

### Maintenance avelumab + best supportive care (BSC) versus BSC alone after platinum-based first-line (1L) chemotherapy in advanced urothelial carcinoma (UC): JAVELIN Bladder 100 phase III interim analysis.

*Thomas Powles, Se Hoon Park, Eric Voog, Claudia Caserta, B.P. Valderrama, Howard Gurney, Haralabos Kalofonos, Sinisa Radulovic, Wim Demey, Anders Ullén, Yohann Loriot, Srikala S. Sridhar, Norihiko Tsuchiya, Evgeny Kopyltsov, Cora N. Sternberg, Joaquim Bellmunt, Jeanny B. Aragon-Ching, Daniel Peter Petrylak, Alessandra di Pietro, Petros Grivas; Barts Cancer Institute, Experimental Cancer Medicine Centre, Queen Mary University of London, St Bartholomew's Hospital, London, United Kingdom; Sungkyunkwan University Samsung Medical Center, Seoul, South Korea; Centre Jean Bernard - Clinique Victor Hugo, Institut Inter-régional de Cancérologie, Le Mans, France; Medical Oncology Unit, Azienda Ospedaliera S. Maria, Terni, Italy; Department of Medical Oncology, Hospital Universitario Virgen del Rocío, Seville, Spain; Department of Clinical Medicine, Macquarie University, Sydney, NSW, Australia; Medical Oncology, University General Hospital of Patras, Patras, Greece; Institute for Oncology and Radiology of Serbia, Belgrade, Serbia; Department of Medical Oncology, AZ KLINA, Brasschaat, Belgium; Patient Area Pelvic Cancer, Theme Cancer, Karolinska University Hospital and Department of Oncology-Pathology, Karolinska Institute, Solna, Sweden; Gustave Roussy, INSERM U981, Université Paris-Saclay, Villejuif, France; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; Yamagata University Faculty of Medicine, Yamagata, Japan; State Institution of Healthcare Regional Clinical Oncology Dispensary, Omsk, Russian Federation; Englander Institute of Precision Medicine, Weill Cornell Medicine, New York, NY; Beth Israel Deaconess Medical Center, Boston, MA; Inova Schar Cancer Institute, Fairfax, VA; Smilow Cancer Center, Yale University, New Haven, CT; Pfizer SRL, Milan, Italy; Department of Medicine, Division of Medical Oncology, University of Washington, Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA*

**Background:** Platinum-based chemotherapy is an active 1L regimen for advanced UC; however, progression-free survival (PFS) and overall survival (OS) are generally short because of chemotherapy resistance. This randomized, phase 3 trial (JAVELIN Bladder 100; NCT02603432) evaluated avelumab (anti-PD-L1) as maintenance therapy following response or stable disease with 1L platinum-based chemotherapy in patients with advanced UC. **Methods:** Eligible patients with unresectable locally advanced or metastatic UC without disease progression after 4-6 cycles of gemcitabine with either cisplatin or carboplatin were randomized 1:1 to receive maintenance avelumab (10 mg/kg IV every 2 weeks) + best supportive care (BSC) or BSC alone, stratified by best response to 1L chemotherapy (complete/partial response vs stable disease) and by visceral vs nonvisceral disease when initiating 1L chemotherapy. The primary endpoint was OS, assessed from randomization in 2 primary populations: all randomized patients and patients with PD-L1+ tumors (Ventana SP263 assay). Secondary endpoints included PFS, objective response, and safety. **Results:** 700 patients were randomly assigned to maintenance avelumab + BSC (n=350) or BSC alone (n=350) and were followed for a median of 19.6 and 19.2 months, respectively. Overall, 358 (51%) had PD-L1+ tumors. Avelumab + BSC significantly prolonged OS vs BSC alone in all randomized patients (hazard ratio [HR] 0.69; 95% CI 0.56, 0.86; 1-sided p=0.0005); median OS with avelumab + BSC vs BSC alone was 21.4 vs 14.3 months, respectively. Avelumab + BSC also significantly prolonged OS vs BSC alone in patients with PD-L1+ tumors (HR 0.56; 95% CI 0.40, 0.79; 1-sided p=0.0003); median OS was not reached vs 17.1 months, respectively. An OS benefit was also observed across all prespecified subgroups. The HR for PFS based on blinded independent central review with avelumab + BSC vs BSC alone was 0.62 (95% CI 0.52, 0.75) in all randomized patients and 0.56 (95% CI 0.43, 0.73) in patients with PD-L1+ tumors. In treated patients in the avelumab + BSC (n=344) vs BSC alone (n=345) arms, respectively, all-causality adverse events (AEs) were reported at any grade in 98.0% vs 77.7% and at grade  $\geq 3$  in 47.4% vs 25.2%, and the most frequent grade  $\geq 3$  AEs were urinary tract infection (4.4% vs 2.6%), anemia (3.8% vs 2.9%), hematuria (1.7% vs 1.4%), fatigue (1.7% vs 0.6%), and back pain (1.2% vs 2.3%). **Conclusions:** JAVELIN Bladder 100 met its primary objective, demonstrating significantly prolonged OS with 1L maintenance avelumab + BSC vs BSC alone in advanced UC in all randomized patients and patients with PD-L1+ tumors. Efficacy benefits were seen across all prespecified subgroups, and the safety profile of avelumab was consistent with previous studies of monotherapy. Clinical trial information: NCT02603432. Research Sponsor: This study was funded by Pfizer as part of an alliance between Pfizer and Merck KGaA, Darmstadt, Germany.

### A randomized phase III trial of systemic therapy plus early local therapy versus systemic therapy alone in women with de novo stage IV breast cancer: A trial of the ECOG-ACRIN Research Group (E2108).

*Seema Ahsan Khan, Fengmin Zhao, Lawrence J. Solin, Lori J. Goldstein, David Cella, Mark Basik, Mehra Golshan, Thomas B. Julian, Barbara A. Pockaj, Christine A Lee, Wajeeha Razaq, Joseph A. Sparano, Gildy V Babiera, Irene Ang Dy, Sarika Jain, Paula Silverman, Carla Fisher, Amye Juliet Tevaarwerk, Lynne I. Wagner, George W. Sledge; Northwestern Memorial Hospital, Chicago, IL; Dana–Farber Cancer Institute, Malden, MA; Albert Einstein Medical Center, Philadelphia, PA; Fox Chase Cancer Center, Philadelphia, PA; Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL; McGill University, Jewish General Hospital Segal Cancer Centre, Montréal, QC, Canada; Brigham and Women’s Hospital and Dana-Farber Cancer Institute, Boston, MA; NRG Oncology, and The Allegheny Health Network Cancer Institute, Pittsburgh, PA; Mayo Clinic, Phoenix, AZ; Swedish Medical Center, Seattle, WA; NSABP Foundation and Peggy and Charles Stephenson Oklahoma Cancer Center, Oklahoma City, OK; Montefiore Medical Center/Albert Einstein College of Medicine/Albert Einstein Cancer Center, Bronx, NY; University of Texas MD Anderson Cancer Center, Houston, TX; St. Luke’s-Roosevelt Hospital, Effingham, IL; Northwestern University Division of Hematology/Oncology, Chicago, IL; University Hospitals Case Medical Center, Cleveland, OH; Indiana University School of Medicine, Indianapolis, IN; University of Wisconsin Carbone Cancer Center, Madison, WI; Wake Forest University Health Sciences, Winston Salem, NC; Stanford University School of Medicine, Stanford, CA*

**Background:** About 6% of newly diagnosed breast cancer patients present with Stage IV disease and an intact primary tumor (IPT). Locoregional treatment (LRT) for the IPT is hypothesized to improve survival based on retrospective analyses, but randomized trials have provided conflicting data. We now report the results of E2108, a Phase 3 trial that examined the worth of LRT for the IPT following initial systemic therapy. **Methods:** Stage IV patients with IPT were registered, treated with optimal systemic therapy (OST) based on patient and tumor characteristics; those who did not progress during 4-8 months of OST were randomized to LRT for the IPT, or no LRT. The primary endpoint was overall survival (OS), with locoregional disease control as a secondary endpoint. Stratified log rank test and Cox proportional hazard model were used to compare OS between treatment groups. Cumulative incidence of locoregional recurrence/progression was estimated and Gray test was used for treatment group comparisons. The trial was designed to detect an improvement in 3 year OS rate from 30% with OST alone to 49.3% for OST+LRT (power 95%, 1-sided alpha 0.05) with full information expected after 152 deaths; the data monitoring committee recommended data release after 80% of full information. **Results:** 390 patients were enrolled between 2/8/11 and 7/23/15, and received OST. Of these, 256 eligible patients were randomized to either continued OST alone (N = 131) or OST+LRT (N = 125). There were 121 deaths and 43 locoregional progression events after a median follow up 59 months (range: 0-91). There was no significant difference in OS (3-year OS rate 68.4% in OST+LRT vs. 67.9% OST alone arm, stratified log-rank  $p = 0.63$ , HR = 1.09, 90% CI: 0.80, 1.49) or in progression-free survival ( $p = 0.40$ ). The locoregional recurrence/progression was significantly higher in the OST alone arm (3-year rate 25.6% vs 10.2%, Gray test  $p = 0.003$ ). Health-related quality of life (HRQOL) measured by FACT-B Trial Outcome Index was significantly worse in the OST+LRT arm than OST alone arm at 18 months post randomization (60% completion, Wilcoxon rank sum test  $p = 0.01$ ), but no difference was observed at time points 6 months (74% completion) or 30 months (56% completion). **Conclusions:** Early local therapy does not improve survival in patients with de novo metastatic breast cancer and an IPT. Although there was a 2.5-fold higher risk of local disease progression without LRT, LRT of the IPT did not lead to improved HRQOL. Clinical trial information: NCT01242800. Research Sponsor: Eastern Cooperative Oncology Group.

### Carfilzomib, lenalidomide, and dexamethasone (KRd) versus bortezomib, lenalidomide, and dexamethasone (VRd) for initial therapy of newly diagnosed multiple myeloma (NDMM): Results of ENDURANCE (E1A11) phase III trial.

Shaji Kumar, Susanna J. Jacobus, Adam D. Cohen, Matthias Weiss, Natalie Scott Callander, Avina A. Singh, Terri L. Parker, Alex R. Menter, Xuezhong Yang, Benjamin Marshall Parsons, Pankaj Kumar, Prashant Kapoor, Aaron Seth Rosenberg, Jeffrey A. Zonder, Edward Anthony Faber, Sagar Lonial, Paul G. Richardson, Robert Z. Orlowski, Lynne I. Wagner, S. Vincent Rajkumar; Mayo Clinic, Rochester, MN; Dana-Farber Cancer Institute, Boston, MA; Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA; ThedaCare, Appleton, WI; University of Wisconsin, Carbone Cancer Center, Madison, WI; MOHPA, Burnsville, MN; Yale University, Hamden, CT; Kaiser Permanente-Lone Tree, Lone Tree, CO; Saint Francis Cancer Center, Greenville, NC; Gundersen Health System, La Crosse, WI; Illinois CancerCare, Peoria, IL; University of California Davis Comprehensive Cancer Center, Sacramento, CA; Department of Malignant Hematology, Barbara Ann Karmanos Cancer Institute/Wayne State University School of Medicine, Detroit, MI; Oncology/Hematology Care, Inc, Cincinnati, OH; Winship Cancer Institute of Emory University, Atlanta, GA; Dana Farber Cancer Institute, Boston, MA; The University of Texas MD Anderson Cancer Center, Houston, TX; Wake Forest University Health Sciences, Winston Salem, NC

**Background:** Bortezomib (btz) combined with lenalidomide (len) and dexamethasone (dex) (VRd) is a standard initial therapy for NDMM. Carfilzomib (cfz), a next-generation proteasome inhibitor, in combination with len-dex (KRd) has shown higher efficacy in phase II trials. This randomized phase III trial was designed to examine if KRd improves progression free survival (PFS) compared to VRd in NDMM (current results), and whether indefinite maintenance with len improves OS compared with two-year maintenance (to be analyzed once data matures). **Methods:** Patients (Pts) with NDMM, were randomized to receive VRd or KRd in a 1:1 fashion for 36 weeks followed by a second randomization (1:1) to indefinite versus two years of len maintenance. Pts without del17p, t(14;16), t(14;20), plasma cell leukemia or high-risk GEP70 profile, were enrolled. VRd arm included btz 1.3 mg/m<sup>2</sup> on days(d) 1, 4, 8, and 11 (d 1, 8 for cycles 9-12), len 25 mg d 1-14, and dex 40 mg d 1, 2, 4, 5, 8, 9, 11, 12 of a 3-week (wk) cycle for 12 cycles, while pts in the KRd arm received cfz 36 mg/m<sup>2</sup> d 1, 2, 8, 9, 15, 16 with len 25 mg daily on d 1-21 and dex 40 mg wkly, in 4 wk cycles for 9 cycles. Maintenance included len 15mg d 1-21 every 4 wks. The study was designed to detect a hazard ratio (HR)=0.75 with 80% power at 1-sided 2.5% alpha and 399 PFS events (progression or death regardless of intervening therapy). **Results:** The study accrued 1087 pts (VRd=542, KRd=545). The median age was 65y. Treatment, efficacy, and toxicity data are in the table. At the second of 3 planned interim analyses, with PFS HR=1.04 (95% CI, 0.8 to 1.3, p=0.74), futility was met. Median PFS was VRd=34.4m and KRd=34.6m; no differences were seen based on age (<65 or ≥65), presence or absence of t(4;14) or ISS stage. The three-year OS (95% CI) was similar: VRd 84% (80 to 88) and KRd 86% (82 to 89). **Conclusions:** In this randomized phase 3 trial, KRd did not improve PFS compared with VRd in NDMM. A significantly higher rate of cardio-pulmonary and renal toxicity was observed with KRd, while neuropathy rates were higher with VRd. VRd remains the standard triplet induction regimen in standard and intermediate risk NDMM, and a suitable backbone for 4 drug combinations. Clinical trial information: NCT01863550. Research Sponsor: U.S. National Institutes of Health.

	VRd	KRd
Median induction duration (mos)	5.9	8.2
<b>Reason off study</b>		
• Disease progression	6%	4%
• Adverse events	17%	9%
• Alternative therapy	18%	14%
• Patient withdrawal	7%	4%
<b>Response</b>		
• ≥ PR	83%	86%
• ≥ VGPR	43%	49%
• ≥ CR	10%	14%
<b>Toxicity Grade ≥3</b>		
• Non-hematological	42%	48%
• Composite Cardiac/ pulmonary/ renal	5%	16%
• Peripheral neuropathy	8%	1%

### **Pembrolizumab versus chemotherapy for microsatellite instability-high/mismatch repair deficient metastatic colorectal cancer: The phase 3 KEYNOTE-177 Study.**

*Thierry Andre, Kai-Keen Shiu, Tae Won Kim, Benny Vittrup Jensen, Lars Henrik Jensen, Cornelis J. A. Punt, Denis Michel Smith, Rocío Garcia-Carbonero, Manuel Benavides, Peter Gibbs, Christelle De La Fouchardiere, Fernando Rivera, Elena Elez, Johanna C. Bendell, Dung T. Le, Takayuki Yoshino, Ping Yang, Mohammed Zulfiqar Husain Farooqui, Patricia Marinello, Luis A. Diaz; Sorbonne University and Saint-Antoine Hospital, Paris, France; University College London Hospital NHS Foundation Trust, London, United Kingdom; Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; Department of Oncology, Herlev Hospital, Herlev, Denmark; Danish Colorectal Cancer Center South, Vejle University Hospital, Vejle, Denmark; Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands; Medical Oncology, Bordeaux University Hospital, Bordeaux, France; Hospital Universitario 12 de Octubre, Madrid, Spain; Hospital Universitario Regional y Virgen de la Victoria, Málaga, Spain; Royal Melbourne Hospital, Melbourne, Australia; Leon Berard Cancer Centre, Lyon, France; Hospital Universitario Marqués de Valdecilla, Santander, Spain; Medical Oncology Department, Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD; National Cancer Center Hospital East, Kashiwa, Japan; MSD China, Beijing, China; Merck & Co., Inc., Kenilworth, NJ; Memorial Sloan Kettering Cancer Center, New York, NY*

**Background:** KEYNOTE-177 (NCT02563002) is a phase 3, randomized open-label study evaluating the efficacy and safety of pembrolizumab (pembro) versus standard of care chemotherapy ± bevacizumab or cetuximab (chemo) as first-line therapy for patients (pts) with microsatellite-instability high/mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC). We present results of the final PFS analysis. **Methods:** A total of 307 pts with MSI-H/dMMR mCRC as determined locally and ECOG PS 0 or 1 were randomly assigned 1:1 to first-line pembro 200 mg Q3W for up to 2 years or investigator's choice of mFOLFOX6 or FOLFIRI Q2W ± bevacizumab or cetuximab (chemo chosen prior to randomization). Treatment continued until PD, unacceptable toxicity, pt/investigator decision to withdraw, or completion of 35 cycles (pembro only). Patients receiving chemo could crossover to pembro for up to 35 cycles after confirmed PD. Primary end points were PFS (RECIST v1.1, central review) and OS. Key secondary end points included ORR (RECIST v1.1, central review), and safety. The data cutoff date for this interim analysis was Feb 19, 2020. The study will continue without changes to evaluate OS. **Results:** At data cutoff, 153 pts were randomized to pembro and 154 to chemo. Median (range) study follow-up was 28.4 mo (0.2-48.3) with pembro vs 27.2 mo (0.8-46.6) with chemo. Pembro was superior to chemo for PFS (median 16.5 mo vs 8.2 mo; HR 0.60; 95% CI, 0.45-0.80;  $P=0.0002$ ). The 12- and 24-mo PFS rates were 55.3% and 48.3% with pembro vs 37.3% and 18.6% with chemo. Confirmed ORR was 43.8% vs 33.1%; median (range) duration of response was not reached (2.3+ to 41.4+) with pembro vs 10.6 mo (2.8 to 37.5+) with chemo. Grade 3-5 treatment related adverse event (AE) rates were 22% vs 66% for pembro vs chemo. One pt in the chemo arm died due to a treatment-related AE. **Conclusions:** Pembro provided a clinically meaningful and statistically significant improvement in PFS versus chemo as first-line therapy for pts with MSI-H/dMMR mCRC, with fewer treatment-related AEs observed and should be the new standard of care for these pts. Clinical trial information: NCT02563002. Research Sponsor: Merck & Co., Inc.

**Osimertinib as adjuvant therapy in patients (pts) with stage IB–IIIA EGFR mutation positive (EGFRm) NSCLC after complete tumor resection: ADAURA.**

*Roy S. Herbst, Masahiro Tsuboi, Thomas John, Christian Grohé, Margarita Majem, Jonathan Wade Goldman, Sang-We Kim, Dominika Marmol, Yuri Rukazenzov, Yi-Long Wu; Medical Oncology, Yale School of Medicine and Yale Cancer Center, New Haven, CT; Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Chiba, Japan; Department of Medical Oncology, Austin Health, Heidelberg, Australia; Klinik für Pneumologie - Evangelische Lungenklinik Berlin Buch, Berlin, Germany; Department of Medical Oncology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA; Department of Oncology, Asan Medical Center, Seoul, Korea, Republic of (South); Late Oncology Statistics, AstraZeneca, Cambridge, United Kingdom; Oncology Research & Development, AstraZeneca, Cambridge, United Kingdom; Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, School of Medicine, South China University of Technology, Guangzhou, China*

**Background:** Osimertinib is a 3rd-generation, CNS-active, EGFR-TKI with superior efficacy to comparator EGFR-TKI (gefitinib/erlotinib) in treatment-naïve EGFRm advanced NSCLC. Approx. 30% of pts with NSCLC present with early stage (I–IIIA) disease; surgery is the primary treatment. Adjuvant chemotherapy is standard of care in pts with resected stage II–III NSCLC and select stage IB pts; however, recurrence rates are high and other therapies are needed. ADAURA (NCT02511106) is a Ph III, double-blind, randomized study assessing the efficacy and safety of osimertinib vs placebo (PBO) in pts with stage IB–IIIA EGFRm NSCLC after complete tumor resection and adjuvant chemotherapy, when indicated. Following Independent Data Monitoring Committee recommendation, the trial was unblinded early due to efficacy; we report an unplanned interim analysis. **Methods:** Eligible pts:  $\geq 18$  years (Japan/Taiwan:  $\geq 20$ ), WHO PS 0/1, primary non-squamous stage IB/II/IIIA NSCLC, confirmed EGFRm (ex19del/L858R), complete resection of primary NSCLC with full recovery from surgery; postoperative chemotherapy was allowed. Pts were randomized 1:1 to osimertinib 80 mg once daily orally or PBO to receive treatment for up to 3 years and stratified by stage (IB/II/IIIA), mutation type (ex19del/L858R), and race (Asian/non-Asian). Primary endpoint: disease-free survival (DFS) by investigator in stage II–IIIA pts. Secondary endpoints: overall survival (OS) and safety. Data cutoff (DCO): 17 Jan 2020. **Results:** Globally, 682 pts were randomized to treatment: osimertinib n=339, PBO n=343. Baseline characteristics were balanced across arms (osimertinib/PBO): stage IB 31/31%, stage II/IIIA 69/69%, female 68/72%, ex19del 55/56%, L858R 45/44%. In stage II–IIIA pts, DFS hazard ratio (HR) was 0.17 (95% CI 0.12, 0.23);  $p < 0.0001$  (156/470 events); 2-year DFS rate was 90% with osimertinib vs 44% with PBO. In the overall population, DFS HR was 0.21 (0.16, 0.28);  $p < 0.0001$  (196/682 events); 2-year DFS rate was 89% with osimertinib vs 53% with PBO. OS was immature (4% maturity) with 29/682 deaths (osimertinib n=9, PBO n=20) at DCO. The safety profile was consistent with the known safety profile of osimertinib. **Conclusions:** Adjuvant osimertinib is the 1st targeted agent in a global trial to show a statistically significant and clinically meaningful improvement in DFS in pts with stage IB/II/IIIA EGFRm NSCLC after complete tumor resection and adjuvant chemotherapy, when indicated. Adjuvant osimertinib provides an effective new treatment strategy for these pts. Clinical trial information: NCT02511106. Research Sponsor: AstraZeneca.

**Clinical impact of COVID-19 on patients with cancer: Data from the COVID-19 and Cancer Consortium (CCC19).**

*Jeremy Lyle Warner, Sam Rubinstein, Petros Grivas, Toni K. Choueiri, Nicole Maria Kuderer, Dimpy Shah, Donna R Rivera, Shilpa Gupta, Mehmet Asim Bilen, Thorvardur Ragnar Halfdanarson, Deborah Blythe Doroshov, Firas Wehbe, Sumit Shah, Yu Shyr, Gilberto Lopes, Corrie Painter, Gary H. Lyman, Michael A. Thompson, Solange Peters, Brian I. Rini; Vanderbilt-Ingram Cancer Center, Nashville, TN; Vanderbilt University Medical Center, Nashville, TN; University of Washington, Seattle, WA; Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA; Advanced Cancer Research Group and University of Washington, Kirkland, WA; University of Texas MD Anderson Cancer Center, Houston, TX; National Cancer Institute, Rockville, MD; Department of Medicine, Masonic Cancer Center, University of Minnesota, Minneapolis, MN; Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, GA; Mayo Clinic, Rochester, MN; Icahn School, New Haven, NY; Northwestern University Feinberg School of Medicine, Chicago, IL; Stanford Cancer Institute, Stanford, CA; University of Miami Health System, Miami, FL; Broad Institute, Cambridge, MA; Fred Hutchinson Cancer Research Center, Seattle, WA; Aurora Cancer Care, Aurora Research Institute, Advocate Aurora Health, Milwaukee, WI; Lausanne University Hospital (CHUV), Lausanne University, Lausanne, Switzerland; Cleveland Clinic Taussig Cancer Institute, Cleveland, OH*

**Background:** There are limited data on COVID-19 in patients with cancer. We characterize the outcomes of patients with cancer and COVID-19 and identify potential prognostic factors. **Methods:** The COVID-19 and Cancer Consortium (CCC19) cohort study includes patients with active or prior hematologic or invasive solid malignancies reported across academic and community sites. **Results:** We included 1,018 cases accrued March-April 2020. Median age was 66 years (range, 18-90). Breast (20%) and prostate (16%) cancers were most prevalent; 43% of patients were on active anti-cancer treatment. At time of data analysis, 106 patients (10.4%) have died and 26% met the composite outcome of death, severe illness requiring hospitalization, and/or mechanical ventilation. In multivariable logistic regression analysis, independent factors associated with increased 30-day mortality were age, male sex, former smoking, ECOG performance status (2 versus 0/1: partially adjusted odds ratio (pAOR) 2.74, 95% CI 1.31-5.7; 3/4 versus 0/1: pAOR 5.34, 95% CI 2.44-11.69), active malignancy (stable/responding, pAOR 1.93, 95% CI 1.06-3.5; progressing, pAOR 3.79, 95% CI 1.78-8.08), and receipt of azithromycin and hydroxychloroquine. Tumor type, race/ethnicity, obesity, number of comorbidities, recent surgery, and type of active cancer therapy were not significant factors for mortality. **Conclusions:** All-cause 30-day mortality and severe illness in this cohort were significantly higher than previously reported for the general population and were associated with general risk factors as well as those unique to patients with cancer. Cancer type and treatment were not independently associated with increased 30-day mortality. Longer follow-up is needed to better understand the impact of COVID-19 on outcomes in patients with cancer, including the ability to continue specific cancer treatments. Research Sponsor: None.

**Thoracic Cancers International COVID-19 Collaboration (TERAVOLT): Impact of type of cancer therapy and COVID therapy on survival.**

*Leora Horn, Jennifer G. Whisenant, Valter Torri, Li-Ching Huang, Annalisa Trama, Luis G. Paz-Ares, Enriqueta Felip, Vera Pancaldi, Alessandro De Toma, Marcello Tiseo, Pilar Garrido, Carlo Genova, Jacques Cadranel, Olivier Michielin, Anne-Marie C. Dingemans, Jan P. Van Meerbeeck, Fabrice Barlesi, Heather A. Wakelee, Solange Peters, Marina Chiara Garassino; Department of Medicine, Vanderbilt Ingram Cancer Center, Nashville, TN; Vanderbilt-Ingram Cancer Center, Nashville, TN; IRCCS Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy; Vanderbilt University Medical Center, Nashville, TN; Istituto Nazionale dei Tumori, Milan, Italy; Hospital Universitario 12 de Octubre, Madrid, Spain; Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; Centre de Recherche en Cancerologie de Toulouse, Toulouse, France; Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Medical Oncology Unit, University Hospital of Parma, Parma, Italy; University Hospital Ramón y Cajal, Madrid, Spain; Lung Cancer Unit, Ospedale Policlinico San Martino, Genoa, Italy; Service de Pneumologie Hôpital Tenon, Paris, France; Center of Personalized Oncology, Lausanne University Hospital (CHUV), Switzerland, Molecular Modeling Group, Swiss Institute of Bioinformatics, Lausanne, Switzerland; Maastricht University Medical Center, Maastricht, Netherlands; Department of Thoracic Oncology, University Hospital Antwerp, Edegem, Belgium; Aix Marseille University, CNRS, INSERM, Marseille, France; Stanford Cancer Institute, Stanford, CA; Lausanne University Hospital (CHUV), Lausanne University, Lausanne, Switzerland*

**Background:** Early reports on cancer patients infected with COVID-19 have suggested a high mortality rate compared to the general population. Patients with thoracic malignancies are considered high risk given their age, preexisting comorbidities, smoking, and pre-existing lung damage in addition to therapies administered to treat their illness. **Method:** We launched a global consortium to collect data on patients with thoracic malignancies diagnosed with COVID-19 infection to understand the impact on this patient population. Goals of this consortium are to provide data for guidance to oncology professionals on treating patients with thoracic malignancies while understanding the risk factors for morbidity and mortality from this novel virus. **Results:** As of April 23, 2020, a total of 295 patients across 59 centers and 9 countries have been entered; median age 68, 31% female, 79% current/former smokers, HTN and COPD most common comorbidities; 73% NSCLC, 14% SCLC, 4% meso and thymic, 49% patients with stage IV disease, majority on chemo or chemo-IO and 24% receiving RT. The use of IO or chemo-IO does not appear to impact risk of hospitalization, while treatment with TKI appears to be associated with a decreased risk of hospitalization. 73% patients required hospitalization, most common therapy given to treat COVID was antibiotics 67%, antivirals 33%, and steroids 30%. **Conclusion:** With an ongoing global pandemic of COVID-19 our data suggest that patients with thoracic malignancies are at high risk for hospitalization. Updated results to be presented will include impact on specific chemo-IO regimens and number of lines of therapy, which may impact hospitalization and risk of death as well as which therapies administered may impact survival in patients treated for COVID-19. Research Sponsor: None.

### **Avelumab in patients with gestational trophoblastic tumors resistant to mono-chemotherapy: Final outcomes of TROPHIMMUN phase II trial, cohort A.**

*Benoit You, Pierre-Adrien Bolze, Jean-Pierre Lotz, Jerome Massardier, Laurence Gladieff, Florence Joly, Touria Hajri, Delphine Maucort-Boulch, Sylvie Bin, Pascal Rousset, Laurent Villeneuve, Adeline Roux, Marine Alves-Ferreira, Daniele Grazziotin, Catherine Mercier, Gilles Freyer, Francois Golfier; Institut de Cancérologie des Hospices Civils de Lyon (IC-HCL), CITOHL, EMR UCBL/HCL 3738, Lyon, GINECO & GINEGEPS, Lyon, France; Centre de Référence des Maladies Trophoblastiques, Hospices Civils de Lyon, Lyon, France; Hôpital Tenon, Paris, France; GINECO, Institut Claudius Regaud, Toulouse, France; Department of Medical Oncology, Centre François Baclesse, Caen, France; Centre de Référence des Maladies Trophoblastiques, Lyon, France; Hospices Civils de Lyon, Lyon, France; Hospice Civils Lyon Unite Rechercher Clinique Pole Information Medicale, Lyon, France; APREC, Hospital Tenon (AP-HP), Paris, France; Centre Hospitalier Lyon-Sud, Pierre-Bénite, France; Centre de Référence des Maladies Trophoblastiques, Centre Hospitalier Lyon-Sud, EMR3738, Université Lyon 1, Lyon, France*

**Background:** Patients with gestational trophoblastic tumors (GTT) resistant to monotherapy are treated with historic chemotherapy regimens known to be effective, but toxic. PD-L1 is constitutively expressed in all GTT subtypes (Bolze et al. *Int J Gynecol Cancer* 2017). HLA-G and natural killer (NK) cells are involved in GTT immune-surveillance. The anti-PD-L1 monoclonal antibody avelumab (Pfizer & Merck KGaA) triggers cytotoxicity through NK cells. The objective of TROPHIMMUN trial was to assess the efficacy of avelumab in patients with chemoresistant GTT. **Methods:** In the cohort A of this academic multicenter trial (NCT03135769), avelumab was given at 10 mg/kg Q2W in patients with GTT resistant to monotherapy. Avelumab was prescribed until hCG normalization, and then for 3 consolidation cycles. The primary objective was the rate of patients with hCG normalization, with a 2 step Simon design. **Results:** 15 patients (median 34 y old) followed by the French Gestational Trophoblastic Center were treated from Dec 2016 to Sept 2019 (stage I/III: 53%/47%; FIGO score 0-4: 33%; score 5-6: 47%; score >6: 20%). They all had progressed with previous methotrexate, and 1 patient with actinomycin-D. They received median 8 avelumab cycles (range: 2-11). The tolerability was favorable. 93 % of patients developed drug-related grade 1-2 toxicities (86% grade 1), mainly including fatigue (33% patients); nausea-vomiting (33%); infusion-related reactions (27%); thyroid disorder (20%); dry eyes (20%) & diarrhea (20%). A grade 3 uterus bleeding (treatment unrelated) was observed in 1 patient. Median follow-up was 30 months. Successful hCG normalizations were obtained in 8 patients (53%, median 9 avelumab cycles), either during avelumab treatment in 7 patients, or after avelumab discontinuation in 1 patient. None presented relapse afterwards, and 1 patient had a subsequent healthy pregnancy. Avelumab resistances requiring switch to chemotherapy were observed in 7 patients (47%), who normalized hCG with subsequent actinomycin-D (42%), or surgery/polychemotherapy (57%). The likelihood of success with avelumab was not related to the FIGO score, or disease stages. **Conclusions:** TROPHIMMUN is the first trial of immunotherapy in GTT patients. The anti-PD-L1 monoclonal antibody avelumab was effective, with a favorable safety profile compared to chemotherapy, in patients with resistance to mono-chemotherapy. About 50 % patients could be cured of their chemoresistant diseases. Avelumab may be a new therapeutic option. Clinical trial information: NCT03135769. Research Sponsor: Merck Serono - Pfizer.

**The pediatric precision oncology study INFORM: Clinical outcome and benefit for molecular subgroups.**

*Cornelis Martinus van Tilburg, Elke Pfaff, Kristian W. Pajtler, Karin P.S. Langenberg, Petra Fiesel, Barbara C. Jones, Gnana Prakash Balasubramanian, Sebastian Stark, Pascal D. Johann, Mirjam Blattner-Johnson, Kathrin Schramm, Natalie Jäger, Andreas von Deimling, Uta Dirksen, Angelika Freitag, Ruth Witt, Peter Lichter, David T.W. Jones, Stefan M. Pfister, Olaf Witt; Hopp Children's Cancer Center Heidelberg (KiTZ), German Cancer Research Center (DKFZ) and Heidelberg University Hospital, Heidelberg, Germany; Princess Máxima Center for Pediatric Oncology, Utrecht, Netherlands; German Cancer Research Center (DKFZ), Heidelberg, Germany; Hopp Children's Cancer Center Heidelberg (KiTZ), German Cancer Research Center (DKFZ), Heidelberg, Germany; Department of Neuropathology, Institute of Pathology, Heidelberg University Hospital (UKHD), National Center for Tumor Diseases (NCT), UKHD and German Cancer Research Center (DKFZ), German Cancer Consortium (DKTK) Core Center Heidelberg, Germany, Heidelberg, Germany; Pediatrics III, West German Cancer Center, University Hospital Essen, German Cancer Consortium (DKTK), Essen, Germany; NCT Trial Center, National Center for Tumor Diseases and German Cancer Research Center (DKFZ), Heidelberg, Germany*

**Background:** Several pediatric precision oncology programs have identified molecular actionable variants. However, the clinical benefit is largely unknown. We here report a target prioritization algorithm and associated clinical outcome. **Methods:** INFORM is a prospective, non-interventional, multi-center, multi-national, and feasibility registry collecting clinical and molecular data. Patients with refractory/relapsed/progressive malignant disease, including primary diagnosis high-risk entities, can be enrolled. Fresh frozen tumor material (incl. germline DNA) was subjected to WES, lcWGS, RNA-Seq, RNA expression array and DNA-methylation. A weekly interdisciplinary molecular board reviewed and prioritized alterations based on a 7-step scale from 'very high' to 'very low', depending on the type of alteration and its entity specific relevance (described by Worst et al. Eur J Cancer 2016). **Results:** To date, more than 1300 patients were enrolled. 525 patients finished follow-up and were included in this analysis. They were enrolled in 72 centers in 8 countries. The median age was 12.0 (range 0 - 40) years. Average turnaround time from submission to report was 25.4 days. Median PFS and OS were 116 (95% CI 105 – 135) and 289 (95% CI 250 – 335) days. The distribution of the highest priority target per patient was: very high 8.0%, high 14.8%, moderate 20.3%, intermediate 23.6%, borderline 14.4%, low 2.5%, very low 1.0% and no actionable target 15.4%. 149 patients received targeted treatment on the basis of identified targets, of which 20 had a very high priority target (mostly ALK, BRAF and NRAS mutations and MET and NTRK-fusions) with a median PFS of 204.5 (95% CI 91.0 – 628.0) compared to 114 (95% CI 103 – 133) days in all other 505 patients ( $p = 0.0095$ ). OS did not show clinically relevant differences. Explorative analysis of the time to progression (TTP) ratio (before compared to after enrollment) showed that patients treated according to a very high priority target had a higher TTP ratio (1.0) compared to all other patients (0.7). Possible predisposition syndromes were identified in 7.8% of patients, half of which were newly diagnosed. Methylation analysis provided a diagnosis refinement in 8% of CNS tumors. **Conclusions:** Pediatric precision oncology in a real world, multi-national setting is feasible. The prioritization algorithm identifies subgroups benefitting from molecularly matched targeted treatment. Still, for the patients without a very high priority target further layers of molecular and functional data should be incorporated in future programs. Research Sponsor: German Cancer Aid, Other Foundation, Ein Herz für Kinder Foundation, German Cancer Consortium (DKTK).