46.7%. Median PFS was 2.9 mo vs 6.1 mo (HR, 1.09, 95% CI, 0.79-1.49). ORR was 25.0% vs 37.8%, and median DOR was 19.3 mo (1.4+ to 33.6+) vs 6.8 mo (1.5+ to 30.4+) for pembro vs chemo, respectively. Conclusions: Collectively, these data indicate that 1L, 2L, and 3L+ pembro monotherapy showed clinically meaningful efficacy in CPS ≥10, with a more durable response than chemotherapy. Clinical trial information: NCT02335411, NCT02370498, and NCT02494583. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

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<td></td>
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<td>ORR, %</td>
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<td>Median (range) DOR, mo</td>
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<td>6.8 (1.5+ to 30.4+)</td>
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The clinical prognostic significance of lymphovascular invasion in gastric cancer.

Hirohito Fujikawa, Takanobu Yamada, Keisuke Koumori, Hayato Watanabe, Kazuki Kano, Yota Shimoda, Yasushi Rino, Munetaka Masuda, Takashi Ogata, Takashi Oshima; Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan; Kanagawa Cancer Center, Yokohama, Japan; Yokohama City University, Yokohama, Japan; Department of Surgery, Yokohama City University, Yokohama, Japan

Background: Lymphovascular invasion (LVI) of malignant tumor is regarded as an initial state of metastasis, including the lymph nodes, and therefore may be a prognostic factor in many malignancies. However, in gastric cancer, according to the current Japanese guidelines, LVI is not clinically useful information, except for in predicting the curability of endoscopic resection, and its clinicopathological characteristics and biological behavior remain unclear. The present study explored the histopathological significance of LVI in gastric cancer and clarified its correlation with the prognosis. Methods: From January 2000 to December 2013, a total of 2090 cases of gastric cancer undergoing radical gastrectomy were enrolled in this study. The correlation of LVI and other histopathological factors with the prognosis was evaluated. Lymphatic vessel invasion (ly) and venous invasion (v) were diagnosed followed the current Japanese classification. LVI positivity (LVIP) and LVI negativity (LVIN) were defined as the presence of lymphatic vessel and/or venous invasion and the absence of LVI, respectively. Results: LVIP was noted in 894 cases (42.8%). The age (p < 0.001), depth of tumor invasion (pT) (p < 0.001), lymph node metastasis (pN) (p < 0.001), and maximum tumor size (p < 0.001) were significantly correlated with the presence of LVI. A multivariate analysis showed that pT (p < 0.001), pN (p < 0.001), and LVI (p = 0.03) were independent risk factors for the prognosis of all patients. On analyzing the significance of every T factor and N factor for the overall survival of LVIP and LVIN cases, no significant difference was recognized in the prognosis among all pT1 patients and pT2-4 patients without nodal metastasis. However, in pT2-4 patients with nodal metastasis, a significant difference was revealed, and the 5-year overall survival rates in LVIP cases were lower than those in LVIN (60.9% [95% confidence interval: 56.3-65.3] vs. 76.7% [95% confidence interval 65.2-84.8], p = 0.005). Conclusions: LVI in gastric cancer is an independent prognostic factor, and its effect tends to be particularly strong in advanced cancer with lymph node metastasis. These patients may therefore require more effective adjuvant therapy. Research Sponsor: None.
Correlation of radiomics of metastatic lesions in gastroesophageal adenocarcinoma (GEA) with tumoral DKK1 mRNA expression and other immune biomarkers in patients (pts) treated with DKN-01.

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Background: Dickkopf-1 (DKK1) modulates Wnt and PI3K/AKT signaling pathways and contributes to an immune suppressive tumor microenvironment. Recently, anti-DKK1 antibody (DKN-01) [D] plus pembrolizumab (P) in GEA tumors has demonstrated clinical activity. Radiomic Quantitative Texture Analysis (QTA) is a non-invasive method for imaging biomarker discovery that can predict molecular drivers of cancer from CT scans obtained during clinical trials. QTA may be a useful tool for predicting DKK1 expression and other immune biomarkers in metastatic lesions from GEA pts treated with DKN-01.

Methods: 13 pts with GEA (12 M; 1F; age 37-81) enrolled in D+P Phase I/II trial with high vs low DKK1 RNA Scope H-Scores (H Score > 35; n = 6 vs H-Score < 35; n = 7) were identified. Metastatic Target lesions (TLs) from baseline CTs with IV contrast underwent additional QTA analysis (TexRAD, CE mark, Essex, UK) after RECIST analysis. ROIs were placed on the TLs and histogram frequency curves (HFC) of the metastatic tumor pixels were generated. First order tumor HFC statistical results (i.e. mean, Standard Deviation-SD, Skewness, Kurtosis, MPP) were correlated with tumoral DKK1 mRNA expression, baseline plasma DKK1 levels and other biomarkers (PD-L1 CPS and MDSCs) along with tumor shrinkage using Pearson’s r correlation (significance p < 0.05). Results: Tumor derived QTA parameter (QTA SD) of the largest metastatic TL from each subject was positively correlated with DKK1 RNAscope H-score (r = 0.661, p value = .014) meaning larger SD texture scores had greater DKK1 expression. Also, tumor derived QTA parameter (QTA MPP) was correlated with baseline plasma DKK1 (r = -0.461, p = 0.005). Finally, QTA SD was correlated with PD-L1 expression (r = 0.630, p = 0.028) and TL shrinkage (r = -0.590, p = 0.034).

Conclusions: Radiomics of GEA tumor metastasis using QTA showed significant correlations between tumor texture, tumor DKK1 mRNA expression and baseline plasma DKK1 suggesting that tumor textures may provide a non-invasive tool for assessing DKK1. Although promising as a imaging biomarker, further studies are required to validate these findings. Clinical trial information: NCT02013154. Research Sponsor: Leap Therapeutics.
Pembrolizumab (pembro) in microsatellite instability-high (MSI-H) advanced gastric/gastroesophageal junction (G/GEJ) cancer by line of therapy.

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Background: Pembro has demonstrated promising antitumor activity in patients (pts) with advanced G/GEJ cancer with PD-L1 CPS ≥1 and CPS ≥10 irrespective of MSI-H status. Here, we examine the antitumor activity of pembro monotherapy vs chemo in pts with MSI-H, advanced G/GEJ cancer in KEYNOTE (KN)-059 (NCT02335411), KN061 (NCT02370498), and KN062 (NCT02494583).

Methods: Eligible pts with advanced G/GEJ cancer with ≥2 prior therapies (KN059 cohort 1; 3L+), 1 prior therapy (KN061; 2L), or no prior therapy (KN062; 1L) were enrolled. In KN059 cohort 1, pts received pembro only. In KN061 pts were randomized to pembro or paclitaxel (chemo), and in KN062 to pembro, pembro + cisplatin+5-FU/cape (chemo), or chemo. Pts received pembro 200 mg Q3W for up to 2 y. MSI-H status was determined centrally by PCR. Endpoints included OS, PFS, ORR, and safety. Data cutoff dates were Aug 8, 2018 (KN059), Oct 26, 2017 (KN061), and Mar 26, 2019 (KN062).

Results: At data cutoff, 259 pts (n = 7 [3%] MSI-H) had enrolled in KN059 cohort 1 (3L+), 592 (27 [5%] MSI-H) in KN061 (2L), and 763 (50 [7%] MSI-H) in KN062 (1L). Median follow-up was 5.6 mo, 7.9 mo, and 11.3 mo, respectively. For the overall study populations, median OS was 5.5 mo for pembro (3L+), 6.7 mo vs 8.3 mo for pembro vs chemo (2L), and 10.6 mo vs 11.0 mo for pembro vs chemo (1L). Median PFS was 2.0 mo (3L+), 1.5 vs 4.1 mo (2L), and 2.0 vs 6.4 mo (1L). ORR was 11.6% (3L+), 11.1% vs 12.5% (2L), and 14.8% vs 37.2% (1L), with median DOR of 16.1 mo, 18.0 vs 5.5 mo, and 13.7 vs 6.8 mo. In pts with MSI-H tumors, OS and PFS were prolonged with pembro vs chemo, with higher ORR (Table).

Conclusions: As with PD-L1 expressers, MSI-H status is a predictive biomarker for pembro monotherapy in advanced G/GEJ cancer irrespective of line of therapy. Clinical trial information: (KN)-059 (NCT02335411), KN061 (NCT02370498), and KN062 (NCT02494583). Merck & Co., Inc., Kenilworth, NJ, USA.

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<th>KN062 (1L)*</th>
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<td>N = 296</td>
<td>N = 256</td>
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<td>Pembro</td>
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<td>mPFS, mo (95% CI)</td>
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<tr>
<td>ORR, %</td>
<td>4 (57.1)</td>
<td>7 (46.7)</td>
<td>8 (57.8)</td>
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<td>m, median; NR, not reached; *Only pembro monotherapy &amp; chemo alone arms included.</td>
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**Background:** FGFR2 and HER2 proteins are well-known molecular targets for cancer therapy, and there are emerging attractive protein-targeted agents such as second generation antibody-drug conjugates. However, there are still limited information about the expression status of FGFR2 and HER2 in gastrointestinal cancer and their relationship to patient background with cancer. In this study, expression status of FGFR2 and HER2 in advanced/metastatic gastric cancer (GC) and colorectal cancer (CRC) were prospectively analyzed in clinical setting. Moreover, eligible patients for the clinical trials of DS-1123 or DS-8201, which are FGFR2- or HER2-targeting anti-cancer agent respectively, were screened.

**Methods:** Patients with advanced/metastatic GC, gastroesophageal junctional cancer (GEJ), and CRC were enrolled. Expression status of FGFR2 and HER2 were prospectively analyzed by IHC and/or FISH. Results: A total of 565 patients (GC; 160, GEJ; 16, CRC; 389) have been enrolled in this study from November 2016 to June 2018. FGFR2 expression (IHC 1+~3+) was observed in 24%, 44%, and 3% of GC, GEJ, and CRC respectively. HER2 expression (IHC 2+, 3+) was observed in 24%, 44%, and 17% of GC, GEJ, and CRC respectively. Expression levels of FGFR2 and HER2 seemed to be not correlated with each other in all 3 types of cancer. Distributions of expression level of FGFR2 or HER2 were slightly different among the histological types in GC. In CRC, distribution of HER2 expression level was also slightly different among the histological types and HER2 expression level was higher in KRAS/NRAS wild type compared to KRAS/NRAS mutant. There was no association between HER2 expression level and primary tumor sites in patients with CRC. Slight concordance of HER2 expression was observed between IHC and FISH in CRC. A total of 7 patients have been enrolled in clinical trials of DS-1123 or DS-8201 through this study based on the analysis findings.

**Conclusions:** This study showed insights into the expression status of FGFR2 and HER2 in GC and CRC as a large-scale prospective analysis. Seven patients who had no standard therapy could access exploratory new drug based on targetable agents through this study. Clinical trial information: 163380. Research Sponsor: Daiichi Sankyo.
Gastric Cancer Registry: A comprehensive patient-reported resource for multidisciplinary and translational genomic approaches to gastric cancer.

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Background: Gastric cancer (GC) is the fifth leading cancer diagnosis and third frequent cause of cancer death globally. GC results from a cascade of molecular and genetic changes owing to environmental and genetic factors. While there are known risks to GC, more is to be learned about its development so to establish effective screens for early stages of cancer. Methods: The Gastric Cancer Registry (GCR) was built to investigate GC and discover informative genomic biomarkers. The GCR comprises medical, family, and social history and genomics data from patients with GC, a family history of GC, and/or a known mutation in the gene CDH1. Samples of saliva and gastric tumors are collected when available. The GCR allows us to leverage several genome sequencing datasets to construct a complete molecular landscape of GC. Early analysis of GC tissue includes whole exome sequencing (WES) to identify mutations, whole genome sequencing (WGS) for copy number variation, and RNA sequencing (RNAseq) for expression profiling. Results are used to inform of clonal neoantigens, microbiome, and immune cell populations. Saliva will be analyzed with linked reads sequencing to unearth germline mutations not picked up in standard clinical gene panels. Results: Datasets from 455 patients and samples from 159 patients have been collected. In a pilot study, we pinpointed specific mutations using WES and revealed extensive changes in genome copy number involving clinically actionable genes through WGS. Most tumors had a high degree of genomic instability and exhibited candidate markers for treatment decisions and response. Additionally, we found that RNAseq revealed tumor subgroups through gene expression signatures. Conclusions: The GCR is an informative resource enabling the identification of biomarkers for GC. With the GCR we are integrating expertise in translational cancer genomics with molecular biology, statistics, and bioinformatics to build a platform for discovery and the development of tools that will ultimately improve the detection, treatment, and prevention of GC. Research Sponsor: Gastric Cancer Foundation.
MT-5111: A novel HER2 targeting engineered toxin body in clinical development.

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Background: Engineered toxin bodies (ETBs) are comprised of a proprietarily engineered Shiga-like Toxin A subunit genetically fused to antibody-like binding domains. MT-5111 is a de-immunized ETB targeting HER2 for solid tumors. MT-5111 works through a novel mechanism of direct cell-kill, via enzymatic ribosome inactivation, and may not be subject to resistance mechanisms that exist for TKI, ADC, or antibody modalities. MT-5111 binds an epitope on HER2 distinct from trastuzumab or pertuzumab, that may provide for combination potential with other HER2 targeting agents. MT-5111 is a 55 kilodalton protein and may have improved tumor penetration capability in solid tumor settings. Methods: HER2 expression and activity of MT-5111 was assessed in vitro by flow cytometry and cell viability assays. Serum exposure and tolerability of MT-5111 was measured in non-human primate (NHP) studies. Results: MT-5111 effectively kills 8/9 cell lines (2 gastric) with moderate to high HER2 surface expression, as well as two additional gastric cell lines with lower HER2 expression. No cytotoxicity is observed on multiple HER2- cell lines. As a protein, MT-5111 is not a substrate of drug efflux transporters that limit efficacy of ADCs. MT-5111 demonstrates effective cell-killing in vitro against cell lines expressing HER2 but resistant to trastuzumab (HCC1954) or T-DM1 (JIMT-1 and gastric SNU-216), highlighting the benefit of a novel mechanism of action to treat resistant disease. MT-5111 binds human and NHP HER2 protein. Based on serum exposure of MT-5111 in NHPs used to model pharmacokinetics, planned MT-5111 dosing in humans is above the IC50 required for HER2-specific cellular cytotoxicity in vitro. MT-5111 has a short half-life that, while allowing for efficient tumor cell targeting, minimizes serum exposure to avoid systemic effects over time. Conclusions: A Phase 1, first in human, open-label dose escalation and expansion study of MT-5111 (NCT04029922) in subjects with HER2+ solid tumors whose disease has progressed after treatment with other approved therapies is open for enrollment. MT-5111 represents a novel HER2 targeted therapy for patients with HER2+ cancers with potential to overcome mechanisms of tumor resistance to existing therapies. Research Sponsor: Molecular Templates, INC.
Utility of PET-CT CMR after neoadjuvant chemotherapy with DCF for esophageal cancer as a predictive factor of recurrence.

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**Background:** PET-CT is considered as standard modality for evaluating metastasis of esophageal cancer before treatment. On the other hand, it is unclear whether PET-CT CMR (complete metabolic response) could be useful for assessment after neoadjuvant chemotherapy. To clarify the utility of PET-CT CMR as an adequate modality of prediction for recurrence after neoadjuvant chemotherapy with DCF for esophageal cancer. **Methods:** Fifty-eight cases of esophageal cancer (cStageII-IVa) who received the esophagectomy with neoadjuvant chemotherapy of DCF since June 2013 in Oita University. We evaluated the clinicopathological factors, RFS and OS between CMR group (n=22, 38%) and non-CMR group (n=36, 62%). **Results:** In the clinical stage before chemotherapy, T-factor was higher in the non-CMR group (p = 0.044), but there were no significant differences of lymph node metastasis (p = 0.27) and stage (p = 0.94) between the two groups. There was no significant difference of the SUV max (16.4 ± 6.5 vs 15.7 ± 6.5, p = 0.98) of the main lesion before chemotherapy and the FDG accumulation rate of lymph nodes (14 cases (63.6%) vs 21 cases) (58.3%), p = 0.69) between the two groups. There were no significant differences of the surgical procedure, lymph node dissection area, number of harvested lymph nodes, amount of bleeding, operation time, curability, and intra/post-operative complications between the two groups. There were 5 cases (15%) with postoperative recurrence in the CMR group (lung 1 case, extra-regional lymph nodes 3 cases, bone 1 case), 17 cases (47%) in the non-CMR group (local 4 cases, lung 3 cases, livers 5 cases, extra regional lymph nodes 6 cases, bone 4 cases, pleura 2 cases), but there was no significant difference between the two groups (p = 0.062). There were significant differences between the two groups for 3-year RFS (81.3 vs 65.3 months, p=0.021) and 3-year OS (93.8 vs 61.6 months, p=0.011). **Conclusions:** PET-CR CMR could not predict recurrence at present. PET-CR CMR cases had better prognosis compared to non-CMR cases in terms of 3-year RFS and 3-years OS. Research Sponsor: None.
Etiological involvement of weak acid reflux in the development of esophageal carcinoma.

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Background: Patients with gastroesophageal reflux disease (GERD) with mixed gastric acid-bile acid reflux are at a high risk of developing reflux-induced esophageal cancer. Increased local production of prostaglandin E2 (PGE2) is etiologically associated with reflux-induced esophageal cancer pathogenesis; however, the underlying mechanism remains unclear. Our aim was to investigate the relationship between PGE2 production in esophageal cells and reflux fluids, particularly gastric acid. The effect of the Kampo medicine Hangeshashinto (HST), which reduced the incidence of reflux-induced esophageal cancer in rats (Surgery 2018), on PGE2 production was also examined.

Methods: Esophageal squamous cell carcinoma were treated for 2 h with acidic culture condition (pH 3.5–6.5) and chenodeoxycholic acid (CDCA; 200, 400 μmol/L), followed by measurement of PGE2 production in the culture medium for the additional 6 h by enzyme-linked immunosorbent assay.

Results: CDCA induced PGE2 production and significantly increased cyclooxygenase-2 (cox-2) expression. However, in weak acidic conditions (pH 4–5), a pH-specific and significant increase in PGE2 production with no increase in cox-2 expression was observed. cPLA2 inhibitor decreased the effect of weak acid stimulation, indicating that the mechanism underlying PGE2 production differs between weak acid and CDCA. In addition, HST significantly inhibited both weak acid- and CDCA-induced PGE2 production.

Conclusions: The synergistic effect of bile acid-induced cox-2 expression and weak acid-induced arachidonic acid production via cPLA2 can cause excessive PGE2 production. Therefore, mixed reflux showing pH 4–5 could contribute to the high incidence of esophageal cancer, which might be prevented by HST treatment. Weak acid reflux around pH 4–5 has been observed in PPI-treated patients, who could exhibit excessive PGE2 production as well as increased risk of reflux-induced esophageal cancer. Research Sponsor: Tsumura&Co.
A clinical scoring system for survival prediction in advanced gastric cancer.

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**Background:** We established a scoring system using easily approachable clinical characteristics at the timing of initiating palliative chemotherapy to achieve accurate overall survival prediction to first-line treatment consisting of fluoropyrimidines in patients with advanced gastric cancer. **Methods:** A total of 1,733 patients were included in the study. The dataset was split into a training (n=1156, 67%) and validation set (n=577, 33%). Top-ranked variables were identified using the Random Forest for Survival algorithm and analyzed into a Cox regression model, thereby constructing the scoring system for predicting overall survival of advanced gastric cancer. **Results:** Five variables were finally included in the scoring system: serum neutrophil-lymphocyte ratio, alkaline phosphatase, albumin level, performance status, and histologic differentiation. The scoring system determined four distinct risk groups in validation dataset with median overall survival of 17.1 month (95% confidence interval [CI] = 14.9 to 20.5 month), 12.9 month (95% CI = 11.4 to 14.6 month), 8.1 month (95% CI = 5.3 to 12.3 month), and 3.9 month (95% CI = 1.5 to 8.2 month), respectively. AUC to estimate discrimination performance of the scoring system was 66.1 for one-year overall survival. **Conclusions:** We developed a simple and clinically useful predictive scoring model in a relatively homogenous population who initiate fluoropyrimidine-containing chemotherapy in advanced gastric cancer. Generalized application of the scoring model will require additional independent validation. None.

<table>
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<tr>
<th>Training Set</th>
<th>Median OS, month (95% CI)</th>
<th>1-year OS, % (95% CI)</th>
</tr>
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<tbody>
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<td>Score0-1</td>
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<td>Score2-3</td>
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<td>26.5 (19.1-36.7)</td>
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<td>Score6-9</td>
<td>3.27 (2.5-4.2)</td>
<td>12.9 (6.9-23.9)</td>
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<table>
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<tr>
<th>Validation Set</th>
<th>Median OS, month (95% CI)</th>
<th>1-year OS, % (95% CI)</th>
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<tr>
<td>Score6-9</td>
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<td>NA (NA-NA)</td>
</tr>
</tbody>
</table>

Median overall survival and probability for one-year overall survival stratified by the risk score.
Effect of proton pump inhibitors on the occurrence and development of gastric cancer and the polarization of macrophages in the microenvironment to M2-type.

Xiao-Qing Lu, Shengxiao Zhang, Huan-Hu Zhang; Breast Surgery, the Second Hospital of Shanxi Medical University, Taiyuan, China; Department of Rheumatology, The Second Hospital of Shanxi Medical University, Taiyuan, China; Department of Digestive Sciences, Shanxi Cancer Hospital, Taiyuan, China

Background: Long-term use of Proton pump inhibitors was associated with an increased gastric cancer(GC) risk in subjects even after HP eradication therapy. In contrast some basic research showed that PPI inhibited the growth of GC. In the tumor-microenvironment (TME), macrophages that are recruited around the tumor are activated to form the tumor-associated macrophages (TAMs), which are the most abundant mononuclear cells in the tumor infiltrating leukocytes. Many studies have shown that TAMs are associated with poor prognosis of tumors. Methods: Immunohistochemistry was used to detect the phenotype of macrophages in patients with gastric cancer treated with PPI or without PPI. Transcriptomics sequencing analyzed the signal pathways that were highly expressed in PPI-treated gastric cancer for further exploring the mechanism of PPI’s main role in gastric cancer cells. In vitro, explore the effects of PPI on gastric cancer cells and the next step on macrophages. The effects of PPI on the growth of gastric cancer and the degree of infiltration and phenotype transformation of macrophages were verified by in vivo experiments. Results: In the gastric cancer tissues treated with PPI, the macrophage phenotype is mostly M2 type, thereby exerting a cancer promoting effects. Transcriptome results showed high expression of genes associated with endoplasmic reticulum stress in gastric cancer tissues after PPI treatment, compared with patients who were not treated with PPI. Among them, GRP78 is a classic marker of endoplasmic reticulum stress. It was not only highly expressed in gastric cancer treated by PPI, but also acted on macrophages through exosomes secreted by gastric cancer cells, and caused macrophage to polarize to M2. Conclusions: PPI caused GC cells to overexpress GRP78 which was secrete into the microenvironment through exosomes, thereby transforming macrophages into M2 type under the action of GRP78. Finally M2 type macrophages promoted the progression of gastric cancer. Research Sponsor: None.
Neutrophil-to-lymphocyte ratio as a prognostic factor and its relationship to patient (pt) outcomes in the RAINBOW trial.

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Background: Neutrophil-to-lymphocyte ratio (NLR/N) reflects underlying levels of systemic inflammation and has prognostic value in advanced gastric cancer (G/GEJ). We investigated the relationship between pretreatment NLR and clinical outcomes in the RAINBOW study of ramucirumab (R) with paclitaxel (P) in G/GEJ. Methods: NLR is defined as the ratio of absolute neutrophil count and absolute lymphocyte count from peripheral blood. Pts in ITT population with baseline NLR were analyzed. As no clear NLR cutoff is established in G/GEJ, multiple cutoffs (4, 5, 6) were evaluated and relationships between baseline NLR and efficacy endpoints examined. Median OS, PFS were estimated using Kaplan Meier method; prognostic effects on OS/PFS of baseline NLR subgroups (sg) and treatment effects on OS/PFS within each baseline NLR sg were evaluated using univariate Cox PH models. Results: Baseline characteristics were generally balanced between high NLR sg. Higher baseline NLR groups were associated with worse outcomes regardless of cutoff (mOS N < 4 vs ≥4: 9.2 (8.1, 10.3) vs 5.6 (4.8, 6.6), HR = 0.61 (0.49, 0.75); N < 5 vs ≥5: 8.6 (7.8, 9.6) vs 5.3 (4.5, 6.5), HR = 0.59 (0.47, 0.75); N < 6 vs ≥6: 8.6 (7.8, 9.6) vs 4.7 (4.2, 5.9), HR = 0.55 (0.43, 0.70)). Consistent treatment benefits (R+P vs Placebo (PB)+P) were observed within high baseline NLR sg (Table). No new safety signals were observed. Conclusions: In this exploratory analysis of RAINBOW, pretreatment NLR (≤4, 5, 6) were independent prognostic factors of improved survival. Treatment benefits with R+P was preserved within high baseline NLR levels defined by different cutoffs and was consistent with ITT results. Clinical trial information: NCT01170663. Research Sponsor: Eli Lilly and Company.
Identification of cancer hallmarks associated with benefit in advanced gastroesophageal adenocarcinoma patients treated with checkpoint blockade.

Emon Elboudwarej, Carrie Brachmann, Daniel V.T. Catenacci, David Cunningham, Eric Van Cutsem, Richard D. Kennedy, Shauna Lambe, Gemma E. Logan, Jean Philippe Metges, Kei Muro, Atsuo Takashima, Zev A. Wainberg, Steven M. Walker, Kensei Yamaguchi, Marianne Zavodovskaya, Scott D. Patterson, Narikazu Boku, Steven M. Walker, ADX; Gilead Sciences, Inc., Foster City, CA; University of Chicago Medical Center and Biological Sciences, Chicago, IL; The Royal Marsden Hospital, Sutton, United Kingdom; University Hospitals Gasthuisberg Leuven and KU Leuven, Leuven, Belgium; ALMAC, Craigavon, United Kingdom; Almac Diagnostics, Craigavon, United Kingdom; Institut de Cancérologie et d’Hematologie, CHU Morvan Pole Régional de Cancérologie, Brest, France; Department of Clinical Oncology, Cancer Center Hospital, Nagoya, Japan; Osaka University, Osaka, Japan; Gastrointestinal Medical Oncology Division, National Cancer Center Hospital, Tokyo, Japan; David Geffen School of Medicine at UCLA, Los Angeles, CA; Department of Gastroenterology, The Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; National Cancer Center Hospital, Tokyo, Japan; Weill Cornell Medicine, New York-Presbyterian Hospital, New York, NY.

Background: The benefit of checkpoint blockade in advanced gastric cancer is limited and biomarkers related to response are needed. Novel gene expression analysis software was used to identify Hallmarks of Cancer associated with clinical benefit following nivolumab treatment in >2nd line advanced gastroesophageal adenocarcinoma (GEA).

Methods: RNA-sequencing data from baseline GEA patient diagnostic tumor samples (103 from NCT02862535; 5 from NCT02862535) were analyzed using the claraT platform (V2.0.0, Almac Diagnostic Services). 62 gene signatures were quantified representing 6 key Hallmarks of Cancer (Avoiding Immune Destruction, Activating Invasion and Metastases, Sustaining Proliferative Signaling, Inducing Angiogenesis, Resisting Cell Death and Genome Instability and Mutation). Clinical benefit (CB) was defined as tumor response or overall survival (OS) > 1 year. HER2 status was from medical records. Survival analyses used cox proportional hazards models. Results: Gene expression signatures (GES) identified 5 molecular subgroups (C1-C5). Rate of CB in each molecular subtype are outlined in Table. C3 and C4 had significantly improved OS compared to C2, (HR = 0.45; p = 0.02 and HR = 0.42; p = 0.02). Greater proportions of HER2+ subjects were present in C4 and C3 vs. C2, with C3 statistically significant (60% vs. 14%; p = 0.012). Gene expression characterized by chromosomal instability (CIN) and homologous recombination repair deficiency (HRD) were associated with HER2(+) (wilcox p = < 0.05). Patients selected by only using CIN & HRD had significant improvement in OS (HR = 0.63; p = 0.03). Conclusions: Interferon-based GES did not predict benefit from immune checkpoint blockade. GES representing HRD and activation of HER2, EGFR and MAPK (each enriched in CIN) were associated with improved survival upon checkpoint blockade in advanced GEA patients. Clinical trial information: NCT02862535. Research Sponsor: Gilead Sciences.

<table>
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<th>C1</th>
<th>C2</th>
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<th>C4</th>
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<tr>
<td>n</td>
<td>18</td>
<td>16</td>
<td>34</td>
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<td>CB</td>
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<td>17.6%</td>
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<td>Associated GES</td>
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<td>None</td>
<td>CIN, HRD, HER2/EGFR/MEK</td>
<td>CIN, HRD, HER2/EGFR/MEK, IFN/IIS</td>
<td>EMT*, TGFb activation</td>
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</table>

*IIS - innate immune signaling; dMMR - mismatch repair deficiency; EMT - epithelial-mesenchymal transition
**Background:** Globally, gastric cancer (GC) is the fourth most prevalent cancer, and the second leading cause of cancer related deaths. Epstein-Barr virus is implicated in the pathogenesis of 5-10% of gastric cancers. Based upon the results obtained from of the cancer genome atlas, EBV related GC is characterized by promoter hypermethylation, PIK3CA mutations (80%) and increased expression of PD-1 and PD-L1, making it an attractive target for molecularly targeted therapy and immunotherapeutic options. As such, a case can be made for routine testing for EBV in all GC patients. University medical center, El Paso is a tax payer funded safety net health system in El Paso country, TX. We conducted a pilot study to characterize the prevalence of EBV associated gastric cancer seen at this facility. 

**Methods:** After obtaining institutional review board (IRB) approval, we identified cases of GC that were diagnosed between January 1, 2008- and December 31-2017. A total of 104 cases were identified of which 17 samples were randomly selected. Pathology specimens were reviewed to identify grade, subtype (intestinal vs diffuse), degree of lymphocytic infiltration and presence/absence of H. pylori. Representative sections from archived tumors were used to perform in-situ hybridization to look for the presence of Epstein-Barr virus. Samples were analyzed using the Rembrandt In situ Hybridization and Detection Universal RISH& HRP Detection Kit for Epstein-Barr early RNA. 

**Results:** The median age of the 17 patients is 63 years with 59% being males. 95% self identified as Hispanic. 41% were smokers, 18% used alcohol. The mean BMI was 27.3. Forty one percent of gastric cancer cases were found in the body, 29% in the antrum, 12% in the cardia, and 6% in the fundus. Forty one percent of cases were Stage IV, 24% stage II, 17% Stage III and 17% Stage I. 95% of cases were high grade, 53% of them had signet ring features. 18% of samples were H. pylori positive. None of the seventeen samples tested positive for EBV. 

**Conclusions:** EBV does not seem to contribute significantly to the pathogenesis of gastric cancer in our local population. As such routine testing for EBV in all gastric cancer patients may not be a cost effective utilization of resources at our hospital. Research Sponsor: Institutional intramural grant.
Genomic correlates of extreme pathologic response following neoadjuvant chemotherapy in locally advanced gastric cancer to reveal distinct vulnerabilities.

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Background: Clinical factors associated with pathologic response (PResp) following neoadjuvant chemotherapy (NCT) in locally advanced gastric cancer (LAGC) are well studied; however, genomic correlates of such response have not been previously investigated. Methods: Evaluable pre-NCT tumor samples from patients with LAGC who underwent resection and demonstrated extreme pathologic response (EPR; $\leq$10% PResp: n = 21, $\geq$80% PResp: n = 19) were sequenced using a targeted exome capture platform. Gene- and signaling pathway-level correlates of EPR and disease-specific survival (DSS) were examined. Results: Of 40 patients, a majority had $cT2/ N^+$ disease and were treated with predominantly platinum (98%) or 5-FU (88%) based NCT regimens. Two patients with MSI-high tumors had $\leq$10% PResp and were excluded from analysis. The EPR cohorts did not differ significantly in demographic or clinical (i.e., tumor location, cT/N status, NCT regimen, extent of gastrectomy, number of lymph nodes examined, or margin status) characteristics. Although EPR cohorts did not differ with respect to tumor differentiation/grade, Lauren classification, proportions of TCGA consensus CIN or GS subtypes, tumors with $\leq$10% PResp were more likely to have vascular ($P < 0.001$) and perineural ($P = 0.007$) invasion. At median follow-up of 31m (IQR 21-57), $\geq$80% PResp was associated with improved DSS compared with $\leq$10% PResp (median NR vs. 32m, $P = 0.04$). On gene-level analysis, tumors with $\leq$10% PResp were significantly more likely to be ERBB2-altered (32% vs 5%, $P = 0.04$) compared with $\geq$80% PResp tumors. Conversely, ARID1A truncating mutations were enriched in tumors with $\geq$80% vs $\leq$10% PResp (32% vs 5%, $P = 0.04$). There was no difference in pathway-level alteration frequency between EPR cohorts. While frequency of oncogenic TP53 alterations was similar between EPR cohorts, TP53-altered tumors were associated with worse DSS vs TP53-wildtype tumors (median 80m vs 24m, $P = 0.005$) in patients demonstrating $\leq$10%, but not $\geq$80%, PResp. Conclusions: Genomic comparison of cohorts demonstrating EPR after NCT in LAGC reveal molecular vulnerabilities with distinct prognostic and therapeutic implications. Research Sponsor: None.
The relevance of neuropilin-1 expression with prognosis according to the histology of gastric cancer.

Ho Seok Seo, Han Hong Lee; Division of Gastrointestinal Surgery, Department of Surgery, College of Medicine, The Catholic University of Korea, Seoul, South Korea; Division of Gastrointestinal Surgery, Department of Surgery, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea

Background: Neuropilin-1 (NRP-1) is known to be related with various types of cancer and considered as a novel tumor marker or a therapeutic target. The aim of the study is to identify the clinical implication of NRP-1 expression in terms of prognosis in gastric cancer. Methods: A total of 265 patients who underwent radical gastrectomy for the treatment of gastric cancer from 2008 to 2011 were included. NRP-1 expression of tumors was determined by immunohistochemistry. Patients’ clinicopathologic characteristics, operation details, and long-term outcomes were retrospectively analyzed. Results: 181 (68.3%) patients showed NRP-1 expression. There was no survival difference according to the NRP-1 expression in all patients. The patients were divided into gland formation (GF) type and no gland formation (nGF) type according to histologic type. NRP-1 expression rates were 65.6% (84/128) and 70.8% (97/137), respectively. In the group of GF, NRP-1 expression was not independent prognostic factor, although patients with NRP-1 expression had better survival outcome. In contrast, patients with NRP-1 expression had worse 5-year survival rate in the group of nGF (p = 0.027) and it was an independent prognostic factor multivariate analysis (HR, 1.923; 95% CI, 1.041 - 3.551). Conclusions: NRP-1 expression in the nGF type gastric cancer predicts a poor prognosis. Research Sponsor: National Research Foundation of Korea.
**Association of ascitic neutrophil to lymphocyte ratio with prognosis in patients with advanced gastric cancer**

Jae-Joon Kim, So Yeon Oh, Kwonoh Park, Sang-Bo Oh; Medical Oncology and Hematology, Department of Internal Medicine, Pusan National University Yangsan Hospital, Yangsan, South Korea; Medical Oncology and Hematology, Department of Internal Medicine, Pusan National University Yangsan Hospital, Pusan National University School of Medicine, Yangsan, South Korea; Medical Oncology and Hematology, Department of Internal Medicine, Pusan National University Yangsan Hospital, Yangsan, South Korea

**Background:** Approximately 40% of metastatic gastric cancer patients develop peritoneal carcinomatosis, and this condition leads patients to grave prognosis. Blood neutrophil to lymphocyte ratio (NLR) is associated with prognosis in various solid tumors, such as non-small cell lung cancer, colorectal cancer, and gastric cancer. We performed this study to investigate the prognostic significance of NLR of ascitic fluid. **Methods:** This is retrospective study. Patients were consecutive included if they; 1) had histologically confirmed gastric adenocarcinoma, poorly cohesive carcinoma, or poorly differentiated carcinoma, 2) were relapsed after curative resection or initially metastatic, 3) had ascites due to peritoneal metastases of gastric cancer, 4) had received paracentesis at least once and the result of ascites exam is available. Patients with clinically active infection in the time of paracentesis is excluded. If multiple times of paracentesis was done, we used initial result. **Results:** From March 2012 to August 2018, total 157 patients who were visited in Pusan National University Yangsan Hospital met the inclusion criteria. Median age is 58 (29-86) years and male patients was 63% (n = 99). In 38.9% (n = 61) patients, gastric cancer was diagnosed in primary site and in ascites synchronously. At the time of first paracentesis, 47.1% (n = 74) of patients had already been received palliative chemotherapy due to metastatic gastric cancer. In the ascites, mean and median NLR is 2.2±6.8 and 0.3 (0-65). All except 3 patients were expired, and the median survival time from paracentesis was 47 (95% confidence interval 38.6-55.4) days. In the Kaplan-Meier survival analysis, patients with higher NLR (>0.33) have shorter survival from paracentesis (39 days, 95% CI 32.5-45.4) in compared to lower NLR ( < 0.33) (61 days, 95% CI 29.4-92.6, log-rank p = 0.011). In the additional analyses, higher neutrophil count (41 vs 72 days, p = 0.045) and lower protein level (32 vs 61 days, p = 0.018) of ascites are also poor prognostic factor. **Conclusions:** High NLR of malignant ascites is poor prognostic factor in patients with gastric cancer. The role of neutrophil in the malignant ascites should be tested in a new perspective. **Research Sponsor:** None.

Predictive role of mismatch repair deficiency (MMR-D) in patients receiving first-line fluoropyrimidine and platinum (F-P) doublet chemotherapy for metastatic and locally advanced unresectable gastric cancers (GC).

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**Background:** Although adjuvant chemotherapy has been known to have a detrimental effect on MMR-D patients (pts) with resectable GC, it is unclear whether palliative chemotherapy for advanced GC would also adversely affect the survival outcome of MMR-D pts. Immune-checkpoint inhibitor (ICI) monotherapy was approved as a standard treatment for ≥ 3rd line of advanced GC and also showed a remarkable efficacy in MMR-D pts regardless of line of therapy. ICI is now being investigated in combination with first-line cytotoxic chemotherapy. Hence, we aim to evaluate the prognostic impact of MMR on cytotoxic chemotherapy in advanced GC. **Methods:** We reviewed our prospective database to identify pts with initially metastatic, recurrent and locally advanced unresectable GC who received F-P doublet from 2015 to 2018. MMR was assessed by immunohistochemistry with previously-collected tumor tissue and correlated with clinical characteristics and survival outcomes. **Results:** Out of 892 pts identified from the database, 543 underwent MMR test [382 initially metastatic (70.3%); 127 recurrent (23.3%); 32 locally advanced unresectable (6.3%)]. Median age was 58 years (range, 24–86) with male comprising 64.0%. MMR-D was found in 4.4% (n = 24) and associated with age > 65 (50% vs 29.9%; P = 0.037), antrum-origin (62.5% vs 34.1%, P = 0.004) and well/moderately-differentiated histology (41.7% vs 25.8%, P = 0.110). According to our prognostic model (Koo DH et al, 2011), MMR-D pts were less likely to be classified into poor-risk group (4.2% vs 16.8%, P = 0.102). In good-risk group, MMR-D pts had significantly shorter PFS (6.0 vs 9.0 months, P = 0.045) and OS (10.1 vs 20.9 months, P = 0.047), while pts in moderate and poor group showed no difference in survival depending on MMR status. **Conclusions:** MMR-D GC showed significantly shorter PFS and OS on F-P doublet in good-risk pts and further investigation is needed to determine underlying molecular mechanisms. With the negative impact of MMR-D on the effect of cytotoxic chemotherapy, exclusion of MMR-D pts should be considered in future trials of ICI and cytotoxic chemotherapy combination. Research Sponsor: None.
A novel gene signature for predicting response to chemoradiotherapy in esophageal adenocarcinoma.

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Background: While neoadjuvant chemoradiotherapy (CRT) has emerged as an important treatment modality in patients with locally advanced esophageal adenocarcinoma (EAC), ~60%-70% of patients do not respond to such treatments; but are exposed to their toxicity nonetheless. This highlights the clinical need for the development of biomarkers that can robustly predict response to CRT and spare others from the toxicity and expense associated with these treatments. Herein, we systematically identified a biomarker signature that predicts response to CRT in EAC patients.

Methods: Using a clinical-trial driven cohort of 25 EAC patients treated with 5-fluorouracil plus carboplatin and concurrent radiation therapy, we performed whole-exome sequencing (WES) in paired biopsy specimens obtained at baseline and 3-6 weeks post-treatment. In addition, we also analyzed the predictive potential of a panel of immune-related genes (TIM3, LAG3, IDO1 and CXCL9) in these matched tissues. Results: In our cohort, based upon RECIST criteria, 14 EAC patients were categorized as non-responders, while 11 were deemed as responders to CRT. Among responders, the most frequently mutated genes were NOTCH1, NOTCH2, NOTCH3, and MLL2; and the overall tumor mutation burden (TMB) was significantly reduced for these genes in post-treatment specimens (P<0.001). In contrast, in non-responders, NFE2L2, KEAP1, FAT1, FAT2, FAT3 and PIK3CA, harbored frequent mutations. Similarly, all four immune-related genes were significantly up-regulated in post-treatment specimens (p<0.05-0.001). Interestingly, the progression-free survival was significantly greater in patients with lower TMB (64.1%, p=0.04) and increased immunogenic scoring (62.7%, p=0.01). We finally constructed a risk-stratification model that comprised of mutational scores from 10 most frequently mutated genes, together with 4 immune-related genes, which achieved an AUC of 0.83 in predicting response to CRT in EAC patients.

Conclusions: Using a systematic biomarker discovery approach, we have developed a novel biomarker signature that robustly predicts response to CRT in EAC patients and has a significant potential for personalized management of EAC patients. Research Sponsor: U.S. National Institutes of Health.
Abdominal obesity and risk for esophageal cancer: A nationwide population-based cohort study of South Korea.

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**Background:** The relationship between overall obesity, as measured by body mass index (BMI), and risk of esophageal squamous cell carcinoma (ESCC) has been reported, and it has a negative correlation. However, the relationship with abdominal obesity, as measured by waist circumference, may be different. We investigated the association between abdominal obesity and ESCC.

**Methods:** Retrospective cohort study with 22,809,722 individuals who had undergone regular health check-ups provided by the National Health Insurance Corporation between 2009 and 2012 (median follow-up period was 6.4 years) in South Korea. Abdominal obesity was defined as a waist circumference over 90 cm for men and 85 cm for women. We estimated hazard ratios (HRs) and 95% confidence intervals (CIs) using Chi-squared test and Cox proportional hazard model adjusted for confounding factors. Primary outcome was newly developed esophageal cancer.

**Results:** After adjusting for BMI, abdominal obesity increased the risk of ESCC (HR 1.29, 95% CI 1.23-1.36). Waist circumference is associated with increased risk of ESCC in a dose-dependent manner (P for trend, 0.0001). We analyzed individuals divided into five categories of BMI. Among individuals with overweight (BMI 23-24.9 kg/m²) and obese I (BMI 25-29.9 kg/m²), abdominal obesity was a risk factor associated with developing ESCC (HR 1.22, 95% CI 1.11-1.34; HR 1.28, 95% CI 1.18-1.39, respectively).

**Conclusions:** Abdominal obesity, not BMI itself, is associated with an increased risk for ESCC. Therefore, reducing abdominal obesity may affect decreasing the development of ESCC. Research Sponsor: None.
Predictive value of the modified systemic inflammation score in patients undergoing curative resection of squamous cell carcinoma of the esophagus.

Mitsuro Kanda, Masahiko Koike, Dai Shimizu, Chie Tanaka, Daisuke Kobayashi, Fuminori Sonohara, Hideki Takami, Yoshikuni Inokawa, Norifumi Hattori, Masamichi Hayashi, Suguru Yamada, Goro Nakayama, Michitaka Fujiwara, Yasuhiro Kodera; Department of Gastroenterological Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan; Nagoya University Graduate School of Medicine, Nagoya, Japan; Nagoya University Graduate School of Medicine, Gastroenterological Surgery, Nagoya, Japan; Nagoya University, Nagoya City, Japan

Background: Inflammation plays a critical role in the development and progression of cancers. Here we aimed to evaluate the clinical significance of the preoperative modified systemic inflammation score (mSIS) to predict long-term outcomes of patients with esophageal squamous cell carcinoma (ESCC).

Methods: We included 443 patients who underwent curative resection of ESCC. The mSIS was formulated according to the serum albumin level (ALB) and lymphocyte-to-monocyte ratio (LMR) as follows: mSIS 0 (ALB ≥ 4.0 g/dL and LMR ≥ 3.4), mSIS 1 (ALB < 4.0 g/dL or LMR < 3.4), and mSIS 2 (ALB < 4.0 g/dL and LMR < 3.4).

Results: Patients were categorized into preoperative mSIS 0 (n = 165), mSIS 1 (n = 183), and mSIS 2 (n = 95) groups. Preoperative mSIS was significantly associated with age, preoperative body mass index, and pathological disease stage. The disease-specific survival times of patients in preoperative mSIS 0, 1, and 2 sequentially shortened (P = 0.009), and mSIS 2 was identified as an independent prognostic factor (hazard ratio 2.63, 95% confidence interval 1.33-5.27, P = 0.0053). In most patient subgroups, the mSIS was associated with greater risk of disease-specific death. A stepwise increase in the prevalence of hematogenous recurrences was directly proportion to the mSIS. When patients were subdivided by mSIS before neoadjuvant treatment, there were no significant differences in disease-specific survival.

Conclusions: Our findings demonstrate that the preoperative mSIS may serve as a powerful prognosticator of ESCC that definitively stratifies clinical outcomes as well as a tool for selecting treatment strategies. Research Sponsor: None.
Tissue levels of steroid hormones and their receptors, prolactin, and SHBG in patients with gastric cancer.

Oleg Ivanovich Kit, Elena M. Frantsiyants, Yuriy A. Gevorkyan, Natalya V. Soldatkina, Nikolay S. Samoylenko; Rostov Research Institute of Oncology, Rostov-on-Don, Russian Federation

Background: Hormones and their receptors are important effectors providing interconnection between the primary tumor and metastatic niches. The aim of the study was to determine levels of steroid hormones and their receptors, prolactin (PRL) and SHBG in tissues of gastric cancer (GC), omentum and peritoneum.

Methods: Levels of steroid hormones and their receptors, PRL and SHBG were determined by ELISA in tissues of primary tumors, omentum and peritoneum in main groups: 1 (M0) – GC T3-4aN0-3M0 (n = 24) and 2 (M1) – GC T3-4aN0-3M1 (n = 21); in tissues of the stomach, omentum and peritoneum – in the control group (non-cancer patients, n = 17).

Results: In GC (M0), estradiol was reduced in primary tumors, omentum and peritoneum by 4.2, 4.0 and 8.6 times, respectively; increased levels of free testosterone (by 18.9, 2.0 and 2.8 times) and PRL (by 8.0, 7.6 and 1.7 times) were observed (p < 0.05). GC (M0) was characterized by high levels of estrogen receptors (ER) α - by 1.2 times (p < 0.05), progesterone (PR) - by 3.5 times and SHBG - by 1.4 times (p < 0.05); tissues of the omentum and peritoneum showed increased levels of ERα - by 2.4 and 3.9 times, ERβ - by 1.5 (p < 0.05) and 2.5 times, PR - by 2.2 and 1.5 times (p < 0.05). GC (M1) had low ERα levels. Conclusions: Decreased levels of estradiol, together with elevated levels of free testosterone and prolactin, in tumor tissues can be considered marking for peritoneal metastases. Correlation between the content of these hormones in the omentum and peritoneum and the presence of metastasis in the organs confirms the “seed and soil” principle. Research Sponsor: None.
Levels of oncofetal proteins in pathological tissues of patients with gastric cancer.

Oleg Ivanovich Kit, Elena M. Frantsiyants, Yuryi A. Gevorkyan, Natalya V. Soldatkina, Nikolay S. Samoylenko; Rostov Research Institute of Oncology, Rostov-on-Don, Russian Federation

Background: Spread to the peritoneal cavity and lymphatic system is the most important factor of gastric cancer prognosis. Successful implantation of cancer cells in a distant place is possible only when cancer cells accept a special kind of molecular invitation sent by some organs. Our purpose was to study levels of CA-19.9, CA-125, CA-72.4 and He-4 in tissues of tumors, peritoneum and omentum in patients with gastric cancer (GC) T3-4aN0-3M1 and T3-4aN0-3M0. Methods: Levels of CA-19.9, CA-125 and CA-72.4 were determined by ELISA in primary tumors, the omentum and peritoneum of patients from main groups 1 (M0) – GC T3-4aN0-3M0 (n = 24) and 2 (M1) – GC T3-4aN0-3M1 (n = 21) and in the stomach, omentum and peritoneum of non-cancer controls (n = 17). Results: Levels of CA-19.9, CA-125 and CA-72.4 were increased, compared to control values, in all studied samples from 1.6 times (CA-72.4) to 180.1 times (CA-19.9). Only CA-19.9 levels differed depending on the metastatic spread: 1.8 times (p<0.05) higher in T3-4aN0-3M1 than in T3-4aN0-3M0. In the omentum tissues, CA-19.9 levels in T3-4aN0-3M1 exceeded the control values by 20 times; in 20 patients with T3-4aN0-3M0, the value was only 4.1 times higher than in controls and 4.8 times lower than in T3-4aN0-3M1; while in 4 patients it did not differ significantly from the value in T3-4aN0-3M1. In the peritoneal tissues, CA-19.9 levels in T3-4aN0-3M1 exceeded the control values by 19.2 times; in 21 patients with T3-4aN0-3M0, the value was only 2.2 times higher than in controls and 8.5 times lower than in T3-4aN0-3M1, while in 3 patients it did not differ significantly from the value in T3-4aN0-3M1. Conclusions: Saturation of peritoneal and omentum tissues with marker oncoproteins is one of the factors associated with metastatic characteristics of gastric cancer, while the CA-19.9 level can serve as informative laboratory tests to predict the nature of the further disease development. Research Sponsor: None.
Conversion surgery for advanced gastric cancer with peritoneal metastasis.

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Background: Patients with peritoneal metastasis have significantly poor prognosis. We have performed pretherapeutic staging laparoscopy (SL) to diagnose peritoneal metastasis for patients with large type 3, type 4 or serosa-invasive gastric cancer. When peritoneal metastasis disappears by chemotherapy for patients with positive peritoneal cytology (CY1) or peritoneal dissemination (P1), we perform the conversion surgery (CS). Methods: We retrospectively analyzed clinical outcomes of 134 patients with advanced gastric cancer who underwent SL between 2005 from 2016. We examined safety and usefulness of CS for patients with CY1 or P1. Results: CY0P0, CY1P0 and P1 were found in 67, 28 and 39 patients, respectively. The median survival time (MST) of patients with CY0P0, CY1P0 and P1 were 39, 21 and 11 months (CY0P0 vs CY1P0; p = 0.029, CY0P0 vs P1; p<0.001, CY1P0 vs P1; p<0.001). In patients with CY1P0, 20 of 26 patients who received chemotherapy underwent the second look SL, and 14 patients (54%) underwent CS (R0) as peritoneal cytology turned negative. These regimens of chemotherapy were S-1/CDDP (n = 9), Docetaxel/CDDP/S-1 (n = 2), SOX (n = 2) and S-1/Docetaxel (n = 1) and the median number of treatment courses was 5 courses. The MSTs of patients with or without CS were 40 months and 11 months (p<0.001). There was no difference in overall survival between patients with CS and patients with CY0P0 at the first SL (p = 0.866). All patients with P1 received chemotherapy, and 11 of these patients underwent the second look SL. As peritoneal metastasis of 7 patients (18%) disappeared by chemotherapy, they underwent CS (R0). The MSTs of patients with or without CS were 31 months and 9 months (p = 0.026). Regarding complications after CS, surgical-site infection and interstitial pneumonia each occurred in one patient (grade II), and intestinal obstruction (grade IIIa) occurred in one patient. There was no mortality. Conclusions: This study suggests that CS is probably safe and may contribute to improve the survival rate of patients with peritoneal metastasis. Moreover, we developed the NSOX regimen, comprised of a combination nab-paclitaxel, S-1 and oxaliplatin, and have performed a phase I/II trial using the NSOX regimen (UMIN000030909). Research Sponsor: None.

Prognostic factors in patients with nonmetastatic gastric cancer treated with contemporary multimodality strategies.

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Background: We conducted a retrospective study to evaluate clinical outcomes in patients with non-metastatic gastric adenocarcinoma (nmGA) treated at two high-volume academic institutions within the University of California (UC) system. Methods: Electronic Health Records and California Cancer Registry of demographic and clinical data were collected for pts with nmGA who underwent surgery with curative intent from 2010-2017. Medical chart reviews were conducted to validate outcomes. We used multivariate Cox regression to determine prognostic factors for cancer recurrence and overall survival. Results: Demographics of study cohort (n = 406): mean age 65 years; 71% male; 58% Caucasian, 26% Asian, 13% Latino. There was an even distribution between pts with locoregionally advanced (defined as pT4 or pN1+) vs. localized (pT1-3, pN0) disease. Tumor histology: 49% intestinal, 19% diffuse, 13% mixed, 19% unknown. Type of surgery: 27% open gastrectomy, 59% laparoscopic, 14% unknown. Multimodality therapy: 29% received perioperative systemic rx alone (48% adjuvant only, 52% neoadjuvant +/- adjuvant), 35% received perioperative systemic rx plus radiation (40% adjuvant only, 60% neoadjuvant +/- adjuvant), 36% underwent surgery only. With median f/u time after surgery of 5 years, 21% of pts developed cancer recurrence and 43% had died. Weight loss prior to diagnosis, locoregional stage, and positive resection margins were a/w recurrence (HR = 1.6-2.5, p < .05). Only locoregional stage was prognostic for worse survival (HR = 2.7, p < .0001). Positive resection margins were seen in 6% of pts and were a/w diffuse histology and tumor size > 4cm (odds ratio = 2.9-8.8, p < .02). Multimodality therapy was not a/w recurrence but was a/w longer survival after adjusting for stage (HR = 0.3, p < .0001). Addition of radiation to systemic rx did not confer further improvements in either recurrence or survival. Conclusions: This study highlights contemporary practice patterns for pts with nmGA and demonstrates a survival benefit with multimodality rx. Additional data are being gathered from other UC medical centers to confirm these findings and explore differences across institutions and ethnicities. Research Sponsor: None.
Relationship between PET response and pathologic response in distal esophageal/gastroesophageal junction (DE/GEJ) cancers.

Irene S. Yu, Shiru Lucy Liu, Yizhou Zhao, Sally CM Lau, Howard John Lim; BC Cancer, Vancouver, BC, Canada; Department of Radiation Oncology, Dalhousie University, Halifax, NS, Canada; Princess Margaret Cancer Center, Toronto, ON, Canada; British Columbia Cancer Vancouver, and CCTG Co-chair, Vancouver, BC, Canada

Background: The utility of PET scans (PETs) to predict outcomes after neoadjuvant treatment of DE/GEJ cancers is unclear. We aimed to explore the relationship between PET response and pathologic/clinical outcomes in a real-world setting. Methods: Patients (pts) with DE/GEJ cancer treated with curative intent perioperative chemotherapy or neoadjuvant chemoradiation followed by surgery in British Columbia from 2009-2018 were included. Retrospective chart review was conducted; pts were stratified into PET responder (R, $\geq 35\%$ decrease in max SUV) and non-responder (NR, $< 35\%$) groups. Chi-square and Kaplan Meier were used to test for associations between variables and outcomes. Results: Of 576 pts identified, 52\% had pre- and post-induction PETs; 232 pts proceeded to surgery and were included for analysis. Treatment regimens comprised of CROSS (72\%), MAGIC (24\%) and FLOT (4\%). Median age was 66 (IQR 57-72), 85\% male, 91\% ECOG 0/1, 62\% GEJ involvement, and 81\% adenocarcinoma histology. Characteristics and treatment regimens were balanced between the PET-R and PET-NR groups (all p $> 0.05$). Median time from end of treatment to PET was 30 days (IQR 22-36); 67\% were PET-R. Pathologic complete response (PCR) rates were similar for PET-R vs. PET-NR (14\% vs. 13\%, p=0.08). The discordance rate between PET vs. pathologic response was 34\% (Table). Aborted surgery rate was higher in the PET-NR group (8\% vs. 3\%, p=0.03); 70\% of aborted cases were due to peritoneal involvement. Median overall survival was similar between the two groups (PET-R 31.5 mo vs. PET-NR 36.1 mo, p=0.62). Conclusions: In our population-based cohort, PET response did not demonstrate prognostic utility and was associated with a significant pathology discordance rate. The role of PET/CT is evolving and the use of post-induction imaging for response assessment and prognostic value may be questionable. Research Sponsor: None.

<table>
<thead>
<tr>
<th>Discordance rates.</th>
<th>Definition</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Tumour Discordance</td>
<td>PET-R, ypT3 or higher</td>
<td>64 (28)</td>
</tr>
<tr>
<td>Nodal Discordance</td>
<td>PET node -, ypN2 or higher</td>
<td>33 (14)</td>
</tr>
<tr>
<td>Primary Tumour and/or Nodal Discordance</td>
<td>As above</td>
<td>79 (34)</td>
</tr>
<tr>
<td>_equivocal</td>
<td>PET-NR, ypT0-2</td>
<td>29 (13)</td>
</tr>
<tr>
<td>EQUIVOCAL</td>
<td>PET node +, ypN0</td>
<td>9 (4)</td>
</tr>
<tr>
<td>EQUIVOCAL</td>
<td>PET node -, ypN1</td>
<td>43 (19)</td>
</tr>
</tbody>
</table>
Clinicopathological features of multifocal gastric carcinoma: A retrospective study.

Xi Zou, Runfeng Zhang, Qi Lei, Aiping Zhou, Chun-Xia Du; Peking Union Medical College Hospital, Chinese Academy of Medical Science and Peking Union Medical College, Beijing, China; National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

**Background:** The occurrence of multifocal gastric carcinoma (MGC) is growing in China, while relevant study remains limited. This study aimed to collect more information of MGC for further research. **Methods:** Patients with MGC treated at China National Cancer Center from January 2010 to December 2017 were enrolled in this retrospective study. A 6-month interval was used to separate synchronous and metachronous foci. **Results:** 103 patients were included, 88 (85.4%) were males. 96 (93.2%) patients had two foci and 7 (6.8%) had three or more foci, contributing a total of 216 tumor foci. 185 (85.6%) foci were adenocarcinoma, 18 (8.3%) were intraepithelial neoplasia, 2 (0.9%) were lymphoepithelioma-like carcinoma and 1 (0.5%) was small cell carcinoma. Intestinal, diffuse, and mixed type accounted for 49.7%, 14.6% and 11.4% respectively, with 24.3% unknown. In 96 patients with 2 foci, 56 (58.3%) patients had synchronous diseases, and 40 (41.7%) had metachronous diseases. The median age at the diagnosis of first tumor was 62 (55-71) years. The median diagnosis interval of metachronous tumor foci was 41.4 (23.5-88.3) months. The locations and sizes of foci are shown in Table. In synchronous cases, 6 foci of accessory tumor were less than 1 cm including one being 0.4 cm. In metachronous cases, 4 foci of second tumor were less than 1 cm. 51 (49.5%) patients were current smokers or ex-smokers, and 44 (42.7%) were regular alcohol consumers. 26 (25.2%) patients had a first-relative family history, including 14 (13.6%) having a family history of gastrointestinal carcinoma. **Conclusions:** The second gastric tumor should be thoroughly detected to avoid missed diagnosis, since the accessory tumor might be rather small. Further genetic research is warranted to explore the potential pathogenesis of MGC. **Research Sponsor:** None.

<table>
<thead>
<tr>
<th>Location</th>
<th>Synchronous</th>
<th>Metachronous</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Major</td>
<td>Accessory</td>
<td>First</td>
</tr>
<tr>
<td>Esophagogastric junction</td>
<td>28</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Upper 1/3 stomach</td>
<td>4</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Middle 1/3 stomach</td>
<td>3</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Lower 1/3 stomach</td>
<td>21</td>
<td>30</td>
<td>14</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td><strong>Size (cm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>4.1</td>
<td>2.6</td>
<td>3.7</td>
</tr>
<tr>
<td>(min-max)</td>
<td>(0.5-8.5)</td>
<td>(0.4-6.5)</td>
<td>(0.9-8.6)</td>
</tr>
</tbody>
</table>

Preoperative muscle strength as a predictor of complications after esophagectomy.

Madison Colcord, Michael D Watson, Nicole Lee Gower, Jennifer H Benbow, Sally Jeanne Trufan, Joshua Hill, Jonathan C. Salo; Levine Cancer Institute, Charlotte, NC; Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC; Levine Cancer Institute, Atrium Health, Charlotte, NC

Background: Sarcopenia has been associated with post-operative complications and length of stay (LOS) in patients undergoing esophagectomy. A variety of methods exist to measure muscle mass and strength, with few comparisons between methods. We compared hand-grip strength (HGS), muscle mass and intramuscular adipose tissue as predictors of post-operative outcomes. Methods: Patients with esophageal cancer undergoing esophagectomy were identified between January 2015 – June 2019 at Levine Cancer Institute. Skeletal muscle index (SMI) and skeletal muscle density (SMD), a measure of intramuscular adipose tissue, were derived from CT. HGS was measured using a dynamometer. Uni- and multivariable GLM analyses were performed. Results: 115 patients (100 male, 15 female) underwent esophagectomy with an average age of 64.3 +/- 9.8. The analysis was stratified by sex due to significant differences in HGS, SMI, and SMD. Among men, univariable analysis revealed a significant association between pre-operative HGS < 25 kg and increased risk of post-operative pneumonia (p = 0.02), ventilation > 48hrs (p = 0.02), LOS (p = 0.002), discharge to home (p = 0.001), and one-year mortality (p = 0.005). All associations except discharge home remained significant in multivariable analyses (Table). Among women, no factors analyzed were significantly associated with postoperative outcomes. Conclusions: HGS is a more powerful predictor of postoperative complications and LOS than either muscle mass or intramuscular adipose tissue among men undergoing esophagectomy. HGS is cost-effective and easily incorporated into routine clinical care, allowing for preoperative intervention to optimize patients for esophagectomy. To better understand the implications in women, additional research with a larger cohort is needed. None.

<table>
<thead>
<tr>
<th>Surgical Outcome</th>
<th>Variable</th>
<th>Odds Ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>Age</td>
<td>1.23</td>
<td>0.018</td>
</tr>
<tr>
<td></td>
<td>Ventilation &gt; 48hrs</td>
<td>0.16</td>
<td>0.045</td>
</tr>
<tr>
<td></td>
<td>Preop Feeding Tube</td>
<td>9.3</td>
<td>0.039</td>
</tr>
<tr>
<td></td>
<td>White Race</td>
<td>25.1</td>
<td>0.011</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>0.78</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>White Race</td>
<td>25.1</td>
<td>0.011</td>
</tr>
<tr>
<td></td>
<td>HGS &lt;25</td>
<td>5.99</td>
<td>0.009</td>
</tr>
<tr>
<td></td>
<td>Pre-op SMD</td>
<td>-</td>
<td>0.015</td>
</tr>
</tbody>
</table>

*Log-transformed
Effect of age on swallowing dysfunction after esophagectomy.

Della Mann, Vishwa Raj, Madison Colcord, Michael D Watson, Sally Jeanne Trufan, Jennifer H Benbow, Nicole Lee Gower, Joshua Hill, Jonathan C. Salo; Levine Cancer Institute, Charlotte, NC; Levine Cancer Institute/Carolina Rehabilitation, Charlotte, NC; Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC; Levine Cancer Institute, Atrium Health, Charlotte, NC

Background: Patients undergoing esophagectomy frequently experience malnutrition, which in combination with the catabolic effects of surgery can result in loss of muscle mass and function. Safe swallowing requires the preservation of muscle mass. Modified barium swallow (MBS) enables assessment of postoperative swallowing impairments. We assessed the incidence and risk factors of swallowing dysfunction post-esophagectomy. Methods: Patients with a MBS post-esophagectomy were identified between January 2015-June 2019 at Levine Cancer Institute at Carolinas Medical Center. Swallowing was evaluated with the Penetration Aspiration Scale. Muscle loss was evaluated with pre-operative hand-grip strength (HGS) and skeletal muscle index (SMI) and skeletal muscle density (SMD) from axial CT images. Uni- and multivariable GLM analyses were performed. Results: 91 patients (79 men, 12 women) underwent esophagectomy with an average age of 64.0 ± 10.1. Pre-operative HGS, SMI, and SMD all decreased with age. Significant differences existed between sexes in HGS, SMI, and SMD, so the cohort was stratified by sex for analysis. Univariate analysis of male patients revealed older age, lower body mass index (BMI), smoking history, prior feeding tube, and lower pre-operative HGS and SMI were associated with aspiration or penetration on MBS. Among women, no factors analyzed were significantly associated with swallowing dysfunction. Conclusions: Swallowing dysfunction after esophagectomy is correlated with increased age and lower BMI. The role of muscle loss in the risk of aspiration after esophagectomy is not clear. Further research is needed to determine the relationship between these factors with the goal of enabling preoperative physiologic optimization and patient selection. None.

Factors associated with aspiration on MBS among men post-esophagectomy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate Odds Ratio</th>
<th>p-value</th>
<th>Multivariable Odds Ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeletal Mass Index</td>
<td>0.96 (0.91-1.01)</td>
<td>0.078</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Prior Feeding Tube</td>
<td>2.48 (0.97-6.37)</td>
<td>0.059</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.11 (1.04-1.17)</td>
<td>0.001</td>
<td>1.1 (1.04-1.17)</td>
<td>0.002</td>
</tr>
<tr>
<td>Smoking Hx</td>
<td>2.67 (1.05-6.60)</td>
<td>0.039</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0.89 (0.82-0.98)</td>
<td>0.005</td>
<td>0.91 (0.83-1.00)</td>
<td>0.039</td>
</tr>
<tr>
<td>HGS &lt;25kg</td>
<td>4.06 (1.47-11.16)</td>
<td>0.007</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

NS: Not significant

A prediction model for pathological findings after neoadjuvant chemoradiotherapy for resectable locally advanced esophageal cancer based on PET images using radiomics and machine-learning.

Yuji Murakami, Yasushi Nagata, Daisuke Kawahara; Hiroshima University Hospital, Hiroshima, Japan; Hiroshima Univ Hosp, Hiroshima, Japan; Hiroshima University Hospital, Japan, Hiroshima, Japan

Background: The pathologic complete response (PCR) rate by neoadjuvant chemoradiotherapy (NCRT) for resectable locally advanced esophageal squamous cell carcinoma (ESCC) is about 40%. If we could predict a PCR from pre-treatment image data, it might be possible to select patients who can be cured by organ-preserving CRT. The purpose of this study is to construct a predictive model for PCR by NCRT in patients with locally advanced ESCC using radiomics and machine-learning.

Methods: We used data of 98 ESCC patients who underwent NCRT and surgery from 2003 to 2016. Firstly, we fused the radiotherapy treatment planning CT images and PET images scanned before treatment. Then using target delineations on planning CT images, we created eight kinds of target regions on PET images. Secondly, we generated a total of 6968 features per patient using the PET image data within these target regions that were preprocessed by radiomics technique. Among them, we extracted the optimal features for machine-learning using the least absolute shrinkage and selection operator (LASSO) logistic regression. Thirdly, artificial neural networks were used as a machine-learning method to create a predictive model. The extracted radiomics features were used as input values, and the information of ‘PCR’ or ‘not PCR’ was used as output values. We used data of randomly selected 58 patients for training and constructed a predictive model. Then we used data of 15 patients to validate the models and created the optimal model. Finally, we evaluated the predictive model using the test data of 25 patients.

Results: By the LASSO analysis, 32 radiomics features were extracted for machine-learning classification. This predictive model predicted pathological findings after NCRT in 24 of 25 test data. The accuracy, specificity and sensitivity in the prediction of PCR after NCRT by this predictive model were 96.0%, 93.8%, and 100%, respectively.

Conclusions: A prediction model based on PET images using radiomics and machine-learning could predict pathological findings after NCRT for resectable locally advanced ESCC. Research Sponsor: Grant-in-Aid for Scientific Research (KAKENHI) (C).
A phase Ib study of near infrared photodynamic therapy (NIR-PIT) using ASP-1929 in combination with nivolumab for patients with advanced gastric or esophageal cancer (GE-PIT study, EPOC1901).

Tomohiro Kadota, Daisuke Kotani, Yusuke Yoda, Miki Fukuimori, Masashi Wakabayashi, Shogo Nomura, NozomuFuse, Akihiro Sato, Tomonori Yano, Kohei Shitara; Department of Gastroenterology and Endoscopy, National Cancer Center Hospital East, Kashiwa, Japan; Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan; Clinical Research Support Office, National Cancer Center Hospital East, Kashiwa, Japan; National Cancer Center Hospital East, Chiba, Japan

**Background:** Near Infrared Photodynamic therapy (NIR-PIT) is a newly developed, molecular targeted cancer therapy based on conjugating a near infrared silica-phthalocyanine dye to a monoclonal antibody, which result in necrotic cell death of targeted cancer cell immediately after exposure to near infrared light. Phase IIa trial of NIR-PIT with RM-1929 (anti-EGFR antibody cetuximab conjugated to IRDye 700DX) showed a 43% objective response rate (ORR) for recurrent head and neck squamous cell carcinoma (Cognetti DM, et al. ASCO 2019 abstr 6014). Meanwhile, PD-1 blockade reverses adaptive immune resistance, resulting in activation of tumor infiltrating lymphocyte after NIR-PIT in syngeneic mouse models (Nagaya T, et al. Cancer immunology research. 2019). The objective of this study is to investigate the safety and efficacy of the NIR-PIT using ASP-1929 (analogous to RM-1929) in combination with nivolumab for advanced gastric or esophageal cancer.

**Methods:** The study is an open-label, single-arm, single-center, Phase Ib clinical trial. Eligible patients are with unresectable esophagogastric squamous cell carcinoma or EGFR positive adenocarcinoma after standard chemotherapy. Dose escalation cohort is designed to determine the recommended dose of laser irradiation energy density in a “3+3” design (50, 75, and 100 J/cm²). Nivolumab of 240 mg on Day 1 and ASP-1929 of 640 mg/m² on Day 8 is administered, and laser irradiation is performed under endoscopy using the laser PIT unit on Day 9. In expansion cohort, approximately 20 patients will be enrolled. The primary endpoint is proportion of incidence of dose-limiting toxicity, and the secondary endpoints are proportion of incidence of adverse events, ORR, local complete response rate, progression-free survival (PFS), local PFS, overall survival, and proportion of incidence of device malfunction. We also investigate several biomarkers using pre- and post-treatment biopsied samples. First patient will be enrolled in December 2019. Clinical trial information: JapicCTI-194969. Research Sponsor: Rakuten Medical, Inc.
Tislelizumab plus chemotherapy versus placebo plus chemotherapy as first-line therapy in patients with locally advanced unresectable or metastatic gastric or gastroesophageal junction (G/GEJ) adenocarcinoma.

Rui-hua Xu, Hendrik-Tobias Arkenau, Yung-Jue Bang, Crystal S. Denlinger, Ken Kato, Josep Tabernero, Jin Wang, Jiang Li, Henry Castro, Markus H. Moehler; Sun Yat-sen University Cancer Center, Guangzhou, China; Sarah Cannon Research Institute, Cancer Institute, University College London, London, United Kingdom; Seoul National University Hospital, Seoul, South Korea; Fox Chase Cancer Center, Philadelphia, PA; National Cancer Center Hospital, Tokyo, Japan; Vall d’Hebron University Hospital and Vall d’Hebron Institute of Oncology, Barcelona, Spain; BeiGene (Beijing) Co., Ltd., Beijing, China; BeiGene USA, Inc., San Mateo, CA; Johannes Gutenberg-University Clinic, Mainz, Germany

Background: First-line standard of care in patients with locally advanced or metastatic G/GEJ adenocarcinoma is fluoropyrimidine- and platinum (plat)-based combination chemotherapy. Despite improved chemotherapy regimens, outcomes remain poor and survival is low. Tislelizumab, an investigational humanized IgG4 monoclonal antibody with high affinity and binding specificity for PD-1, was engineered to minimize binding of FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. Previous reports from early phase studies suggested tislelizumab, as a single agent and combined with chemotherapy, was generally well tolerated and had antitumor activity in patients with advanced solid tumors, including G/GEJ cancer. Methods: This randomized, placebo-controlled phase 3 study (NCT03777657) is designed to evaluate plat/fluoropyrimidine + tislelizumab vs plat/fluoropyrimidine + placebo as first-line therapy for patients with locally advanced or metastatic G/GEJ adenocarcinoma. Adult patients (n=720) from ~160 centers will be randomized 1:1 to receive tislelizumab (200 mg IV Q3W) or placebo as first-line therapy in combination with chemotherapy. Oxaliplatin (130 mg/m² IV Q3W) + capecitabine (1000 mg/m² orally BID for 2 weeks) or cisplatin (80 mg/m² IV Q3W) + 5-fluorouracil (800 mg/m²/day IV on Days 1-5 Q3W) will be used as backbone chemotherapy on an individual basis. Chemotherapy will be administered for up to 6 cycles; capecitabine maintenance therapy is optional for patients who received capecitabine and oxaliplatin. Progression-free and overall survival are primary endpoints of the study. Secondary endpoints will include overall response rate, quality-of-life outcomes, and the safety/tolerability profile of combination therapy. Exploratory endpoints include disease control rate, time to response, and an analysis of potential predictive biomarkers including PD-L1 expression; the VENTANA PD-L1 (SP263) assay will be used for PD-L1 expression analysis. This study is actively enrolling. Clinical trial information: NCT03777657. Research Sponsor: BeiGene, Co., Ltd.
A global phase II trial-in-progress with bavituximab plus pembrolizumab in patients with advanced gastric or gastroesophageal cancer.

Background: The majority of gastric cancer (GC) patients fail to derive sufficient benefit from currently available therapies. Pembrolizumab received accelerated approval in 2017 as a third-line therapy in PD-L1 positive GC patients with an ORR of 13.3%. Further studies in second- and third-line GC patients showed comparable outcomes when pembrolizumab was combined with chemotherapy. Bavituximab, an investigational, chimeric monoclonal antibody designed to inhibit the immunosuppressive effects of phosphatidylserine (PS), is being evaluated in combination with pembrolizumab in patients with advanced gastric and gastroesophageal junction (GEJ) cancer. Bavituximab binds in a high-affinity complex with β2-glycoprotein and PS to reverse immunological non-responsiveness and activate multiple immune cell receptors, including TIMS and TAMS. Data from the Phase III Sunrise second-line lung cancer study indicated that patients who progressed on study treatment with bavituximab plus docetaxel and continued with a checkpoint inhibitor showed significantly improved overall survival. Cumulative data suggest that bavituximab may potentiate pembrolizumab-mediated checkpoint inhibition, potentially increasing overall clinical benefit.

Methods: This phase 2, multicenter, open-label, single-arm global study is designed to assess the safety, tolerability and efficacy of the bavituximab-pembrolizumab combination in advanced gastric or GEJ adenocarcinoma patients, regardless of PD-L1 status, who have progressed on or after at least one prior standard therapy. Patients must be treatment naive for checkpoint inhibitors. The study, started in August 2019, consists of an initial 3+3 de-escalation safety cohort to confirm the expansion cohort dose. A total of 80 patients will be enrolled. Primary endpoints will assess antitumor activity of the treatment combination on objective response rate using RECIST1.1, safety and tolerability. Secondary endpoints will evaluate antitumor characteristics, pharmacokinetics, and immunogenicity. Exploratory objectives include the evaluation of a novel biomarker signature panel and its relationship to efficacy outcomes. Research Sponsor: Oncologie, Inc.
A phase II trial of [fam-] trastuzumab deruxtecan (T-DXd, DS-8201a) in subjects with HER2-positive, unresectable, or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma.

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Background: Despite attempts, no HER2-directed therapies have been approved for gastric or GEJ cancer after disease progression on trastuzumab. [Fam-] trastuzumab deruxtecan (T-DXd, DS-8201a) is a novel HER2-targeted antibody-drug conjugate composed of a humanized monoclonal antibody specifically targeting HER2, a cleavable tetrapeptide-based linker (drug-to-antibody ratio of ≈8), and a potent topoisomerase I inhibitor payload. In a phase 1 study, T-DXd (5.4 or 6.4 mg/kg) showed promising antitumor activity in a variety of tumor types, including a confirmed objective response rate (ORR) of 43% among subjects with extensively pretreated HER2-positive gastric cancer (Shitara et al. Lancet Oncol. 2019;20(6):827-836). Here we describe the phase 2 trial evaluating the efficacy and safety of T-DXd in subjects with HER2-positive gastric/GEJ cancer previously treated with trastuzumab (NCT04014075). Methods: This is a single-arm, open-label, multicenter, phase 2 study in subjects with centrally confirmed, HER2-positive (immunohistochemistry [IHC] 3+ or IHC 2+/in situ hybridization positive), unresectable or metastatic gastric/GEJ cancer that progressed on or after first-line therapy with a trastuzumab-containing regimen. HER2 status will be confirmed by a fresh biopsy before enrollment. Subjects are excluded if they received anticancer therapy after a first-line trastuzumab-containing regimen. HER2 status will be confirmed by a fresh biopsy before enrollment. The study began in August 2019 and will recruit ≈72 subjects from 25 to 30 sites in North America and Europe. T-DXd at 6.4 mg/kg will be administered intravenously once every 3 weeks until disease progression. The primary efficacy endpoint is confirmed ORR by independent central review (ICR) using RECIST v1.1 criteria. Secondary endpoints include duration of response and progression-free survival by ICR and investigator assessment, ORR by investigator assessment, and overall survival. Additional endpoints include safety, disease control rate, and pharmacokinetic analyses. Health-related quality of life will also be measured. Clinical trial information: NCT04014075. Research Sponsor: Daiichi Sankyo.
Phase II study of the combination of abemaciclib and pembrolizumab in locally advanced unresectable or metastatic gastroesophageal adenocarcinoma: Big Ten Cancer Research Consortium BTCRC-GI18-149.

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**Background:** Metastatic gastroesophageal adenocarcinoma (GEA) has poor prognosis. Overall survival (OS) remains around 12 months (mo) with current therapies. Pembrolizumab is approved for advanced GEA that has progressed on at least 2 prior lines of systemic therapy. However, the majority of patients progress on this treatment, and less than 15% of patients experience objective response (OR). This study will evaluate efficacy of pembrolizumab in combination with cyclin-dependent kinase 4/6 (CDK4/6) inhibitor, abemaciclib, in patients with advanced GEA. Preclinical studies have demonstrated that CDK4/6 inhibitors can increase anti-tumor immunity and can synergize with immune checkpoint inhibitors. Based on these data, we hypothesize that abemaciclib will augment response to pembrolizumab in GEA. **Methods:** This is a multi-institutional, single arm, open label, phase II study of abemaciclib in combination with pembrolizumab in patients with advanced GEA who have progressed or were intolerant to at least 2 prior lines of therapy. Patients previously treated with immune checkpoint inhibitors or with microsatellite unstable tumors will be excluded. Treatments will be given on a 21 day cycle until disease progression or intolerable toxicities. Pembrolizumab, 200 mg intravenously, will be given on day 1, and abemaciclib, 150 mg, will be taken orally twice a day on days 1-21. Primary endpoint is progression free survival (PFS). Secondary endpoints include PFS rate at 6 mo, disease control rate, OS and OR rate. Correlative endpoints will examine relationship between PDL1 status, genomic signature and treatment response. Saliva samples will be collected for microbiome analysis. Archival tumor tissue and blood samples will be banked for future studies. A total of 31 evaluable subjects will be enrolled to detect an anticipated increase in the median PFS from 2 months (null hypothesis) to 4 months with 80% power at the one-sided 0.05 significance level. The trial is open to enrollment. Clinical trial information: NCT03997448. Research Sponsor: Eli Lilly.
Tislelizumab plus chemotherapy as first-line treatment for unresectable, locally advanced recurrent/metastatic esophageal squamous cell carcinoma.

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Background: Esophageal squamous cell carcinoma (ESCC) is the predominant histological subtype of esophageal cancer, particularly in Asian countries. Inhibition of the PD-1/PD-L1 axis has demonstrated antitumor activity in patients with advanced unresectable or metastatic ESCC. Tislelizumab, an investigational humanized IgG4 monoclonal antibody with high affinity and binding specificity for PD-1, was engineered to minimize binding to FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. Results from early phase clinical studies suggest tislelizumab, as a single agent or in combination with chemotherapy, was generally well tolerated and had antitumor activity in patients with solid tumors, including ESCC. Methods: This global, phase 3, randomized, placebo-controlled, double-blind study (NCT03783442) is designed to evaluate the efficacy and safety of tislelizumab plus chemotherapy as first-line treatment of unresectable, locally advanced recurrent or metastatic ESCC. Adult patients with histologically confirmed unresectable ESCC, or locally advanced recurrent/metastatic disease with a ≥6 month treatment-free interval, are eligible; palliative radiation administered ≥4 weeks from study initiation is allowed. Patients who received prior anti-PD-(L)1, anti-PD-L2, or first-line therapy are ineligible. Patients (n=480) will be randomized 1:1 to receive tislelizumab 200 mg IV every 3 weeks (Q3W) plus investigator-chosen chemotherapy (ICC) or placebo plus ICC. ICC options include: platinum (plat; cisplatin 60-80 mg/m² or oxaliplatin 130 mg/m² IV Q3W) + 5-FU 750-800 mg/m² by continuous IV infusion over 24 hours for 5d Q3W; or plat + capecitabine 1000 mg/m² orally BID for 14d Q3W; or plat + paclitaxel 175 mg/m² IV Q3W. Progression-free and overall survival are primary endpoints; secondary endpoints include objective response rate, duration of response, and health-related quality of life. Safety will be assessed by monitoring adverse events, physical examinations, vital signs, and electrocardiograms. This study is actively enrolling. Clinical trial information: NCT03783442. Research Sponsor: BeiGene, Co., Ltd.
KEYNOTE-811 pembrolizumab plus trastuzumab and chemotherapy for HER2+ metastatic gastric or gastroesophageal junction cancer (mG/GEJc): A double-blind, randomized, placebo-controlled phase III study.

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Background: Combination therapy with the anti-HER2 antibody trastuzumab plus fluoropyrimidine and platinum is the current standard of care for patients with HER2+ mG/GEJc. We hypothesize that combination anti-PD-1 and anti-HER2 therapy will result in T-cell activation, augment antibody-dependent, cell-mediated cytotoxicity, and potentiate antitumor immune response in HER2+ patients. A phase 2 study in HER2+ mG/GEJc demonstrated the safety and preliminary efficacy of trastuzumab/pembrolizumab/chemotherapy; the objective response rate was 87%, and the disease control rate was 100% (Janjigian YY, ASCO GI 2019). KEYNOTE-811 (ClinicalTrials.gov, NCT03615326), a global, multicenter, randomized, placebo-controlled, phase 3 study, is underway. Methods: Key eligibility criteria are age $\geq$18 years; previously untreated unresectable or metastatic HER2+ (centrally confirmed IHC 3+ or IHC 2+/ISH $\geq$ 2.0) G/GEJ cancer; life expectancy $> 6$ months with RECIST v1.1 measurable disease; and adequate organ function and performance status (ECOG PS of 0 or 1). Patients will be randomly assigned 1:1 to receive chemotherapy with pembrolizumab 200 mg intravenously (IV) or placebo with trastuzumab 6 mg/kg (after 8 mg/kg load) every 3 weeks (Q3W) up to 2 years or until intolerable toxicity or disease progression. Investigator-choice chemotherapy will include day 1 cisplatin 80 mg/m² IV and 5-fluorouracil 800 mg/m²/day IV (days 1-5) or oxaliplatin 130 mg/m² IV and capecitabine 1000 mg/m² BID days 1-14 (Q3W). Primary end points are progression-free survival and overall survival. Secondary end points are objective response rate, duration of response, and safety and tolerability. Adverse events are graded per CTCAE v4.0 and will be monitored for 30 or 90 days after treatment. Patients will be followed up for survival. Planned enrollment is approximately 692 patients. Clinical trial information: NCT03615326. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.
Phase II study of trifluridine/tipiracil (FTD/TPI) and oxaliplatin as induction chemotherapy (IC) in resectable esophageal and gastroesophageal junction adenocarcinoma (EGAC).

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Background: Neoadjuvant chemoradiation (CRT) followed by surgery is a standard approach for localized EGAC. Despite multimodality treatment, 5-year overall survival (OS) is less than 50%, with pathologic complete response (pCR) rates of 20%. Achievement of pCR is associated with an improved OS. We propose to use a novel combination of FTD/TPI and oxaliplatin as IC. We hypothesize that IC before CRT will increase the pCR rate in localized EGAC. Methods: This is an open-label, multicenter phase II trial. Patients (pts) with potentially resectable loco-regional EGAC are eligible. Pts. should have adequate organ function, ECOG performance status of 0 – 1, age < 76 years, and endoscopic ultrasound-determined node-positive disease with any T-stage, or T3-T4a with any N stage. Pts. with T4b or M1 disease will be excluded. Pts. will receive three cycles of IC with FTD/TPI and oxaliplatin. Based on the maximum tolerated dose (MTD) observed in a phase I trial, FTD/TPI will be administered 35 mg/m² BID, days 1–5 every 14 days, with a fixed dose of oxaliplatin 85 mg/m² (day 1). Pts will then undergo concurrent CRT (standard radiation dose of 5040 cGy will be utilized) with weekly Carboplatin (AUC 2) and Paclitaxel (50 mg/m²) for 6 weeks followed by surgery. Our primary objective is to evaluate the pCR rate. The secondary objectives include evaluation of 2-year disease-free survival (DFS), 2-year OS, and assessment of toxicities of the IC. As a correlative endpoint, circulating tumor DNA level will be correlated with disease recurrence and metabolic response on PET CT. Assuming a historic pCR rate of 20% with standard CRT, 41 pts (enrollment of up to 45 pts accounting for non-evaluable pts) are needed to show a 15% increase in pCR with IC with 80% power at one-sided significance level of $\alpha = 0.1$. In stage 1, $n_1 = 22$ evaluable pts will be enrolled. If there is 5 or more pCRs, an additional $n_2 = 19$ pts will be enrolled in stage 2. If 12 or more pCRs are observed in the total $n = 41$ evaluable pts, then the proposed treatment regimen will be considered promising for further study. We anticipate accrual over a 2-year period from 3 sites. Clinical trial information: NCT04097028. Research Sponsor: National Comprehensive Cancer Network (NCCN) Oncology Research Program.
A phase I open-label study to investigate safety and tolerability, efficacy, pharmacokinetics, pharmacodynamics, and immunogenicity of MT-5111 in subjects with HER-2 positive tumors.

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Background: Engineered toxin bodies (ETBs) are proprietarily engineered from a Shiga-like Toxin A subunit fused to antibody-like binding domains. ETBs can force receptor internalization, self-route to the cytosol, and induce cell-kill via inactivation of ribosomes. MT-5111 is a 55 kDa de-immunized ETB targeting HER2, and may not be subject to resistance mechanisms that exist for TKI, ADC, or antibodies. It binds a HER2 epitope distinct from trastuzumab or pertuzumab, could be combined with other HER2 targeting agents, and may have improved tumor penetration. Methods: MT-5111 is evaluated as monotherapy in subj with confirmed HER2+ locally advanced or metastatic cancers. The primary objective is to determine the maximum tolerated dose in subjects (subj) with advanced HER2-positive tumors. Secondary endpoints are PK, tumor response and immunogenicity. Part 1 will escalate doses to identify MTD in up to 42 subj. Part 2 will further evaluate MT-5111 at the MTD in up to 98 subj. All subj will receive MT-5111 on Days 1, 8, and 15 of each 21-day cycle until disease progression, unacceptable toxicity, death, withdrawal of consent or another reason for withdrawal. Part 1 will include subj with any HER2+ solid cancers. Part 2 will enroll 3 expansion cohorts: HER2+ breast (BC), HER2+ gastroesophageal cancer (GEA), and other HER2+ solid cancers. HER2+ must be demonstrated on metastatic lesions in case of metastases. Tumors tested by immunohistochemistry (IHC) must have IHC status of 2+ or 3+, regardless of in-situ hybridization (ISH) results; for BC and GEA, if no IHC is available, ISH per ASCO-CAP guidelines is used. Subj with HER2+ BC should have had at least 2 lines of HER2-directed therapy; subj with HER2+ gastric cancer should have received trastuzumab or have been intolerant to trastuzumab. Subj with evaluable disease may be included in Part 1; in Part 2, all subj must have at least 1 measurable lesion per RECIST 1.1. ECOG should be 0-1, and bone marrow, hepatic, renal, cardiac function should be adequate. Further details can be found on clinicaltrials.gov (NCT04029922). Enrollment has begun in September 2019. Clinical trial information: NCT04029922. Research Sponsor: Molecular Templates.
A phase Ib study of alofanib, an allosteric FGFR2 inhibitor, in patients with advanced or metastatic gastric cancer.

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Background: Fibroblast growth factor receptor 2 (FGFR2) is amplified or overexpressed in 3% to 61% of patients with gastric cancer and associated with a poor prognosis. Acquired mutations in FGFR2 develop resistance to multikinase inhibitors. Besides, resistance to monoclonal antibodies depends on the type of FGFR2 isoforms IIIc or IIIb expressed by cancer cells. Alofanib (RPT835) is a novel selective allosteric inhibitor of FGFR2. Alofanib could bind to the non-active site of FGFR2 extracellular domain and had an inhibitory effect on FGF2-induced phosphorylation of FRS2α. On preclinical models no severe organ and function test changes were observed. Based on these results, alofanib has advanced into clinical evaluation. Methods: RPT835GC1B is a Phase Ib study, being conducted in at least four sites in Russia, evaluating the safety and preliminary efficacy of alofanib in patients with advanced and metastatic gastric adenocarcinoma pretreated with ≥ 1 previous lines of therapy. This trial consists of two parts. The standard dose-escalation part (design 3+3) aims to establish the maximum tolerated dose (MTD) or recommended phase 2 dose (R2PD) as a primary endpoint. The first part of the study includes a 28-day period when alofanib is administered daily intravenously for 5-days followed by a 2-day interval (rest). There are five dose levels: 50, 100, 165, 250, and 350 mg/m². The dose-expansion phase accrues additional 20 patients, where comprehensive information to be collected. Secondary endpoints include pharmacokinetic parameters, rate of adverse events, progression-free survival, overall survival, and objective response rate. All patients will receive alofanib until disease progression or unacceptable toxicity. FGFR2 amplification, fusion, and overexpression will be assessed as well. Clinical trial information: NCT04071184. Research Sponsor: Skolkovo Foundation. Ruspharmtech.
EORTC 1707 VESTIGE: Adjuvant immunotherapy in patients with resected gastric cancer following preoperative chemotherapy with high risk for recurrence (ypN+ and/or R1): An open-label randomized controlled phase II study.

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Background: Gastroesophageal adenocarcinoma patients with metastatic lymph nodes (ypN+) or a microscopically incomplete surgical resection (R1) following neoadjuvant chemotherapy are at high risk of disease recurrence. Current practice is to continue with the same perioperative chemotherapy used prior to surgery, despite these suboptimal outcomes. Immune checkpoint blockade with nivolumab and ipilimumab has demonstrated activity in advanced gastroesophageal adenocarcinoma. We hypothesise that high risk (ypN+ and/or R1) post resection gastroesophageal adenocarcinoma patients who are treated with nivolumab and ipilimumab will have better disease free survival than patients who continue with standard post-operative chemotherapy. Methods: VESTIGE is an ongoing, international, open label randomized phase II study designed to evaluate the efficacy of adjuvant nivolumab plus ipilimumab versus standard post-operative chemotherapy in high risk (ypN+ and/or R1) post resection gastroesophageal adenocarcinoma patients. Eligible patients (n=240) will be randomised 1:1 to receive post-operative adjuvant chemotherapy (identical regimen as pre-operatively) or nivolumab 3mg/kg IV q2w plus ipilimumab 1mg/kg IV q6w x 1 year. Key inclusion criteria include ypN+ and/or R1 status following neoadjuvant chemotherapy plus surgery and an adequate pre-specified surgical resection. The primary endpoint of the study is disease free survival, with secondary endpoints of overall survival, safety, toxicity and quality of life. The trial will recruit 240 patients at 24 number of sites in the Czech Republic, France, Germany, Israel, Italy, Norway, Poland, Portugal, Spain, and United Kingdom. Recruitment commenced July 2019 and is anticipated to take 30 months. The VESTIGE translational research programme includes collection of pre-treatment biopsies, post-chemotherapy resection specimens and serial liquid biopsy on treatment to explore biomarkers predictive of immune checkpoint blockade efficacy. Clinical trial information: NCT03443856. Research Sponsor: BMS.
Margetuximab (M) combined with anti-PD-1 (MGA012) or anti-PD-1/LAG-3 (MGD013) +/- chemotherapy (CTX) in first-line therapy of advanced/metastatic HER2+ gastroesophageal junction (GEJ) or gastric cancer (GC).

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Background: Trastuzumab (T), a monoclonal antibody (mAb) targeting HER2, is standard of care palliative 1st-line therapy for advanced HER2+ GEJ/GC patients (pts). M, an Fc-engineered anti-HER2 mAb, targets the same HER2 epitope but with higher affinity for both 158V (high binding) and 158F (low binding) alleles of activating Fc receptor CD16A. M coordinately enhanced both innate and adaptive immunity, including antigen-specific T-cell responses to HER2. PD-1 and LAG-3 are T-cell checkpoint molecules that suppress T-cell function. MGA012 (INCMGA00012) is a humanized, hinge-stabilized, IgG4 anti-PD-1 mAb blocking binding of PD-L1 or PD-L2 to PD-1. MGD013 is a humanized Fc-bearing bispecific tetravalent protein that binds to both PD-1 and LAG-3, inhibiting their respective ligand binding. We previously reported that a CTX-free regimen of M+PD-1 blockade was well tolerated in GEJ/GC pts, and induced a 30% objective response rate (ORR). This was 2- to 3-fold greater than in historical controls with checkpoint inhibitors alone. This registration-directed trial assesses efficacy, safety, and tolerability of M+checkpoint inhibition ± CTX in metastatic/locally advanced, treatment-naive, HER2+ GEJ/GC pts.

Methods: This is a 2-cohort, adaptive open-label phase 2/3 study. The first single arm, CTX-free cohort A evaluates M+MGA012 in HER2+ (immunohistochemistry [IHC] 3+) and PD-L1+ (excluding microsatellite instability high) pts. After 40 pts are evaluated for response/safety, 60 more pts will be enrolled if the threshold for continuation is met. In randomized cohort B, HER2+ (IHC 3+ or 2+/fluorescent in situ hybridization+) pts are enrolled irrespective of PD-L1 status. Part 1 randomizes pts to 1 of 4 arms (50 pts each): control arm (T+CTX) or 1 experimental arm (M+CTX; M+CTX+MGA012; M+CTX+MGD013). CTX is investigator’s choice XELOX or mFOLFOX-6. Part 2 consists of control (T+CTX) vs 1 experimental arm (M+CTX) + either MGA012 or MGD013, depending on results from part 1; with 250 pts each. The primary efficacy endpoint for cohort A (both parts) is ORR per RECIST 1.1; for cohort B part 2 it is overall survival. Research Sponsor: MacroGenics, Inc.
Sgnlva-005: Open-label, phase II study of ladiratuzumab vedotin (LV) for advanced aerodigestive tract malignancies.

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**Background:** LIV-1 is a transmembrane protein with putative zinc transporter and metalloprotease activity. It has been linked to the epidermal-to-mesenchymal transition that leads to malignant progression and metastasis. Ladiratuzumab vedotin (LV), also known as SGN-LIV1A, is an investigational antibody-drug conjugate (ADC) targeting LIV-1 that is composed of a humanized IgG1 monoclonal antibody conjugated to monomethyl auristatin E (MMAE) via a protease-cleavable linker. MMAE-linked ADCs can induce mitotic arrest and immunogenic cell death. In a phase 1 study, LV was well tolerated and showed antitumor activity in heavily pretreated patients (pts) with metastatic breast cancer (Modi et al 2017). The current study was initiated to evaluate LV in previously treated pts with advanced upper aerodigestive tract malignancies. **Methods:** SGNLVA-005 (NCT04032704) is an open-label, phase 2 study evaluating LV monotherapy (2.5 mg/kg IV every 3 weeks) for pts with the following advanced malignancies: gastric and gastroesophageal junction (GEJ) adenocarcinoma, esophageal squamous cell carcinoma, small cell lung cancer, non-small cell lung cancer (NSCLC)-squamous, NSCLC-nonsquamous, and head and neck squamous cell carcinoma. Up to approximately 30 pts with unresectable locally advanced or metastatic disease, measurable disease per RECIST v1.1, an ECOG score of 0 or 1, and adequate organ function are enrolling in each of the cohorts. Pts in the gastric and GEJ adenocarcinoma and esophageal squamous cell carcinoma cohorts must have received no more than 1 prior line of platinum-based cytotoxic chemotherapy and pts in the gastric and GEJ adenocarcinoma cohort should have received prior anti-PD(L)1 therapy if indicated. The study consists of a 2-stage design that includes a Bayesian predictive probability of success approach to determine futility criteria. Study objectives include objective response rate (primary); safety and tolerability, disease control rate, duration of response, progression-free and overall survival, and pharmacokinetics and immunogenicity (all secondary); and pharmacodynamics. Study enrollment is ongoing in North America. Pts will also enroll in Europe and Asia. Clinical trial information: NCT04032704. Research Sponsor: Seattle Genetics, Inc.
A phase II study of futibatinib (TAS-120) in patients (pts) with advanced (adv) solid tumors harboring fibroblast growth factor receptor (FGFR) genomic aberrations.

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Background: FGFR genomic aberrations are known to drive oncogenesis in multiple tumor types via FGFR signaling pathway dysregulation. Futibatinib is an oral, highly selective, irreversible FGFR1-4 inhibitor that has shown potent antiproliferative activity against FGFR-deregulated tumors of diverse tissue origins in preclinical studies. In a phase 1 dose-escalation/expansion study, futibatinib showed promising antitumor activity and tolerability in previously treated pts with tumors harboring FGFR aberrations. This phase 2 study was designed to evaluate the efficacy and safety of futibatinib in pts with tumors harboring FGFR aberrations. The study will enroll pts in multiple cohorts based on diagnosis and FGFR aberration status; cohorts enrolling pts with adv solid tumors are reported here.

Methods: In this global, open-label, phase 2 study, pts (≥18 years; Eastern Cooperative Oncology Group performance status of 0 or 1) will be enrolled in cohort A (~60 pts with metastatic/locally adv solid tumors, except primary brain tumors or intrahepatic cholangiocarcinoma, harboring FGFR1-4 rearrangements and with disease progression after standard treatment) or cohort B (~35 pts with metastatic/locally adv gastric tumors harboring FGFR2 amplifications and with ≥2 prior therapies). Key exclusion criteria are clinically significant alterations in calcium-phosphorus homeostasis, ectopic mineralization/calcification, and prior FGFR inhibitor treatment. Pts will receive 20 mg futibatinib once daily in a continuous 28-day cycle until disease progression, unacceptable toxicity, or other discontinuation criteria are met. The primary endpoint is objective response rate (ORR) per independent central review. Secondary endpoints include ORR per investigator, disease control rate, duration of response, progression-free survival, overall survival, and safety. The anticipated start date is in April 2020. Research Sponsor: Taiho Oncology.

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Background: Oesophagogastric (OG) cancers represent a significant health burden and leading cause of cancer related death. Prognosis in advanced disease is poor and novel therapies are needed to improve outcomes. Molecular features of advanced OG cancer suggest that assessment of DDR (DNA damage repair) targeted agents is warranted. Specifically, ATM and ARID1A defects and mutational scars indicative of homologous recombination defects are present in a subset of OG cancers and are associated with polyadenosine 5’-diphosphoribose polymerase inhibitor (PARPi) sensitivity. Methods: SOlar is a multi-centre, open-label, single arm, phase II study of olaparib, a PARPi, in patients with advanced oesophageal, gastro-oesophageal junction and gastric adenocarcinoma. The trial will use a single-arm Simon two-stage design to evaluate the anti-tumour activity of olaparib in advanced OG cancers. The primary endpoint is disease control rate (DCR) at 8 weeks by RECIST v1.1. To rule out a DCR of \( \leq 15\% \) while aiming for DCR \( \geq 30\% \) (alpha = 0.09, power = 89\%), 54 patients must be recruited in total. An interim analysis will take place when 27 patients have been accrued, dosed and followed until the 8-week disease evaluation. If 4 or fewer patients have disease control (DC) the study will be terminated. If 5 or more patients have DC in the final analysis then it will be concluded that the treatment has shown anti-tumour activity compatible with 30\% and an investigation of potential biomarkers of response will be carried out. Secondary endpoints are ORR, DoR, OS, PFS, time to radiological progression and safety. This highly translational study incorporating serial tumour biopsies will investigate candidate predictive biomarkers of PARPi sensitivity with the aim of identifying responder/non-responder subpopulations. Further exploratory objectives will investigate the predictive role of early FDG-PET/CT in assessing tumour response and the creation of an organoid biobank. The trial opened to recruitment in July 2019 and will recruit up to 54 patients over 3 years. Clinical trial information: NCT03829345. Research Sponsor: AstraZeneca. The study is sponsored by The Royal Marsden Hospital.
A phase II study evaluating safety and efficacy of niraparib in patients with previously treated homologous recombination (HR) defective or loss of heterozygosity (LOH) high-metastatic esophageal/GEJ/proximal gastric adenocarcinoma: A Big Ten Cancer Research Consortium study.

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**Background:** Adenocarcinoma of esophagus (EAC) and GEJ is the fastest rising cancer in the US. The outcomes are extremely poor with median overall survival (OS) being 12 mo in patients (pts) with metastatic disease. The standard first line treatment for metastatic EAC is platinum-based regimen with median progression free survival (PFS) of 6 mo. Second line options are associated with limited efficacy. An analysis of TCGA has shown 40% of EAC harboring abnormalities in HR genes, most likely resulting from chronic acid reflux induced DNA damage. HR dysregulation is commonly associated with high LOH. Sensitivity to PARP inhibition has been shown to be a surrogate for HR defects or BRCAness phenotype. Clinically PARP inhibitors have shown activity in HR defective prostate and ovarian cancers. These findings provide the basis for this study.

**Methods:** Pts with metastatic esophageal/GEJ/proximal gastric adenocarcinoma, previously treated with 1 line of platinum containing chemotherapy, and harboring high LOH and/or deleterious alteration(s) in HR genes (BRCA1/2, PALB2, ATM, BARD1, BRIPI, CDK12, CHEK2, FANCA, RAD51, RAD51B, RAD51C, RAD51D, RAD54L, NBN, ARID1A, GEN1) are eligible for this study. Pts can be prescreened at the time of diagnosis of locally advanced or metastatic disease by genomic analysis of the most recent available tumor tissue. Pts will receive oral niraparib until disease progression or unacceptable toxicity. Primary objective is response rate (RR). Secondary objectives are safety and tolerability, progression free survival (PFS), and disease control rate (DCR). Exploratory objectives include correlation between high LOH and response to niraparib, mechanisms of resistance to PARP inhibition, EZH2 expression and its correlation with response and resistance to PARP inhibition, and analysis of germline HR gene mutations and correlation with response to niraparib. Estimated sample size is 43. The study has recently opened to accrual at Indiana University with intended collaboration with 2 additional sites. Clinical trial information: NCT03840967. Research Sponsor: Tesaro, Inc.
A pilot study of avelumab in Epstein-Barr virus-associated gastric cancer.

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Background: Gastric Cancer (GC) is the third most common cause of cancer related deaths worldwide. The median overall survival of patients with stage 4 disease is approximately 1 year. Current accepted treatment approach with chemotherapy is applied with little consideration for known genetic or biologic heterogeneity. Whilst immune-based approaches in GC look promising it is clear that single-agent PD1/PDL1 inhibition benefit a minority. We must clarify a means of identifying prospectively those patients who may benefit from this treatment. A recent landmark paper by The Cancer Genome Atlas (TCGA) proposed a classification of GC into four subtypes: Epstein-Barr-virus (EBV)-positive, microsatellite instable (MSI), chromosomal instable (CI), and genomically stable (GS). Two of the four – EBV and MSI subtypes – are likely to be immunogenic and amenable to PD1/PDL1 inhibition. Recent advances have shown EBV-positive tumors to be infiltrated by lymphocytes and be enriched for PDL1.

Methods: This single centre single-arm pilot study in gastric or junctional adenocarcinoma will explore the hypothesis that administering anti-PDL1 therapy (Avelumab) in a prospectively identified population enriched for potential responders will result in improved outcomes. The anticipated frequency of EBV associated-GC (c10%) means that approximately N = 100 patients will be screened to identify N = 10 participants. If a positive signal for efficacy is seen this will provide a basis for a larger, multicentre study. Previously treated Patients with confirmation of stage 4 EBV- positive gastric or oesophago-gastric adenocarcinoma meeting eligibility criteria will be enrolled. Avelumab will be administered at a dose of 10mg/kg IV every 14days. Primary endpoint is to determine the 6-month progression free survival (PFS) of Avelumab in EBV-associated GC. Secondary endpoints include overall response rate, overall survival, median PFS time and feasibility/accrual rate at 12 months. Exploratory endpoints will be to evaluate changes in immune parameters in the peripheral blood over time. Kaplan-Meier methods for primary efficacy endpoint with two-tailed one-sample proportion test will be used to evaluate the evidence to reject the null hypothesis. Clinical trial information: 2018-002085-39. Research Sponsor: MERCK.
A multicenter phase II trial of tumor treating fields plus chemotherapy for first-line treatment of gastric adenocarcinoma.

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Background: Gastric carcinoma (GC) is the third-leading cause of death in China (291,000 deaths in 2015). Current therapies include surgery, chemotherapy, radiotherapy and targeted therapy, which prolong PFS and OS to 6 months and 8-14 months, respectively. Tumor Treating Fields (TTFields) are a non-invasive, regional antimitotic treatment modality approved by the FDA for glioblastoma and malignant pleural mesothelioma. TTFields at specific frequency (100-500 kHz) are delivered via transducer arrays placed on the skin of the upper abdomen, back, right and left hypochondriac regions where the primary tumor lesion is located. TTFields were effective in preclinical models of gastric cancer and there are several ongoing Phase 3 trials of TTFields in multiple solid tumors. In this phase 2, single arm, open-label, multi-center study, we will investigate for the first time the efficacy and safety of TTFields concomitant with XELOX (oxaliplatin/capecitabine) as the first-line treatment of GC.

Methods: Patients (N = 50) with histologically confirmed unresectable, locally advanced or metastatic Gastroesophageal Junction (GEJ) or Gastric Adenocarcinoma (GC), aged ≥ 18 years, ECOG PS 0-1, who had no previous systemic treatment for the recurrent or metastatic disease will be enrolled. Patients will receive TTFields (150 kHz via the NovoTTF-100L (P) medical device for average monthly use of 18 hrs/day) plus XELOX chemotherapy (Oxaliplatin: 130 mg/m² on day 1 every 3 weeks; Capecitabine: 1000 mg/m², PO, BID on day 1-14 every 3 weeks). For HER-2 positive patients, trastuzumab is allowed. The primary endpoint is investigator-assessed Objective Response Rate (ORR) per RECIST 1.1. Secondary endpoints are time to tumor progression (TTP), progression-free survival (PFS), overall survival (OS), and 12-month OS rate. Adverse events (AEs) will be graded for severity according to CTCAE 5.0. Based on the historical ORR data in first-line chemotherapy in GC, we assumed that ORR will be higher than 45% with TTFields concomitant with chemotherapy. At least 45 patients need to be enrolled to ensure the lower boundary is 30% of the 95% CI. Estimating a patient dropout rate of 10%, 50 patients will be actually enrolled. Research Sponsor: Novocure and Zai Labs.
A phase III trial in progress comparing tislelizumab plus concurrent chemoradiotherapy (cCRT) with placebo plus cCRT in patients with localized esophageal squamous cell carcinoma (ESCC).

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Background: In China, esophageal cancer (EC) ranks as the eighth most common cancer and the sixth most common cause of cancer related death. The predominant histological subtype of EC is ESCC. At first diagnosis, more than half of patients (pts) with ESCC are unfit for surgery. An alternative to surgery is cCRT; however, many pts experience local failure or distant metastasis after cCRT. As such, innovative therapies are needed. Tislelizumab, an investigational humanized monoclonal antibody with high affinity and specificity for PD-1, was engineered to minimize binding to FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. In previous studies, tislelizumab, as a monotherapy and in combination with chemotherapy, was generally well tolerated and had antitumor activity in pts with ESCC. Methods: This phase 3, randomized, double-blind, placebo-controlled study (NCT03957590) is designed to compare the efficacy of tislelizumab versus placebo in combination with cCRT. Patients with histologically confirmed localized ESCC for whom cCRT is suitable and surgery is unsuitable/declined are being enrolled. Approximately 316 Chinese pts will be randomized 1:1 to receive tislelizumab (200 mg IV Q3W) or placebo (IV Q3W) in combination with cisplatin (25 mg/m² IV on Days 1-3 of each 3-week cycle) plus paclitaxel (135 mg/m² IV Q3W) and radiotherapy at a total dose of 50.4 Gy. An Independent Data Monitoring Committee will be established to assess the safety/tolerability of tislelizumab plus cCRT in the first 20 enrolled pts; monitoring across the study will occur at regular intervals thereafter. Progression-free survival (PFS), assessed by a Blinded Independent Review Committee per RECIST v1.1, is the primary endpoint. Secondary efficacy endpoints include overall response rate, duration of response, and overall survival. Incidence and severity of adverse events (CTCAE V5.0) and HRQoL are additional secondary endpoints. Exploratory endpoints include PFS rate at Years 1 and 2, pharmacokinetic profile, and predictive biomarker analyses. Clinical trial information: NCT03957590. Research Sponsor: BeiGene, Ltd.