8001 **Oral Abstract Session**

ATLAS: A phase 3 randomized trial of carfilzomib, lenalidomide, and dexamethasone versus lenalidomide alone after stem-cell transplant for multiple myeloma.

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Background: Treatment following autologous stem cell transplantation (ASCT) for multiple myeloma (MM) remains an area of active investigation. We have shown that extended post-ASCT treatment with carfilzomib, lenalidomide, and dexamethasone (KRd) after KRd induction improved the depth and duration of response (Jasielec et al, Blood 2020), suggesting a benefit of post-ASCT KRd therapy. Here we directly compare that strategy to standard lenalidomide (R) maintenance. **Methods:** This international open-label phase 3 randomized trial recruited newly-diagnosed MM patients (pts) who received any induction therapy for up to 12 months (mo) followed by single ASCT and achievement of at least stable disease within 100 days afterward. Pts were randomized to receive either KRd or R, stratified by post-transplant response (≥VGPR vs < VGPR) and cytogenetic risk [standard risk (SR) vs high [HR: presence of t(4;14), t(14;16), or del(17p)]. Pts randomized to KRd received carfilzomib 36 mg/m^2 on days (D) 1,2,8,9,15,16 for 4 cycles (C) then D1,2,15,16 starting C5; R 25 mg D1-21, and dexamethasone 20 mg D1,8,15,22 in 28-day cycles. KRd pts with SR who reached IMWG-defined MRD-negativity after C6 de-escalated therapy to R alone after C8 (KRd- > R); the rest continued KRd through C36 followed by R alone until progression. Pts randomized to R received lenalidomide 10 mg C1-3 and then 15 mg daily. The primary objective was to compare progression free survival (PFS) rate between the two arms. Based on historical PFS rates, a sample size of 180 Pts was calculated to provide 85% power with 2-sided alpha 0.05. **Results:** 180 pts were enrolled (R n = 87; KRd n = 93) through 10/21/20; data cutoff was 12/31/21. Pt characteristics in the KRd and R arms were balanced for median age (58 vs 59 yrs), >VGPR (88% vs 92%), and HR (23% vs 21%). After 6 cycles, 47% pts in the KRd arm and 29% in the R arm achieved MRD-negativity (p = 0.017). 34 KRd pts eligible for de-escalation converted to R alone after C8 and were analyzed on the KRd arm per intention-to-treat. At median follow-up of 33.8 mo, 23 pts (25%) on the KRd arm and 38 pts (44%) on the R arm progressed; estimated median PFS was 59.0 mo for KRd vs 41.4 mo for R (Hazard Ratio 0.56, logrank p = 0.026). At cutoff, 90% of KRd and 87% of R pts were alive; no deaths were treatment-related. All-grade toxicities were generally comparable between arms. The most common grade 3+ AEs and those of special interest were neutropenia (KRd 47%; R 59%), thrombocytopenia (KRd 13%; R 7%), infections (KRd 15%; R 6%), cardiovascular toxicities (KRd 4%, R 5%), and secondary malignancies (KRd 2, R 2). **Conclusions:** This is the first randomized phase 3 trial demonstrating superior PFS with extended post-transplant KRd therapy compared to R maintenance. Therefore, MRD/risk-adapted post-ASCT extended KRd treatment may represent a new standard of care. Clinical trial information: NCT02659293. Research Sponsor: Amgen, Pharmaceutical/Biotech Company.

8002 **Oral Abstract Session**

Daratumumab carfilzomib lenalidomide and dexamethasone as induction therapy in high-risk, transplant-eligible patients with newly diagnosed myeloma: Results of the phase 2 study IFM 2018-04.

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Background: High-risk (HR) cytogenetic is associated with poor outcome in transplant eligible (TE) newly diagnosed myeloma multiple myeloma (NDMM). The triplet combination carfilzomib lenalidomide and dexamethasone (KRD) plus transplantation demonstrated high efficacy with favorable safety profile in TE-NDMM patients (FORTE). The addition of daratumumab (Dara) to frontline therapy also improved response rate and progression free-survival in TE-NDMM patients (CASSIOPEIA, GRIFFIN). Double transplant also improved outcome of HR TE NDMM patients (EMN02, STAMINA). The phase 2 trial 2018-04 from the Intergroupe Francophone du Myelome (IFM) is evaluating an intensive strategy with Dara-KRD induction and consolidation plus double transplant in HR TE NDMM (NCT03606577). **Methods:** HR MM was defined by the presence of del17p, t(4;14) and/or t(14;16). Stategy includes Dara-KRD induction (6 cycles), autologous stem cell transplantation (ASCT), Dara-KRD consolidation (4 cycles), second ASCT, Dara-lenalidomide maintenance. The primary endpoint was the feasibility of this intensive strategy. Here, we report efficacy and safety analysis of Dara-KRD induction. **Results:** Fifty patients with previously untreated NDMM were included from july 2019 to march 2021 in 11 IFM centers Median age was 57 (range 38 -65). ISS stage 3 was present in 12 (24%) patients. Based on inclusion criteria, all patients had HR cytogenetic, including 17p deletion (n = 20, 40%), t(4;14) (n = 26, 52%) or t(14;16) (n = 10,20%). Forty-six patients completed Dara-KRD induction. Two patients discontinued treatment due to severe adverse event (COVID-19 infection, n = 1 ; drug-induced hepatitis, n = 1) and 2 patients discontinued treatment due to disease progression. Grade 3-4 treatment related adverse event (> 5% of patients) were neutropenia (38%), anemia (14%), thrombocytopenia (8%), infection (6%), renal insufficiency (6%) and deep-vein thrombosis (6%). Two patients (6%) experienced stem-cell collection failure. Overall response rate was 96%, including 92 % > very good partial response. Among 37 (/46) evaluable patients post induction, Minimal Residual Disease negativity rate (NGS, 10^{-5}) was 62%. **Conclusions:** Dara-KRD as induction prior ASCT is safe and allows deep responses in TE NDMM patients with high-risk cytogenetic profile. IFM 2018-04 study is ongoing and longer follow-up is needed to evaluate safety and efficacy of the overall strategy with Dara-KRD induction and consolidation plus double transplant in this subset of HR patients. Clinical trial information: NCT03606577. Research Sponsor: Celgene/BMS, Amgen, Janssen.

8003 **Oral Abstract Session**

Phase 1 study of CART-ddBCMA in relapsed or refractory multiple myeloma.

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Background: Chimeric Antigen Receptor (CAR) T cell therapies targeting B-cell maturation antigen (BCMA) have demonstrated benefit in patients (pts) with relapsed and/or refractory Multiple Myeloma (RRMM). CART-ddBCMA is an autologous anti-BCMA CAR T cell therapy that utilizes a novel, synthetic binding domain, called a D-Domain, instead of a typical scFv binder. The objective of this first-in-human trial is to assess the safety and efficacy of CART-ddBCMA. **Methods:** This is a Phase 1, multicenter, open label, dose escalation trial for pts with RRMM who have received ≥3 prior regimens or are triple-refractory. After apheresis, bridging therapy is allowed during manufacturing. Pts receive fludarabine and cyclophosphamide (30/300 mg/m^2/day) days -5 to -3 and CART-ddBCMA infusion on day 0. Dose escalation was performed at 100 (DL1) and 300 (DL2) x 10^6 (± 20%) CAR+T cells, followed by expansion of DL1. The primary endpoint is incidence of adverse events (AEs), including dose-limiting toxicities (DLTs). Additional endpoints are depth and duration of response (IMWG Criteria), minimal residual disease (MRD, clonoSEQ), progression-free (PFS) and overall survival (OS). Pts with 1- and 3-months follow-up were eligible for safety and efficacy analysis, respectively. **Results:** As of January 25, 2022, 25 pts received CART-ddBCMA, with median age 66 (range: 44-76), after a median of 5 prior lines of therapy (3-16), including 10 (40%) with extramedullary disease (EMD). Median follow-up was 9.8 (2-23.7) months. Overall, 25 pts (19 DL1; 6 DL2) were evaluable for safety and 24 (18 DL1; 6 DL2) for efficacy analysis. All pts experienced CRS, but only 1 pt (in DL2) had grade (gr) 3 CRS. All other CRS cases were gr ≤2, with no cases of gr ≥3 CRS in DL1. Four pts experienced ICANS (2, gr ≤2; 2, gr 3), with 1 gr 3 case in each of DL1 (5%) and DL2 (17%). Standard management resulted in resolution of CRS/ICANS within 30 days in all cases without sequelae. The ORR = 100%, sCR/CR rate = 67%, and ≥VGPR rate = 88%. Conversion to CR/sCR has occurred with longer follow-up, as late as month 9 in this trial. At time of data-cut 5 pts in DL1 with PR/VGPR have < 9 months follow-up, with 4 (of 4 evaluable) negative at $\geq 10^{-5}$ for MRD. Overall, 17 of 20 (85%) evaluable pts have achieved best MRD response of $\geq 10^{-5}$. In the dose escalation pts (i.e., those with longest follow-up, n = 12), the ORR and CR/sCR rate was 100% and 75%, respectively, despite 58% (7/12) EMD in this group. Of the first 6 pts dosed in DL1, 4 (67%) continue in ongoing sCR beyond 18 months, including 3 with EMD. Median duration of response, PFS and OS were not evaluable at the time of data-cut because 19 of 24 evaluable pts (79%) remain in ongoing response. **Conclusions:** CART-ddBCMA administration, to date, has demonstrated clinical activity, including 100% ORR with rates of CR/sCR and ≥VGPR of 67% and 88%, respectively. Durable responses beyond 18 months have been observed, including in pts with EMD. Clinical trial information: NCT04155749. Research Sponsor: Arcellx.

8004 **Oral Abstract Session**

Phase I open-label single arm study of GPRC5D CAR T-cells (OriCAR-017) in patients with relapsed/refractory multiple myeloma (POLARIS).

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Background: GPRC5D, a type-C 7-pass transmembrane receptor protein, is predominantly expressed on malignant plasma cells from MM patients. The autologous GPRC5D-directed CAR-T cell (OriCAR-017), owning to an additional proprietary Ori element, is the 2nd generation CAR-T cell with improvement in expansion and durability. **Methods:** The primary objective of this study was to evaluate safety and tolerability of OriCAR-017. Key enrolment criteria included measurable MM adults, R/R or intolerant to established therapies. Patient received lymphodepleting chemotherapy with fludarabine 30mg/m^2/d and cyclophosphamide 300mg/m^2/d for 3 days followed by a single infusion of OriCAR-017. The trial followed 3+3 design with 1×10^6/kg, 3×10^6/kg and 6×10^6/kg CAR^+ T cells cohorts. **Results:** Eleven patients were enrolled and underwent apheresis during June 9, 2021 and January 31, 2022. 9pts have completed infusion and 8pts available for efficacy and safety evaluation, the 9th pt completed infusion at January 23, 2022. 2 pts were suspended infusion due to rapid disease progression. Of the 9 infused pts, median age 65 years (range41-71) and a median of 6 (range3-17) prior therapy lines; 3 (33.0%)/1 (11.0%) triple-class/penta-drug exposed; 2 (22.0%)/1 (11.0%) triple-class/penta-drug refractory; 4 (44.0%) prior BCMA CART therapy. Five out of 6pts had high-risk cytogenetic profiles including 2pts with del(17p). No dose-limiting toxicities occurred. The most common TEAEs were neutropenia (G3/4 100%), thrombocytopenia (G3/4 100%), leukopenia (G3/4 100%), lymphopenia (G3/4 100%) and anemia (G3/4 87.5%). All pts experienced CRS with 7pts in G1, 1pt in G2. All CRSs were rapidly relieved after conventional intervention(tocilizumab and steroids). The median onset time was 3 days (range0-8), median duration 6 days (range5-8). No neurologic toxicities were reported. No nail disorders were reported. 8pts avaliable for efficacy evaluation, median follow up time was 109.5 days (range32-195 days). A 100.0% ORR were observed with 3pts CR/sCR, 2pts VGPR, 3pts PR. Three out of 4pts with prior BCMA CAR-T therapy were available for efficacy evaluation-1sCR, 1VGPR, 1PR. After infusion, 8pts were MRD negative in the bone marrow by flow cytometry (10^{-5}) at day 28, 5pts continued at month 3 and 1pt at month 6. Robust OriCAR-017 expansion in peripheral blood by using qPCR for 8pts, median peak was 507,463.6copies/ml (range152093.7 – 1121996.9), median time to peak expansion was 10 days (range7-14). **Conclusions:** In this phase I study, OriCAR-017 was showed safe and impressive efficacy in RRMM patients. Majority of AEs were transient and manageable. 100% ORR and 100% MRD negative rate, along with favorable safety support OriCAR-017 to be a competitive therapy for RRMM. Furthermore, patients who had relapsed from BCMA CAR-T therapy may still benefit from OriCAR-017. Clinical trial information: NCT05016778. Research Sponsor: Oricell Therapeutics Co., Ltd.

8005 **Oral Abstract Session**

Updated results of a multicenter first-in-human study of BCMA/CD19 dual-targeting fast CAR-T GC012F for patients with relapsed/refractory multiple myeloma (RRMM).

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Background: GC012F is a B cell maturation antigen (BCMA)/CD19 dual-targeting CAR-T developed on the novel FasT CAR-T platform with overnight manufacturing and designed to improve depth of response and efficacy. Data was presented at ASCO and EHA 2021 for initial 19 pts. We present updated data for study (NCT04236011; NCT04182581) with longer follow up and 9 additional pts treated (n = 28) in 3 different dose levels. **Methods:** From October 2019 to November 2021, 28 heavily pretreated RRMM pts (age 27-76) median of 5 prior lines (range 2-9) were treated on a single-arm, open label, multicenter Investigator Initiated Trial receiving a single infusion of GC012F. 89.3% (25/28) were high risk (HR- mSMART), 8 pts had EM disease, 3 had never achieved a CR including after transplant, 1 pts presented with plasma cell leukemia, 24/28 pts were refractory to last therapy, 3 pts primary refractory. 9/28 pts had received prior anti-CD38, 27/28 pts prior IMiDs. 26/28 pts were refractory to PI, 26/28 pts to IMiDs. After lymphodepletion over 2-3 days (30 mg/m^2/d, 300mg/ m^2/d Flu/Cy) GC012F was administered as single infusion at 3 dose levels: 1x10^5/kg (DL1) n = 2, 2x10^5/kg (DL2) n = 10 and 3x10^5/kg (DL3) n = 16. **Results:** As of Jan 26th 2022, 28 pts - median follow-up (f/u) 6.3 mths (1.8-29.9) - had been evaluated for response. Overall response rate (ORR) in DL1 was 100% (2/2)- DL 2 -80% (8/10) DL 3 -93.8% (15/16) with 27 pts MRD negative by flow cytometry (sensitivity 10^{-4}-10^{-6}). 100% of MRD assessable pts (27/27) achieved MRD negativity. One patient out of 28 could not get assessed. At d28, 21/24 assessable patients were MRD negative (81.5%), 4/28 pts could not get d28 MRD assessment f/u due to COVID-19 restrictions however were assessed at a later timepoint. To date best response is MRD- sCR in 21/28 patients**(**75.0%) across all dose levels. Some pts after short f/u show responses that are still deepening. Cytokine Release Syndrome (CRS) was mostly low grade: gr 0 n = 3 (10.7%), gr 1-2 n = 23 (82.1%), gr 3 n = 2 (7.1%) – no gr 4/5 CRS and no ICANs were observed (Graded by ASBMT criteria). Median duration of CRS was 3 d (1-8 d). PK results showed no difference amongst dose levels DL1 to DL3. Overall, CAR-T median Tmax was 10 d (range 8-14 d), median peak copy number (Cmax) was 97009 (16,011-374,346) copies /μg DNA with long duration of persistence of up to d793 (data cut-off). CAR-T geometric mean $AUC_{0\text{-}28}$ for DL1, DL2 and DL3 were 468863, 631540 and 581620 copies/μg DNA$\times$day, respectively. Pts continue to be monitored for safety and efficacy including DOR. **Conclusions:** BCMA-CD19 dual FasT CAR-T GC012F continues to provide deep and durable responses with a favorable safety profile in additional RRMM pts across all dose levels demonstrating a very high MRD negativity rate including in pts refractory to anti-CD38, PI and IMIDs. GC012F is currently being studied in earlier lines of therapy as well as additional indications. Clinical trial information: NCT04236011; NCT04182581. Research Sponsor: Gracellbiotechnologies.

8006 **Oral Abstract Session**

Initial safety results for MagnetisMM-3: A phase 2 trial of elranatamab, a B-cell maturation antigen (BCMA)-CD3 bispecific antibody, in patients (pts) with relapsed/refractory (R/R) multiple myeloma (MM).

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Background: Elranatamab (PF-06863135) is a humanized bispecific antibody that targets both BCMA-expressing MM cells and CD3-expressing T cells. MagnetisMM-3 (NCT04649359) is an open-label, multicenter, non-randomized, phase 2 study to evaluate the safety and efficacy of elranatamab monotherapy in pts with R/R MM. Initial safety results are presented. **Methods:** MagnetisMM-3 enrolled pts who are refractory to at least 1 proteasome inhibitor, 1 immunomodulatory drug, and 1 anti-CD38 antibody. Pts were assigned to 1 of 2 independent, parallel cohorts: those naïve to BCMA-directed therapies (Cohort A) and those with previous exposure to BCMA-directed antibody-drug conjugates or CAR-T cells (Cohort B). Pts received subcutaneous elranatamab 76 mg QW on a 28-d cycle with a 2-step-up priming dose regimen administered during the first week. Dose modifications were permitted for toxicity. Treatment-emergent adverse events (TEAEs) were graded by CTCAE (v5.0), and cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) by ASTCT criteria. **Results:** As of the data cutoff on Dec 31, 2021, 60 pts in Cohort A had received ≥1 dose of elranatamab; the last pt's first dose was ~2 months prior to the cutoff. Median age was 69.0 y (range, 44–89), 48.3% were male, 63.3% were white, 18.3% were Asian and 11.7% were Black/African American. At baseline, 60.0% of pts had an ECOG performance status 1–2 and pts had received a median of 5 (range, 2–12) prior therapies. Median duration of elranatamab treatment was 9.57 wks (range, 0.1–46.1); median relative dose intensity was 87.4% (range, 23.1–101.4). TEAEs were reported in 100% (Grade [G] 3/4, 75.0%) of pts. Most common (≥30%) hematologic TEAEs were neutropenia (36.7% [G3/4, 35.0%]), anemia (36.7% [G3/4, 30.0%]) and thrombocytopenia (30.0% [G3/4, 21.7%]). Among pts who received the 2-step-up priming regimen (n = 56), CRS and ICANS, respectively, were reported in 58.9% (G3/4, 0%) and 3.6% (G3/4: 0%); of those pts, 57.6% (n = 19/33) and 100% (n = 2/2) received tocilizumab and/or steroids. Most common (≥30%) non-hematologic TEAE, other than CRS/ICANS, was fatigue (31.7% [G3/4, 3.3%]). Infections were reported in 46.7% (G3/4: 18.3%) of pts; most frequently reported were upper respiratory tract infections (11.7% [G3/4: 0%]). Discontinuations due to adverse events were reported in 5.0% of pts. No pts permanently discontinued treatment due to CRS or ICANS. There were 10 deaths; causes were MM progression (n = 8), septic shock (n = 1) and unknown (n = 1). Data will be updated at the time of presentation to include ~90 pts. **Conclusions:** Preliminary results of MagnetisMM-3 in pts with R/R MM and no prior BCMA-targeted treatment suggest that 76 mg QW elranatamab with a 2-step-up priming regimen is well tolerated, with no G ≥3 CRS or ICANS observed. Clinical trial information: NCT04649359. Research Sponsor: Pfizer.

8007 **Oral Abstract Session**

Teclistamab, a B-cell maturation antigen (BCMA) x CD3 bispecific antibody, in patients with relapsed/refractory multiple myeloma (RRMM): Updated efficacy and safety results from MajesTEC-1.

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Background: The BCMA × CD3 bispecific antibody teclistamab (tec; JNJ-64007957) redirects CD3+ T cells to mediate T-cell activation and subsequent lysis of BCMA-expressing myeloma cells. The multicohort, open-label, phase 1/2 MajesTEC-1 study is investigating safety/efficacy of tec in patients (pts) with RRMM who previously received ≥3 lines of therapy (LOT). In phase 1, the recommended phase 2 dose (RP2D) of tec was identified as a weekly subcutaneous dose of 1.5 mg/kg preceded by step-up doses of 0.06 and 0.3 mg/kg. Initial results from pts treated with the tec RP2D in phase 1/2 (no prior exposure to an anti–BCMA-targeted treatment), demonstrated that tec was well tolerated with encouraging efficacy. Here we present updated results from pts treated at the RP2D, including additional pts and longer follow-up. **Methods:** Eligible pts were aged ≥18 years, had documented MM (per IMWG criteria), and had received ≥3 prior LOT including a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 antibody. Prior BCMA-targeted therapy was not permitted in Phase 1. Pts received tec at the RP2D. The primary endpoint was overall response rate (assessed per IMWG 2016 criteria). Adverse events (AEs) were graded per CTCAE v4.03 (cytokine release syndrome [CRS] and ICANS graded per ASTCT guidelines). Data cutoffs for safety and efficacy (N = 165) were Sep 7 and Nov 9, 2021, respectively. **Results:** Median pt age was 64 y (range 33–84); 58% were male, and median prior LOT was 5 (range 2–14); 100% were triple-class exposed, 70% were penta-drug exposed, 78% were triple-class refractory, and 30% were penta-drug refractory. ORR was 64% (95% CI 56–72), with a complete response or better achieved in 30% of pts. Responses were durable and deepened over time; median duration of response (DOR) was not reached. The 12-mo DOR rate was 66% (95% CI 49–79). The majority of pts who responded to treatment in the first cycle had a reduction in soluble BCMA. The most common hematologic AEs were neutropenia (65%; grade 3/4: 57%), anemia (50%; grade 3/4: 35%), thrombocytopenia (38%; grade 3/4: 21%), and lymphopenia (34%; grade 3/4: 32%). Infections occurred in 104 pts (63%; grade 3/4: 35%). The most common nonhematologic AE was CRS (72%; grade 3: 0.6%; no grade 4/5); median time to CRS onset (range) was 2 days (1–6) and median duration was 2 days (1–9). Five pts (3%) reported a total of 9 ICANS events (all grade 1/2; 7 were concurrent with CRS; all resolved). There were no treatment-related deaths. No pts required a teclistamab dose reduction due to AEs. **Conclusions:** Current data with ~9 months of follow-up reaffirm the deep and durable responses that have been observed with tec in pts with highly refractory MM, with no new safety signals. Additional data with longer follow-up, including subgroup analyses and PFS, will be presented. Clinical trial information: NCT04557098. Research Sponsor: Janssen Research & Development, LLC.

8008 **Oral Abstract Session**

Major risk factors associated with severe COVID-19 outcomes in patients with multiple myeloma: Report from the National COVID-19 Cohort Collaborative (N3C).

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Background: Patients with multiple myeloma (MM), an age-dependent neoplasm of antibody-producing plasma cells, have compromised immune systems due to multiple factors that may increase the risk of severe COVID-19. The NCATS' National COVID Cohort Collaborative (N3C) is a centralized data resource representing the largest multi-center cohort of ~12M COVID-19 cases and controls nationwide. In this study, we aim to analyze risk factors associated with COVID-19 severity and death in MM patients using the N3C database. **Methods:** Our cohort included MM patients within the N3C registry diagnosed with COVID-19 based on positive PCR or antigen tests or ICD-10–CM. The outcomes of interest include all-cause mortality (including discharge to hospice) during the index encounter, and clinical indicators of severity (hospitalization/ED visit, use of mechanical ventilation, or extracorporeal membrane oxygenation/ECMO). **Results:** As of 09/10/2021, the N3C registry included 690371 cancer patients, out of which 17791 were MM patients (4707 were COVID-19+). The mean age at diagnosis was 65.9yrs, 57.6% were >65yo, 46.4% were females, and 21.8% were Blacks. 25.6% had a Charlson Comorbidity Index (CCI) score of ≥2. 55.6% required an inpatient or ED visit, and 3.65% required invasive ventilation. 11.4% developed acute kidney injury during hospitalization. Multivariate logistic regression analysis showed histories of pulmonary disease (OR 2.2; 95%CI: 1.7-2.8), renal disease (OR 1.8; 95%CI: 1.4-2.4), and black race ($p<0.001$) were associated with higher risk of severity. Interestingly, smoking status was significantly associated with a lower risk of severity (OR 0.7; 95%CI: 0.5-0.9). Further, protective association was also observed between COVID-19 severity and blood or marrow transplant (BMT) (OR 0.52; 95%CI: 0.4-0.7), daratumumab therapy (OR 0.64; 95%CI: 0.42-0.99) and COVID-19 vaccination (OR 0.28; 95%CI: 0.18-0.44). IMiDs were associated increase in the risk of COVID-19 severity (OR 2.1; 95%CI: 1.6-2.7). 2.3% of N3C-myeloma COVID-19+ patients died within the first 10 days, while 4.95% died within 30 days of COVID-19 hospitalization. Overall, the survival probability was 90.5% across the course of the study. Multivariate cox proportional hazard model showed that CCI score ≥2 (HR 4.4; 95%CI: 2.2-8.8), hypertension (HR 1.6; 95%CI: 1.02-2.4), IMiD (HR 2.6; 95%CI: 1.8-3.8) and proteasome inhibitor (HR 1.6; 95%CI: 1.1-2.5) therapy were associated with worse survival. COVID-19 vaccination (HR 0.195; 95%CI: 0.09-0.45) and BMT (HR 0.65; 95%CI: 0.4-0.995) were associated with lower risk of death. **Conclusions:** We have identified previously unpublished potential risk factors for COVID-19 severity and death in MM as well as validated some published ones. To the best of our knowledge, this is the largest nationwide study on multiple myeloma patients with COVID-19. Research Sponsor: None.

8009 **Clinical Science Symposium**

Phase II study of umbilical cord blood–derived natural killer (CB-NK) cells with elotuzumab, lenalidomide, and high-dose melphalan followed by autologous stem cell transplantation (ASCT) for patients with high-risk multiple myeloma (HRMM).

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Background: Despite the introduction of several novel agents over the past decade, patients with HRMM continue to have relatively poor outcomes. In a first-in-human study, we previously showed the feasibility of using CB-NK cells up to a dose of 1 x 10^8 cells/kg in MM patients undergoing high-dose melphalan (200 mg/m^2; Mel200) plus lenalidomide and ASCT (NCT01729091). Lenalidomide enhances NK cell function and antibody-mediated cell toxicity against tumor targets. Our preclinical data showed that *ex vivo* expanded NK cells demonstrated higher elotuzumab-mediated cytotoxicity against myeloma targets than non-expanded cells, and the addition of elotuzumab to lenalidomide augmented the CB-NK cell ADCC against MM1.S myeloma targets. Hence, we aimed from this expansion part of the phase 2 clinical trial to determine the efficacy of CB-NK cells combined with elotuzumab/lenalidomide for HRMM undergoing ASCT. **Methods:** Patients with HRMM, ages 18-75 years, were eligible. HRMM defined as: disease relapse within 18 months of ASCT; fluorescence in situ hybridization (FISH) showing t(4:14), t(14:16), t(14:20), deletion (del) 17/17p or gain (amp) 1q; del(13) by conventional cytogenetic analysis; high-risk signatures as determined by the GEP-70 or EMC-92 gene expression profiles. With day 0 defined as day of stem cell infusion, treatment consisted of IV elotuzumab 10 mg/kg (days -15 and -8), oral lenalidomide 10 mg (days -8 to -2 prior to ASCT), Mel200 on day -7, and CB-NK cells on day -5. The primary endpoints were best response rate (≥VGPR) and minimal residual disease (MRD) at 3 months after ASCT, as defined per the IMWG criteria. MRD was tested by using 8-color multiparametric flow cytometry validated to a sensitivity level of 0.001% (1 cell in 100,000). **Results:** Thirty patients, with a median age of 63 (range, 40-72) years, were enrolled between 03/2018 and 01/2021. 97% had R-ISS stages 2/3, 40% had ≥2 high-risk genetic abnormalities, and 23% had del TP53. Most (80%) received induction therapy with bortezomib or carfilzomib + lenalidomide + dexamethasone, 1 patient had prior ASCT, and 4 received >1 prior line of therapy. Before ASCT, 73% had VGPR or better (40% in CR/sCR) and 40% had negative MRD. At 3 months after transplant, 97% achieved ≥VGPR (76%, CR/sCR) and 75% had negative MRD. At median follow-up of 26 (range, 12-44) months, only 4 patients progressed (3 had positive MRD after ASCT). The 2-year PFS and OS rates were 83% and 97%, respectively. No unexpected serious adverse effects attributable to NK cells were noted. **Conclusions:** CB-derived expanded NK cells plus elotuzumab/lenalidomide combined with Mel200 and ASCT results in excellent and durable hematologic and MRD responses in HRMM patients. Furthermore, PFS and OS rates compare favorably to published outcomes for HRMM patients. Clinical trial information: NCT01729091. Research Sponsor: Moonshot Program, Pharmaceutical/Biotech Company.

8000 **Oral Abstract Session**

Ixazomib and daratumumab without dexamethasone (I-Dara) in elderly frail RRMM patients: A multicenter phase 2 study (IFM 2018-02) of the Intergroupe Francophone du Myélome (IFM).

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Background: Frail patients with multiple myeloma have an inferior outcome, especially in the relapse setting. This adverse prognosis is mainly related to a high discontinuation rate due to treatment (Tx) related adverse events. The aim of this phase 2 study is to evaluate efficacy and tolerability of Ixazomib-Daratumumab (I-Dara) without Dexamethasone in elderly frail patients with relapsed myeloma (RRMM) (NCT03757221). **Methods:** Ixa-Dara naïve RRMM patients received oral Ixazomib (4 mg: days 1, 8, 15), IV Daratumumab (16 mg/kg; days 1, 8, 15, 22, cycles 1-2; days 1, 15, cycles 3-6; days 1, cycles 7+) and IV Methylprednisolone before Daratumumab (100 mg at day 1, 8, cycle 1 and then 60 mg). They were enrolled after 1 or 2 prior therapy if their frailty score was ≥ 2 by IMWG score. The primary endpoint was ≥ very good partial response rate (VGPR) at one year. Secondary endpoints included ORR, PFS, OS & toxicity according to NCI-CTCAE version 5. **Results:** Sixty-three patients were screened and 55 enrolled between 03/2018 and 09/2021. Patient were at first (n = 36) or second relapse (n = 19). Thirty-three patients (60%) were previously exposed to bortezomib, 37 (67%) were previously exposed to lenalidomide (Len) and 20 (36 %) were refractory to Len. Median age was 82 (72-93). All patients had a frailty score ≥2 and 13 (24 %) had a 3 or 4 frailty score. In 41 patients ISS at diagnosis was stage I (n = 11), II (n = 18) or III (n = 12). Seventeen (36%) patients harbored high-risk (HR) cytogenetic, including t(4;14) (n = 8) or del17p (n = 10). The median duration of Tx among 28 pts with ongoing Tx was 10 months [5-32] at data cutoff (February, 2)]. The median duration of Tx among 27 pts who stopped Tx was 6 months [0-18]: 18 had progressive disease. Nine patients died during the study: Daratumumab-related bronchospasm (D1C1); Ixazomib-related overdose (C2); sepsis (n = 4), progressive disease (n = 3). Regarding toxicity, 27 pts had a ≥grade 3 AE (49%). The most common grade 3-4 toxicities were thrombocytopenia (n = 9), other cytopenias (n = 4), infection (n = 8), hypertension (n = 3) and gastrointestinal disorders (n = 3). Fourteen out of 28 were SAE including 5 infections, 1 bronchospasm, 1 acute respiratory failure and 2 ixazomib overdoses. Overall response rate, including minimal response, was 86 % with a ≥VGPR rate of 32 % in the whole group. In Len refractory patients the ORR was 82 % and ≥VGPR 41%, in HR cytogenetic patients ORR was 85 % and ≥VGPR 46%. With a median follow-up of 11.6 months median PFS is 16 months and median OS NR (76% estimated at one year). **Conclusions:** In this elderly frail population Ixa-Dara is a feasible combination with favorable efficacy profile even in Len refractory and HR cytogenetic patients. Early toxicity remains a concern in this population eventhough more manageable with Dara SC. Clinical trial information: NCT03757221. Research Sponsor: Janssen and Takeda companies.

8011 **Poster Discussion Session**

Daratumumab (DARA) + lenalidomide, bortezomib, and dexamethasone (RVd) in transplant-eligible newly diagnosed multiple myeloma (NDMM): A post hoc analysis of sustained minimal residual disease (MRD) negativity from GRIFFIN.

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Background: In the primary analysis of the phase 2 randomized GRIFFIN study, DARA + RVd (D-RVd) improved the stringent complete response (sCR) rate by end of consolidation for transplant-eligible NDMM (42.4% vs 32.0%; 1-sided $P = 0.068$). With longer follow-up (median, 38.6 mo), D-RVd vs RVd improved MRD-negativity (10^{-5}) rates in clinically relevant subgroups (ISS stage III, 71% vs 36%; high cytogenetic risk, 44% vs 29% [del17p, t(4;14), or t(14;16)]; revised high cytogenetic risk, 55% vs 32% [del17p, t(4;14), t(14;16), t(14;20), or gain 1q]). Here we present a post hoc analysis of sustained MRD negativity (median follow-up, 38.6 mo) in the same subgroups and in patients (pts) with ≥CR. **Methods**: Transplant-eligible NDMM pts were randomized 1:1 to 4 D-RVd/RVd induction cycles, ASCT, 2 D-RVd/RVd consolidation cycles, and 2 years of maintenance therapy with lenalidomide (R) ± DARA. For induction/consolidation (21-day cycles), pts received R (25 mg PO Days [D] 1-14), V (1.3 mg/m^2 SC D1, 4, 8, 11), and d (40 mg PO weekly) ± DARA (16 mg/kg IV D1, 8, 15 of Cycles 1-4 and D1 of Cycles 5-6). In maintenance (28-day cycles), pts received R (10 mg PO D1-21; if tolerated, 15 mg in Cycles 10+) ± DARA (16 mg/kg IV Q8W/Q4W or 1800 mg SC per protocol amendments). The primary endpoint was sCR rate by end of consolidation. **Results**: The following features were balanced among randomized pts (D-RVd, n = 104; RVd, n = 103): high cytogenetic risk (16; 14), revised high cytogenetic risk (42; 37), gain 1q (34; 28), and ISS stage III (14; 14). Sustained MRD-negativity rates at 10^{-5} lasting ≥6 and ≥12 months were higher for D-RVd vs RVd among all high-risk subgroups (Table). D-RVd was superior to RVd for rates of sustained MRD negativity lasting ≥12 months for pts with ≥CR (53.7% vs 20.3%) and sCR (59.1% vs 17.4%; Table). Among all pts with sustained MRD negativity, only 1 D-RVd pt subsequently had disease progression, and 1 RVd pt died. Additional data on MRD at 10^{-6} and PFS will be presented. **Conclusions**: MRD data in GRIFFIN show that the addition of DARA to RVd induction/consolidation and R maintenance may lead to durable MRD-negativity (10^{-5}) rates in pts with transplant-eligible NDMM with high cytogenetic risk, ISS stage III, and those who achieve ≥CR or sCR, however larger studies are needed. Clinical trial information: NCT02874742. Research Sponsor: Janssen Oncology, AFT (https://acknowledgments.alliancefound.org).

Sustained MRD negativity (10^{-5} by NGS), n/N (%)	D-RVd ≥6 mo	D-RVd ≥12 mo	RVd ≥6 mo	RVd ≥12 mo
Overall (ITT)	50/104 (48.1)	46/104 (44.2)	15/103 (14.6)	13/103 (12.6)
High cytogenetic risk	4/16 (25.0)	3/16 (18.8)	2/14 (14.3)	2/14 (14.3)
Revised high cytogenetic risk	15/42 (35.7)	14/42 (33.3)	7/37 (18.9)	6/37 (16.2)
Gain 1q	14/34 (41.2)	13/34 (38.2)	5/28 (17.9)	4/28 (14.3)
ISS stage III	7/14 (50.0)	6/14 (42.9)	2/14 (14.3)	2/14 (14.3)
≥CR	48/82 (58.5)	44/82 (53.7)	14/59 (23.7)	12/59 (20.3)
sCR	43/66 (65.2)	39/66 (59.1)	10/46 (21.7)	8/46 (17.4)

8012 **Poster Discussion Session**

A phase II study of daratumumab with weekly carfilzomib, pomalidomide, and dexamethasone in relapsed and refractory multiple myeloma.

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Background: Daratumumab (dara), carfilzomib (K), pomalidomide (P), and dexamethasone (d) are established in relapsed multiple myeloma (MM) with activity in 3-drug combinations including: dara Kd; dara Pd; and KPd. The paradigm in relapsed/refractory disease is moving towards more intensive and well-tolerated combinations to achieve deeper and more durable responses while ensuring tolerability. Quadruplet regimens are now becoming standard in newly diagnosed MM, and we explored a 4-drug regimen in relapsed disease. Preliminary results of a phase 2 study of dara KPd with a twice/week schedule of K showed an ORR of 86% in pts with a median of 1 prior line (Jasielec et al., ASH 2020). Here we report an ongoing study of dara with *weekly* KPd (dara wKPd) to improve the accessibility of this regimen. **Methods:** This phase 2 study (NCT04176718) will enroll up to 43 pts with relapsed/refractory MM who have received at least 1 prior therapy, including both lenalidomide and a proteasome inhibitor. Prior therapy with dara, K, or P was permitted except for K and P given together as last line of therapy. Dara wKPd was given on a 28-day schedule. Dara was given according to the dara Pd schedule. An initial cohort received dara 16 mg/kg iv (with first dose split over two days); the trial was amended to dara 1800 mg sc. K 56 mg/m^2 iv was given weekly on days 1, 8, 15; for C1D1, dose was 20 mg/m^2. P 4 mg was given po on days 1-21. Dex 40 mg was given weekly with the dose split over two days. Treatment was until progression or unacceptable toxicity. The primary endpoints are overall response and the safety profile of dara wKPd. Secondary endpoints include PFS. **Results:** At time of data cutoff, 24 pts were enrolled; median age was 65 (range 42-73), and median number of prior regimens was 2 (range 1-3). All pts were refractory to their last line of therapy and had prior lenalidomide and bortezomib. Additional prior therapies included: pomalidomide (54%), carfilzomib (13%), ixazomib (46%), cyclophosphamide (4%), auto SCT (29%). High risk FISH was present (out of 24 pts): del 17p (13%); t(14;16) (8%); gain of 1q (46%). Median follow up was 8.4 months. 2 pts came off study due to neutropenia leading to delay in treatment. Grade 3-4 hematologic AEs included neutropenia (46%) and thrombocytopenia (25%). There was 1 episode of febrile neutropenia. Common non hematologic AEs (all; grade 3-4) included fatigue (42%; 0%); dyspnea (38%; 4%); increase in ALT/AST (29%; 8%); insomnia (21%; 0%); neuropathy (17%; 0%). 22 pts were evaluable for response, with an overall response rate of 95% (PR 23%, VPGR 68%, CR 5%). Median PFS at 12 months was 86.2% (95% CI, 70%-100%). **Conclusions:** Dara wKPd shows some of the highest response rates (95%) reported to date in relapsed/refractory MM. This likely reflects the incorporation of 4 active drugs in 1 regimen and builds on the efficacy of dara-based triplet regimens, with manageable toxicity and convenience of weekly K. Clinical trial information: NCT04176718. Research Sponsor: Amgen, Janssen.

8013 **Poster Discussion Session**

Efficacy and safety of teclistamab (tec), a B-cell maturation antigen (BCMA) x CD3 bispecific antibody, in patients (pts) with relapsed/refractory multiple myeloma (RRMM) after exposure to other BCMA-targeted agents.

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Background: Tec (JNJ-64007957) is a BCMA x CD3 bispecific antibody (Ab) that redirects CD3+ T cells to mediate T-cell activation and subsequent lysis of BCMA-expressing myeloma cells. MajesTEC-1 is a multicohort, open-label phase 1/2 study of tec in pts with RRMM who previously received ≥3 prior lines of therapy (LOT). Results from a pooled analysis of phase 1 and phase 2 cohort A (median follow-up 7.8 mo) demonstrated an overall response rate (ORR) of 62.0% in pts with no prior anti-BCMA treatment (tx). We present initial results from cohort C, in which pts had prior exposure to an anti-BCMA tx. **Methods:** Eligible pts (age ≥18 y) had documented MM per IMWG criteria and had received ≥3 prior LOT including a PI, an IMiD, an anti-CD38 Ab, and an anti-BCMA tx (chimeric antigen receptor T [CAR-T] or Ab drug conjugate [ADC]). Pts were enrolled into a Simon's stage design, receiving weekly subcutaneous tec 1.5 mg/kg preceded by step-up doses of 0.06 and 0.3 mg/kg. Primary endpoint was ORR (per IMWG 2016 criteria). AEs were graded per CTCAE v4.03; cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) were graded per ASTCT guidelines. **Results:** As of Sep 7, 2021, 38 pts in cohort C received tec (63% male; median age 63.5 y [range 32–82]; median prior LOT 6 [range 3–14]). 32 (84%) pts were refractory to last LOT; 25 (66%) were refractory to an anti-BCMA tx. Of 25 pts evaluated for efficacy, 16 (64%) had prior ADC, 11 (44%) prior CAR-T (2 pts received both). With median follow-up of 6.9 mo (range 0.7–8.7), ORR was 40% (95% CI 21–61). 5 pts (20%) achieved a complete response or better. The ORR (95% CI) was 38% (15–65) in ADC-exposed pts and 45% (17–77) in CAR-T–exposed pts. Most responses occurred rapidly; 7/25 pts had responses that deepened over time. Median time (range) to first and best response was 1.2 mo (0.2–4.9) and 2.1 mo (1.1–5.7), respectively. Median duration of response was not reached. The safety profile was comparable with that observed in BMCA tx-naive pts, with no new safety concerns. 16 pts (42%; grade 3/4 26%) had infections. Most common AEs (n = 38) were CRS (63%; all grade 1/2; median [range] time to CRS onset: 3 d [2–6], duration of CRS: 2 d [1–4]), neutropenia (55%; grade 3/4 50%), thrombocytopenia (42%; grade 3/4 29%), anemia (39%; grade 3/4 29%), and lymphopenia (40%; grade 3/4 37%). One pt had grade 3 ICANS that resolved with supportive care; pt remains on tx. No pts developed anti-tec Abs. Baseline BCMA expression was comparable with that observed in BCMA tx-naive pts. Updated efficacy and safety data will be presented for 40 pts. **Conclusions:** Initial results of serial targeting of BCMA with tec following ADC or CAR-T tx suggest a promising ORR with responses occurring early and deepening over time. A well-tolerated safety profile was observed in pts previously treated with anti-BCMA tx. Clinical trial information: NCT04557098. Research Sponsor: Janssen Research & Development, LLC.

8014 **Poster Discussion Session**

Elranatamab, a BCMA-targeted T-cell redirecting immunotherapy, for patients with relapsed or refractory multiple myeloma: Updated results from MagnetisMM-1.

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Background: Elranatamab (PF-06863135) is a bispecific molecule that activates and redirects the T-cell mediated immune response against multiple myeloma (MM), a plasma cell dyscrasia characterized by expression of B-cell maturation antigen (BCMA). MagnetisMM-1 (NCT03269136), the ongoing Phase 1 first-in-human study for elranatamab, was designed to characterize safety, pharmacokinetics (PK), pharmacodynamics, and efficacy for patients (pts) with relapsed or refractory MM. **Methods:** Elranatamab was given subcutaneously (SC) at doses from 80 to 1000μg/kg either weekly or every 2 weeks (Q2W). Treatment-emergent adverse events (TEAEs) were graded by Common Terminology Criteria for Adverse Events (v4.03) and cytokine release syndrome (CRS) by American Society for Transplantation and Cellular Therapy criteria. PK, cytokine and soluble BCMA profiling, and lymphocyte subset analyses were performed. Response was assessed by International Myeloma Working Group (IMWG) criteria. Minimal residual disease (MRD) was assessed by next generation sequencing at a sensitivity of 1×10^{-5} in accordance with IMWG criteria. **Results:** A total of 55 pts received single-agent elranatamab SC at a dose ≥215μg/kg as of 1-Nov-2021. Median age was 64 (range 42-80) years, and 27% of pts were Black/African American or Asian. Median number of prior regimens was 6 (range 2-15), 91% were triple-class refractory, 56% had prior stem cell transplantation, 27% had high cytogenetic risk, and 22% received prior BCMA-targeted therapy. The most common TEAEs regardless of causality included CRS, neutropenia, anemia, injection site reaction, and lymphopenia. With pre-medication and a single priming dose (600μg/kg or 44mg), the overall incidence of CRS at the recommended dose (1000μg/kg or 76mg) was 67% and limited to Grade 1 (33%) or Grade 2 (33%), with no events Grade 3 or higher. Exposure was dose dependent and Q2W dosing achieved exposure associated with anti-myeloma efficacy. Cytokine increases occurred with the first dose and were reduced by pre-medication. Soluble BCMA decreased with disease response, elranatamab therapy was associated with increased peripheral T cell proliferation, and median time to response was 36 days (range 7-73). With a median follow-up of 8.1 months (range 0.3-21) and including only IMWG confirmed responses, 31% of pts achieved complete response or better and the overall response rate was 64% (95% CI 50-75%). For responders (n = 35), median duration of response was not yet reached, but the probability of being event-free at 6 months was 91% (95% CI 73-97%). Single-agent elranatamab induces durable clinical and molecular responses, and updated data including MRD assessment will be presented. **Conclusions:** Elranatamab shows a manageable safety profile and achieves durable clinical and molecular responses for pts with relapsed or refractory MM. Clinical trial information: NCT03269136. Research Sponsor: This study was sponsored by Pfizer.

8015 **Poster Discussion Session**

Efficacy and safety of talquetamab, a G protein-coupled receptor family C group 5 member D x CD3 bispecific antibody, in patients with relapsed/refractory multiple myeloma (RRMM): Updated results from MonumenTAL-1.

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Background: G protein-coupled receptor family C group 5 member D (GPRC5D), which has limited expression in normal human tissue but is highly expressed on malignant plasma cells, is a promising target for multiple myeloma (MM) immunotherapy. Talquetamab (JNJ-64407564) is a first-in-class, bispecific IgG4 antibody that binds to both GPRC5D and CD3 receptors, mediating T-cell–activated lysis of GPRC5D+ MM cells. Here we report updated results with additional patients (pts) and longer follow-up from MonumenTAL-1, a phase 1 trial of talquetamab in RRMM (NCT03399799). **Methods:** Eligible pts had RRMM or were intolerant to standard therapies; prior B-cell maturation antigen-directed therapies were permitted. The primary objectives were to identify the recommended phase 2 doses (RP2Ds) (part 1) and assess talquetamab safety and tolerability at the RP2Ds (part 2). Collective safety, efficacy, PK, and PD data supported 2 RP2Ds for talquetamab: 405 μg/kg SC QW (n = 30) and 800 μg/kg SC Q2W (n = 44). Step-up dosing was used to mitigate against severe cytokine release syndrome (CRS); required premedications were limited to step-up doses and the first full dose of talquetamab. Adverse events (AEs) were graded by CTCAE v4.03 with CRS events graded per Lee et al 2014 criteria. Investigators assessed responses per International Myeloma Working Group criteria. **Results:** As of Jan 17, 2022, pts in the 405 μg/kg/800 μg/kg groups, respectively, received a median of 6 /5 prior lines of therapy, 100%/98% were triple-class (TC) exposed, 77%/75% were TC refractory. Median follow-up (range) was 11.7 (1.0–21.2)/4.2 (0.7–13.7) months. Most AEs were grade 1 or 2. The most common AEs were cytopenias and CRS. Cytopenias (including neutropenia [67%/36%; grade 3/4: 53%/23%]) were reversible, mostly confined to step-up and cycle 1–2 doses, and generally resolved within 1 week. Infections occurred in 47%/34% (grade 3/4: 7%/9%) of pts. CRS (77%/80%; grade 3: 3%/0%) mostly occurred during step-up dosing. Skin-related and nail disorder AEs occurred in 83%/75% of pts (most commonly skin exfoliation: 37%/39% [all grade 1 and 2]). Dysgeusia (63%/57%) was generally mild and managed with dose adjustments. The overall response rates in response-evaluable pts were 70% (21/30 pts)/64% (28/44 pts); very good partial response or better rate: 57%/52%; median time to first confirmed response (range): 0.9 (0.2–3.8)/1.2 (0.3–6.8) months. Median duration of response will be reported. No pts died due to drug-related AEs. The PK and PD profiles of both RP2Ds appear comparable. **Conclusions:** These data show that both RP2Ds of talquetamab have comparable safety, efficacy, and pharmacokinetic profiles and confirm talquetamab as a novel, first-in-class therapy with highly promising efficacy in a heavily pretreated RRMM pt population. Clinical trial information: NCT03399799. Research Sponsor: Janssen Research & Development, LLC.

8016 **Poster Discussion Session**

Comparative efficacy of teclistamab (tec) versus current treatments (tx) in real-world clinical practice in the prospective LocoMMotion study in patients (pts) with triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM).

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Background*:* Pts with TCE RRMM who have been exposed to ≥3 lines of therapy (LOT) have a poor prognosis and limited tx options. Tec is a B-cell maturation antigen × CD3 bispecific antibody being evaluated in MajesTEC-1 (NCT04557098), a single-arm, phase 1/2 study in pts with RRMM who were TCE to an immunomodulatory drug, a proteasome inhibitor, and an anti-CD38 antibody and received ≥3 LOT. Since MajesTEC-1 lacks a control arm, we assessed the comparative efficacy of tec vs tx currently used in real-world clinical practice (RWCP) by creating an external real-world control arm from LocoMMotion (NCT04035226), a prospective study of RWCP efficacy and safety outcomes in pts with TCE RRMM who received ≥3 LOT. **Methods:** An external control arm for MajesTEC-1 was created from pts in LocoMMotion (248 pts, clinical cutoff May 21, 2021) who met MajesTEC-1 eligibility criteria. Individual pt-level data from MajesTEC-1 were included from 150 pts treated with tec (1.5 mg/kg weekly) at a clinical cutoff of Sep 7, 2021. Inverse probability of tx weighting with average tx effect on the treated was used to adjust for imbalances in baseline covariates of prognostic significance (refractory status, International Staging System stage, time to progression on prior LOT, extramedullary disease, number of prior LOT, time since diagnosis, average duration of prior LOT, age, hemoglobin, lactate dehydrogenase, creatinine clearance, Eastern Cooperative Oncology Group performance status, gender, type of MM, and prior transplant). Comparative efficacy of tec vs RWCP was estimated for overall response rate (ORR), very good partial response (VGPR) rate, complete response or better (≥CR) rate, duration of response (DOR), progression-free survival (PFS), and overall survival (OS). For binary endpoints (ORR, VGPR rate, and ≥CR rate), relative effect of tec vs RWCP was estimated with an odds ratio, transformed into a response-rate ratio (RR) and 95% confidence interval (CI), derived from weighted logistic regression. A weighted Cox proportional hazards model was used to compute hazard ratios (HRs) and 95% CIs for time-to-event endpoints (DOR, PFS, and OS). **Results:** Baseline characteristics were well balanced between the 2 cohorts after reweighting the external RWCP cohort. Pts treated with tec had improved outcomes vs tx used in RWCP: ORR (RR 2.31; 95% CI 1.75–2.87; $P<$ 0.0001), VGPR rate (RR 5.54; 95% CI 3.38–7.70; $P<$ 0.0001), ≥CR rate (RR 91.50; 95% CI 12.66–661.43; $P<$ 0.0001), DOR (HR 0.17; 95% CI 0.08–0.36; $P<$ 0.0001), PFS (HR 0.47; 95% CI 0.34–0.67; $P<$ 0.0001), and OS (HR 0.69; 95% CI 0.46–1.05; $P=$ 0.08). **Conclusions***:* Tec showed significantly improved efficacy over RWCP for almost all outcomes, highlighting its potential as a highly effective tx option for pts with TCE RRMM who have been exposed to ≥3 LOT. Research Sponsor: Janssen Global Services, LLC.

8017 **Poster Discussion Session**

Safety and clinical activity of belantamab mafodotin with lenalidomide plus dexamethasone in patients with relapsed/refractory multiple myeloma (RRMM): DREAMM-6 arm-A interim analysis.

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Background: Belantamab mafodotin (belamaf; BLENREP) is a B-cell maturation antigen-targeting antibody–drug conjugate approved for patients (pts) with RRMM as monotherapy at 2.5 mg/kg Q3W. Preclinical data demonstrate synergy between belamaf and lenalidomide (Len), suggesting added benefit when combined with standard of care such as Len + dexamethasone (Dex). DREAMM-6 (NCT03544281) Arm A is evaluating belamaf in combination with LenDex in pts with RRMM. **Methods:** This ongoing, two-part, two-arm, open-label study included pts with RMMM previously treated with ≥1 line of therapy (LOT). Pts received 4 belamaf doses/schedules (1.9 mg/kg Q8W or Q4W; 2.5 mg/kg Q4W or Q4W SPLIT dose [50% on Days (D)1, 8] IV) in combination with Len (20 mg PO D1–21) and Dex (20 mg PO/IV D1, 8, 15, 22). Primary objectives were safety (including treatment-related [TR]AEs related to the combination belamaf and LenDex), tolerability, and efficacy (including overall response rate [ORR] defined as ≥partial response). **Results:** As of this interim analysis (data cut: July 23, 2021), 45 pts received ≥1 dose (12 at 1.9 mg/kg Q8W; 4 at 1.9 mg/kg Q4W; 16 at 2.5 mg/kg Q4W; 13 at 2.5 mg/kg Q4W SPLIT). Across cohorts, the median age was 68 y (range: 36–80). Thirteen pts (29%) had high-risk cytogenetics and 6 (13%) had extramedullary disease. Median prior LOT was 3 (range: 1–11) and 26 (58%) had prior Len treatment. The median duration of follow-up and ORR ranged across cohorts (Table). The median duration of response was only reached in the 1.9 mg/kg Q4W cohort (11.1 mo [95% CI: 3.7–not reached [NR]). At the time of data cut, median progression-free survival was not reached in the 1.9 mg/kg Q8W or 2.5 mg/kg Q4W cohorts. Gr ≥3 TRAEs occurred in 42–85%. Gr ≥3 keratopathy occurred in 0 pts in 1.9 mg/kg Q8W, 1 pt (25%) in 1.9 mg/kg Q4W, 8 pts (50%) in 2.5 mg/kg Q4W, and 6 pts (46%) in 2.5 mg/kg Q4W SPLIT cohorts. **Conclusions:** Belamaf + LenDex had a tolerable safety profile, with no new safety signals identified in pts with RRMM. AEs, including keratopathy, were common but manageable with dose modifications. Encouraging clinical activity is observed with this combination in pts with RRMM. Follow-up/correlative studies are ongoing. Funding: GSK (Study 207497); drug linker technology licensed from Seagen Inc.; mAb produced using POTELLIGENT Technology licensed from BioWa. Clinical trial information: NCT03544281. Research Sponsor: GlaxoSmithKline.

Follow-up, ORR, and safety.

n, (%), unless specified	Belamaf 1.9 mg/kg Q8W + LenDex n=12	Belamaf 1.9 mg/kg Q4W + LenDex n=4	Belamaf 2.5 mg/kg Q4W + LenDex n=16	Belamaf 2.5 mg/kg Q4W SPLIT + LenDex n=13
Duration of follow-up, median, mo	3.4	17.4	16.2	12.0
ORR	5 (42)	3 (75)	10 (63)	9 (69)
≥Very good partial response	2 (17)	2 (50)	8 (50)	5 (38)
Gr ≥3 TRAEs	5 (42)	2 (50)	13 (81)	11 (85)
AEs leading to dose interruption/delay	11 (92)	3 (75)	13 (81)	12 (92)
Serious TRAEs	2 (17)	0	3* (19)	3 (23)

*Includes 1 fatal serious TRAE (febrile neutropenia).

8018 **Poster Discussion Session**

Safety and clinical activity of belantamab mafodotin with pembrolizumab in patients with relapsed/refractory multiple myeloma (RRMM): DREAMM-4 Study.

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Background: Belantamab mafodotin (belamaf; BLENREP), a B-cell maturation antigen (BCMA) targeted antibody–drug conjugate approved for adult patients with RRMM, has a multimodal mechanism that eliminates myeloma cells via direct cytotoxicity and a systemic anti-tumor immune response, which may be augmented by an immune checkpoint inhibitor. DREAMM-4 (NCT03848845) assessed safety and clinical activity of belamaf with pembrolizumab (pembro) in RRMM. **Methods:** This was a Phase I/II, single-arm, open-label study of adults with RRMM after ≥3 lines of therapy (LOT, including anti-CD38 monoclonal antibody, proteasome inhibitor, and immunomodulator). Part 1 established the dose of belamaf 2.5 mg/kg with pembro 200 mg, both IV Q3W up to 35 cycles, for the Part 2 expansion. Primary efficacy endpoint was investigator-assessed overall response rate (ORR, ≥partial response [PR] per IMWG criteria by investigator). Secondary endpoints included duration of response (DoR), progression-free survival (PFS), adverse events (AEs) per NCI-CTCAE v4.03, and pharmacokinetics (PK). **Results:** This primary analysis of all treated pts (as of Oct 18, 2021) included 34 pts (6 in Part 1 and 28 in Part 2). In both parts, median prior LOT was 5 (range 3–13); 10 pts (29%) had high-risk cytogenetics and 9 (26%) had extramedullary disease. ORR was 47%, with most responses (10/16 pts) ≥ very good PR (VGPR, Table). Median follow-up was 14.7 months (mo); median (95% CI) DoR was 8.0 (2.1–not reached) mo; median PFS was 3.4 (1.4–5.6) mo. Most pts had ≥1 AE (any grade [Gr]: 97%; Gr ≥3: 74%) and treatment-related AE (TRAE, any Gr: 97%; Gr ≥3: 65%). Most common (≥35%) AEs were keratopathy (any Gr: 76%; Gr ≥3: 38%), vision blurred (any Gr: 38%; Gr ≥3: 0%), and thrombocytopenia (any Gr: 35%; Gr ≥3: 29%). AEs led to dose delays (65%) and dose reductions (32%), but not discontinuation. Nine pts had a serious AE (SAE); 4 pts had ≥1 SAE related to study treatment. Two pts had immune-related AEs of Gr 1 (gout and autoimmune hypothyroidism). Preliminary PK and soluble BCMA data were consistent with single-agent belamaf therapy. **Conclusions:** Belamaf + pembro demonstrated a favorable ORR compared with single-agent belamaf in heavily pre-treated RRMM. No new TRAEs were identified; AE frequency and severity were similar to single-agent belamaf. Correlative biomarker studies are ongoing. Clinical trial information: NCT03848845. Research Sponsor: GSK (205207), Pharmaceutical/Biotech Company.

Response, n (%)	Belamaf 2.5 mg/kg + pembro 200 mg Q3W Part 2 (N=28)	Belamaf 2.5 mg/kg + pembro 200 mg Q3W Parts 1 and 2 (N=34)
ORR, n (%) [95% CI]	12 (43) [25.4–62.8]; p=0.4490	16 (47) [29.8–64.9]
≥VGPR, n (%) [95% CI]	7 (25) [10.7–44.9]	10 (29) [15.1–47.5]
sCR	0	0
CR	2 (7)	4 (12)
VGPR	5 (18)	6 (18)
PR	5 (18)	6 (18)
SD	6 (21)	8 (24)
PD	8 (29)	8 (24)
NE	2 (7)	2 (6)

CR, complete response; NE, not evaluable; PD, progressive disease; sCR, stringent CR; SD, stable disease.

8019 **Poster Discussion Session**

Synergistic effects of low-dose belantamab mafodotin in combination with a gamma-secretase inhibitor (nirogacestat) in patients with relapsed/refractory multiple myeloma (RRMM): DREAMM-5 study.

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Background: Preclinical data demonstrate that nirogacestat, a gamma-secretase inhibitor, may increase cell-surface levels of a B-cell maturation antigen (BCMA) and reduce soluble BCMA levels, which could enhance anti-BCMA agent activity in multiple myeloma. In the DREAMM-5 (NCT04126200) Phase I/II platform trial belantamab mafodotin (belamaf; BLENREP), a BCMA-targeting antibody-drug conjugate, is being evaluated in combination with nirogacestat to determine if the combination can result in similar efficacy and an improved ocular safety profile compared to the currently approved belamaf schedule (single agent dose 2.5 mg/kg Q3W) in patients with RRMM which showed a 31% overall response rate (ORR) and 44.5% Gr3/4 keratopathy (BLENREP US prescribing information). **Methods:** This cohort within the DREAMM-5 nirogacestat combination sub-study has a sequential dose-exploration (DE) phase evaluating 0.95 mg/kg Q3W belamaf with 100 mg BID nirogacestat continuously, followed by a randomized cohort expansion (CE) comparing the combination to a belamaf 2.5 mg/kg Q3W arm. **Results:** Preliminary results from the 10 patients (pts) in the DE cohort with low-dose belamaf + nirogacestat are presented in this abstract. Pts had a median (range) of 4.5 (3–10) prior lines of therapy. At time of data cut-off (Nov 15, 2021), pts received a median (range) of 7 cycles (1–26). The ORR was 60% (n=6/10) and 20% (n=2) achieved a very good partial response (Table). The key emergent adverse events (AEs) included ocular events (n=7 [70%]; ≥Grade [Gr] 3, n=2 [20%] of which Gr 3 keratopathy was reported in 1 pt [10%]), diarrhea (n=7 [70%]; Gr 3, n=1 [10%]) and hypophosphatemia (n=7 [70%]; Gr 3, n=1, [10%]). There were 2 Grade 5 AEs, neither of which were related to study treatment. No pt permanently discontinued study due to treatment related AEs. **Conclusions:** Encouraging clinical activity and a manageable safety profile is observed with low dose belamaf (0.95 mg/kg Q3W) + nirogacestat (100 mg BID continuously) in pts with RRMM. This ongoing sub-study is actively recruiting patients and will continue to evaluate belamaf + nirogacestat efficacy and safety. Updated results will be reported at the congress. Funding: GSK (208887); drug linker technology licensed from Seagen Inc.; mAb produced using POTELLIGENT Technology licensed from BioWa. Clinical trial information: NCT04126200. Research Sponsor: GSK 208887.

Response and safety.

	DE Cohort N=10n (%)
Overall response rate	6 (60)
Very good partial response	2 (20)
Partial response	4 (40)
AEs (Gr ≥3)	8 (80)
Diarrhea	Gr 1/2: 6 (60)Gr 3: 1 (10)
Hypophosphatemia	Gr 1/2: 6 (60)Gr 3: 1 (10)
Ocular events[a]	Gr 1/2: 5 (50) Gr 3: 2 (20)
Keratopathy	Gr 1/2: 1 (10)Gr 3: 1 (10)

[a]CTCAE5 (based on visual acuity and ocular symptoms and reported by investigators).

8020 **Poster Discussion Session**

Biological correlative analyses and updated clinical data of ciltacabtagene autoleucel (cilta-cel), a BCMA-directed CAR-T cell therapy, in lenalidomide (len)-refractory patients (pts) with progressive multiple myeloma (MM) after 1–3 prior lines of therapy (LOT): CARTITUDE-2, cohort A.

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Background: Cohort A of the multicohort phase 2 CARTITUDE-2 (NCT04133636) study is evaluating cilta-cel safety and efficacy in pts with MM who received 1–3 prior LOT and were len-refractory – a difficult-to-treat population with poor prognosis. We present updated results. **Methods:** Pts had progressive MM after 1–3 prior LOT, including a PI and IMiD, were len-refractory, and had no prior exposure to BCMA-targeting agents. A single cilta-cel infusion (target dose 0.75×10^6 CAR+ viable T cells/kg) was given post lymphodepletion. Safety and efficacy were assessed, and the primary endpoint was MRD negativity at 10^{-5}. Management strategies were implemented to minimize risk of movement/neurocognitive AEs (MNTs). Pharmacokinetic (PK) analyses (C_{max} and T_{max} of CAR+ T-cell transgene levels in blood) are being conducted, as well as analyses of levels of CRS-related cytokines (eg, IL-6) over time, peak levels of cytokines by response and CRS, association of cytokine levels with ICANS, and CAR+ T cell CD4/CD8 ratio by response, CRS, and ICANS. **Results:** As of January 2022 (median follow-up [MFU] 17.1 mo [range 3.3–23.1]), 20 pts (65% male; median age 60 y [range 38–75]) received cilta-cel. Pts received a median of 2 (range 1–3) prior LOT, and a median of 3.5 y (range 0.7–8.0) since MM diagnosis. 95% were refractory to last LOT, and 40% were triple-class refractory. ORR was 95%, 90% achieved CR or better, and 95% had ≥VGPR. Median times to first and best response were 1.0 mo (range 0.7–3.3) and 2.6 mo (range 0.9–13.6), respectively. 16 pts were MRD-evaluable, all of whom achieved MRD negativity at 10^{-5}. Median DOR was not reached and 12-mo event-free rate was 79%. The 12-mo PFS rate was 75%. Median time to onset of CRS was 7 d (range 5–9) and occurred in 95% of pts (gr 3/4: 10%), with median duration of 3 d (range 2–12). Neurotoxicity occurred in 30% of pts (5 gr 1/2; 1 gr 3/4). 3 pts (15%) had ICANS (all gr 1/2); 1 pt had gr 2 facial paralysis. No MNTs were seen. 1 death occurred due to COVID-19 (assessed as tx-related by the investigator), 2 due to progressive disease, and 1 due to sepsis (not related to tx). Preliminary PK analyses indicate that peak expansion of CAR-T cells occurred at d 10.5 (range 8.7–42.9) and median persistence was 153.5 d (range 57.1–336.8). **Conclusions:** At a longer MFU of 17.1 mo, a single cilta-cel infusion led to deepening and durable responses in pts with MM who had 1–3 prior LOT and were len-refractory. Follow-up is ongoing. Updated and in-depth PK, cytokine, and CAR-T subset analyses and clinical correlation will be presented and provide novel insights into biological correlates of efficacy and safety in this pt population. This pt population is being further evaluated in the CARTITUDE-4 study (NCT04181827), which has concluded enrollment. Clinical trial information: NCT04133636. Research Sponsor: Janssen Research & Development, LLC, Pharmaceutical/Biotech Company.

8021 **Poster Discussion Session**

Correlative analysis to define patient profiles associated with manufacturing and clinical endpoints in relapsed/refractory multiple myeloma (RRMM) patients treated with idecabtagene vicleucel (ide-cel; bb2121), an anti-BCMA CAR T cell therapy.

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Background: The anti-BCMA autologous CAR T cell therapy ide-cel has achieved deep and durable responses in RRMM patients (Munshi, N Engl J Med 2021). Prior studies have described the correlation between patient characteristics and clinical outcomes from CD19 CAR T cell therapy (Finney, J Clin Invest 2019; Fraietta, Nat Med 2018). We sought to define patient profiles correlated with manufacturing and clinical endpoints in RRMM patients treated with ide-cel in clinical trials using unsupervised clustering and multivariate machine learning across multiple key variable domains. **Methods:** Clinical and manufacturing data were harmonized across 164 RRMM patients treated with ide-cel in KarMMa (NCT03361748) and KarMMa-2 cohort 1 (NCT03601078). Based on individual multivariate importance, 10 selected peripheral blood mononuclear cell (PBMC), drug product (DP), and in-process cell growth variables were used to define patient clusters. Random forest classifiers were generated to identify patient characteristics associated with manufacturing and clinical endpoints. Wilcoxon rank sum and Kruskal-Wallis tests were used to compare 2 and 3+ categorical groups; Cox proportional hazards were used to compare groups with time-to-event data. **Results:** Using an unsupervised method, 4 patient clusters were identified that represented 10%, 57%, 15%, and 18%, respectively, of the total 164 patients. Cluster 4 was the most favorable and was characterized by a higher frequency of T cells in PBMCs; increased T-cell size during manufacturing; higher DP T-cell transduction, potency, and vector copy number; and ultimately a > 3-fold higher CAR T cell yield compared with the least favorable cluster 1. Cluster 2 contained most patients and was associated with intermediate manufacturing endpoints. Patients in cluster 4 had a higher complete response rate, longer progression-free survival, and were defined by lower tumor burden, higher absolute lymphocyte count (ALC), and longer washout period after alkylator treatment, among others (Table). **Conclusions:** The current study identified patient profiles in RRMM using accessible laboratory or medical history data that correlated with longitudinal outcomes. These findings may inform patients likely to achieve improved outcomes with CAR T cell therapy. Clinical trial information: NCT03361748. Research Sponsor: 2seventy bio, formerly bluebird bio, Pharmaceutical/Biotech Company.

Select patient variables across clusters.

Variable Median [Q1-Q3]	Cluster 1 n = 17	Cluster 2 n = 94	Cluster 3 n = 24	Cluster 4 n = 29
Monoclonal protein (g/L)†	12.08 [8.07-21.33]	10.73 [5.50-21.51]	7.36 [4.95-13.38]	7.00 [4.65-11.07]
ALC (10^9/L)†	0.50 [0.29-0.78]	0.85 [0.54-1.36]	0.67 [0.49-0.86]	0.91 [0.62-1.26]
Patients with alkylator exposure within 6 months*(%)	47	31	29	24

†Assessment at screening timepoint *Time of last exposure is measured relative to date of apheresis.

8022 **Poster Session**

Prognostic value of early bone marrow MRD status in CAR-T therapy for myeloma.

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Background: Bone marrow (BM) assessment of minimal residual disease (MRD) is being considered as a surrogate endpoint in clinical trials and is prognostic for survival in multiple myeloma (MM). Timing of BM assessment is variable across Chimeric Antigen Receptor T cell (CART) therapy trials and differs from standard of care practice. BM myeloma cell clearance can be detected by month 1 post CART, even before serum immunofixation becomes negative. BM is still hypocellular at month 1, thus prognostic value of MRD negative (MRDneg) at this timepoint is unclear. We examined impact of Day 30 MRD status in patients (pts) who received CART at Mayo Clinic. **Methods:** Medical records were reviewed retrospectively for MM pts who received CART between 8/2016 and 6/2021. PFS and OS were plotted by Kaplan-Meier method. **Results:** Sixty MM pts received CART and had BM biopsy at month 1. Median age was 62 yrs, 53% were male, and 78% were BM MRDneg by flow cytometry. Baseline demographics were similar between MRDneg and MRD+ (Table). Overall, 85% (40/47) who were month 1 BM MRDneg had i/u FLC<normal. Patients who achieved CR/sCR had higher rates of BM MRDneg (100% vs 61%, p<0.001) and i/u FLC< normal (89% vs 58%, p<0.001). At month 1, 24/60 (40%) pts had hypocellular BM. Serial BM samples at month 3 (n=35), 6 (n=28) and 12 (n=23) showed MRDneg rate of 93% (25/27), 56% (9/16) 58% (7/12), respectively.. Rate of hypocellularity was 54% (19/35), 32% (9/28) and 30% (7/23), respectively. Among the MRDneg/hypocellular pts at month 1, hypocellular BM was seen in 8/11 (73%) pts at month 3 and 2/4 (50%) pts at month 6 and 12. Compared to MRD+, pts who had BM MRDneg at months1 had longer PFS (Table). PFS was not statistically significantly different between pts who had BM MRDneg and were either hypocellular or not. MRDneg pts with i/u FLC<normal at months1 had better median PFS compared to those who did not. (MRD+:2.9 months (1.2-NR). MRDneg/FLC>normal: 4.9 months (2.3-NR). vs MRDneg/FLC<normal:17.9 months (11.8-NR), p<0.0001). **Conclusions:** Hypocellular BM is common in the 3 months post CART. Regardless of BM cellularity, BM MRDneg at month 1 correlates with deep response and prolonged PFS. Majority of BM MRDneg pts at month 1 also had FLC<normal. BM MRDneg status and FLC normalization were associated with longer survival. Our data support the continued evaluation of BM early post CART infusion as a prognostic tool. Research Sponsor: None.

Patient demographics and outcomes.

Variable	All pts (N=60)	MRDneg (N=47)	MRD+ (N=13)	P- Value
High risk cytogenetics, n(%)	28 (70)*	21 (70)	7 (70)	1.0
ISS Stage II/III, n (%)	14 (31)	11 (31)	3 (30)	0.9
Bridging therapy, n (%)	46 (77)	39 (83)	7 (54)	0.03
Plasmacytoma, n(%)	16 (27)	14 (30)	2 (15)	0.3
Cytokine release syndrome, all grade, n (%)	45 (75)	36 (77)	9 (69)	0.6
ICANS, all grade, n(%)	13 (22)	11 (23)	2 (15)	0.5
FLC depletion, n(%)	43 (72)	40 (85)	3 (23)	<0.001
Best response- CR/sCR, n(%)	27 (45)	27 (57)	0 (0)	<0.001
Progression free survival (95% CI)	10.4 (6.0-17.9)	17.5 (10.4-NR)	2.9(1.2-NR)	<0.0001

8023 **Poster Session**

Association of socioeconomic status with adherence to oral agents in patients with multiple myeloma.

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Background: The introduction of novel oral immunomodulatory drugs has improved the overall survival rates of patients with multiple myeloma (MM). Poor adherence to oral therapies may lead to drug resistance, poor response to treatment and other downstream effects. It is unknown if socioeconomic status (SES) mediates adherence to oral MM agents. **Methods:** This is a retrospective review of newly diagnosed adult patients with MM with drug coverage through a large pharmacy benefit manager (PBM) who received oral MM agents between September 1, 2016 and September 1, 2020. Patients were excluded if they were not eligible for PBM benefits for the 6 months prior to or the 12 months after the index date and if they had a stem cell transplant based on a proxy signal. Adherence was defined as an annual medication possession ratio between 0.8 and 1.2. An SES composite index was developed using ZIP code level factors in a K-means clustering algorithm. Multivariable logistic regression for adherence was conducted using the SES-index and controlled for other patient-specific demographics. **Results:** In total, 6,602 patients were enrolled in the study, of which, 4,211 (64.5%) were defined as adherent. There were significant unadjusted differences in age (67.89 vs 64.06, p<0.00001), ZIP code-based SES index (p=0.00049), census region (p<0.00001) and insurance plan type (p<0.00001). Results from multivariable logistic regression are shown in table. Patients residing in Very Low SES ZIP codes were significantly less likely to be adherent to oral MM agents compared to those residing in Very High SES locations. Odds of adherence increased as patient's age increased. Increasing polypharmacy was negatively associated with oral MM agent adherence. **Conclusions:** Aside from patients residing in Very Low SES ZIP codes, ZIP code-based SES measures were not associated with worse adherence. Other mediating factors include younger age and number of co-prescribed medications. Further investigations of adherence to oral MM agents with clinically relevant outcomes are warranted. Research Sponsor: None.

Variable	OR (95% CI)	p-value
Zip code SES composite index		
Very Low	0.75 (0.56–1)	0.048
Low	0.81 (0.62–1.07)	0.14
Medium	0.85 (0.64–1.12)	0.24
High	0.9 (0.68–1.19)	0.47
Very High	*(reference)*	-
Age		
< 50	0.79 (0.64–0.97)	0.022
50–64	*(reference)*	-
65–84	1.71 (1.5–1.94)	< 0.00001
≥85	2.11 (1.58–2.83)	0.00001
Polypharmacy		
None (<10)	*(reference)*	-
Mild (10–13)	0.66 (0.57–0.76)	< 0.00001
Moderate (14–18)	0.46 (0.4–0.53)	< 0.00001
Extreme (≥19)	0.34 (0.29–0.39)	< 0.00001

8024 **Poster Session**

Pomalidomide, bortezomib, and dexamethasone in lenalidomide-pretreated multiple myeloma: A subanalysis of OPTIMISMM by frailty.

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Background: Patients (pts) with multiple myeloma (MM) are likely to be older adults, and advanced age is associated with lower survival rates, in part due to comorbidities and frailty. Results from the phase 3 OPTIMISMM trial (NCT01734928) demonstrated that pomalidomide (P) in combination with bortezomib + dexamethasone (Vd) significantly improved progression-free survival (PFS) in lenalidomide (LEN)-pretreated pts with relapsed/refractory MM (RRMM) vs Vd, irrespective of age and Eastern Cooperative Oncology Group performance status (ECOG PS). Here, we report results from a post hoc analysis assessing outcomes of PVd vs Vd in pts with RRMM by frailty status. **Methods:** Pts with MM and 1–3 prior lines of therapy (including a LEN-containing regimen) who had been randomized 1:1 to PVd or Vd were assessed for frailty. Frailty scores were calculated using age (≤ 75 yr = 0; 76–80 yr = 1; > 80 yr = 2), the Charlson Comorbidity Index (≤ 1 = 0; > 1 = 1) and ECOG PS (0 = 0; 1 = 1; ≥ 2 = 2). Pts were classified as non-frail (NF; combined score: 0 or 1) or frail (F; combined score: ≥ 2). PFS, overall response rate (ORR), and safety outcomes were assessed by treatment group and frailty status. **Results:** In the intent-to-treat population (N = 559) (data cutoff Oct 26, 2017), 93/281 (33.1%) pts who received PVd and 93/278 (33.5%) who received Vd were frail. Baseline characteristics were similar between treatment groups within each frailty subgroup. Median PFS was longer with PVd vs Vd in NF ($P = 0.001$) and F ($P = 0.006$) subgroups (Table). ORR was higher with PVd vs Vd in NF ($P < 0.001$) and F ($P < 0.001$) subgroups. Incidence of grade ≥ 3 (G3) treatment-emergent adverse events (TEAEs) was higher with PVd vs Vd in NF (88.1 vs 61.3%) and F (96.8 vs 87.9%) subgroups; peripheral neuropathy, acute renal failure, and hypertension were the most common. Treatment discontinuation due to G3 TEAEs was greater with PVd vs Vd in NF (19.2 vs 18.5%) and F (30.1 vs 20.9%) subgroups. PVd had a longer median treatment duration vs Vd in NF (8.8 vs 5.7 mo) and F (8.9 vs 4.3 mo) subgroups. **Conclusions:** Frail pts with RRMM who received PVd had longer PFS and higher ORR than pts who received Vd, consistent with the overall OPTIMISMM results. Frail pts experienced more G3 TEAEs and treatment discontinuations with PVd vs Vd, but treatment duration was longer with PVd vs Vd. Clinical trial information: NCT01734928. Research Sponsor: Celgene, a Bristol-Myers Squibb Company.

Efficacy outcomes for pts in OPTIMISMM who received PVd vs Vd, by frailty level.

	NF PVd (n = 180)	NF Vd (n = 179)	F PVd (n = 93)	F Vd (n = 93)
Median PFS, mo	14.7	8.3	9.7	5.1
ORR,[a] n (%)	149 (82.8)	96 (53.6)	74 (79.6)	39 (41.9)
sCR	7 (3.9)	1 (0.6)	2 (2.2)	1 (1.1)
CR	22 (12.2)	8 (4.5)	9 (9.7)	1 (1.1)
VGPR	69 (38.3)	28 (15.6)	31 (33.3)	11 (11.8)
PR	51 (28.3)	59 (33.0)	32 (34.4)	26 (28.0)
SD	23 (12.8)	63 (35.2)	9 (9.7)	41 (44.1)
PD	3 (1.7)	11 (6.1)	8 (8.6)	5 (5.4)
OR for ORR (95% CI)[b]	4.45 (2.68–7.39)[c]		6.63 (3.18–13.83)[c]	

[a]ORR includes PR or better; [b]OR calculated as PVd vs Vd; [c]$P < 0.001$.

8025 **Poster Session**

Subcutaneous (SC) isatuximab administration by an on-body delivery system (OBDS) in combination with pomalidomide-dexamethasone (Pd) in patients with relapsed/refractory multiple myeloma (RRMM): Interim phase 1b study results.

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Background: Intravenous (IV) isatuximab (Isa) + Pd is approved for the treatment of RRMM patients (pts). SC delivery would optimize convenience of administration. Prior results showed that SC Isa administered by syringe pump has efficacy and safety profiles comparable to IV Isa; the recommended Phase 2 dose (RP2D) was 1400 mg (IMW21 P-207). **Methods:** This multicenter Phase 1b study evaluated safety, PK and efficacy of SC vs IV Isa + Pd in RRMM pts after ≥2 prior treatment lines. Pts were randomized 2:1 to SC1000 mg or IV 10 mg/kg and to SC1400 mg or IV. An expansion cohort was later implemented with SC Isa administered at the RP2D via OBDS, a wearable bolus injector applied to the abdomen by a healthcare professional. Primary endpoints (EPs) were safety, including injection site reactions (ISRs), and PK. Main secondary EPs were overall response rate (ORR) and progression-free survival (PFS). **Results:** 56 pts were randomized and treated: 12 Isa IV, 12 Isa SC1000, 10 Isa SC1400 and 22 OBDS pts. At study entry, ISS stage II–III was 67% in IV, 33% in SC1000, 60% in SC1400 and 50% in OBDS pts. On Jan 20, 2022, 33% IV, 25% SC1000, 50% SC1400 and 86% OBDS pts remained on treatment. Due to sequential accrual, median follow-up (FU) was longer in IV (20.6 mo) and SC1000 (23.8 mo) than SC1400 (18.1 mo) and OBDS (6.5 mo) pts. Infusion reactions (IRs) were infrequent (≤10% in each cohort, all Grade [G] 2), only at first IV or SC infusion/injection, with no IRs in OBDS. Local tolerability of OBDS was very good, with 5 (22.7%) pts experiencing 7 ISR episodes, all G1, out of 305 administrations (2.3%): 5 injection site erythemas, 1 injection site hemorrhage, and 1 injection site induration. Median duration of OBDS injection was 10 min. Incidence of G4 neutropenia was lower in SC1000 (42%) vs the other cohorts (55–60%). The lower % of ≥G3 treatment-related AEs in OBDS (77%) vs the other cohorts (≥80%) may be due to shorter FU. Best overall responses are shown in table; longer FU is needed for OBDS pts. Median PFS was 22 mo in IV, 12.5 mo in SC1000 and not reached in SC1400 and OBDS pts. PK and CD38 receptor occupancy results in OBDS pts are consistent with those observed in SC1400 with pump. **Conclusions:** SC Isa administered by OBDS shows a safety profile consistent with IV administration with no IRs and excellent local tolerability. Efficacy in the SC cohorts was comparable to the Phase 3 ICARIA results. Isa SC administration by OBDS is well tolerated, requires a short duration of injection and provides a convenient hands-free option. Clinical trial information: NCT04045795. Research Sponsor: Sanofi.

Efficacy.

%	IV n=12	SC 1000 n=12	SC 1400 n=10	OBDS n=22	SC 1400 + OBDS (RP2D) n=32
ORR	66.7	66.7	80.0	77.3	78.1
CR	16.7	25.0	20.0	13.6	15.6
≥VGPR	50.0	41.7	40.0	40.9	40.6
PR	16.7	25.0	40.0	36.4	37.5

CR complete response, *VGPR* very good partial response, *PR* partial response.

8026 **Poster Session**

Safety and efficacy of daratumumab use in patients with renal impairment and hemodialysis.

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Background: Targeting CD38 in multiple myeloma (MM) using daratumumab-based regimens can prolong remission in both the newly diagnosed and relapsed settings. However clinical trials have excluded patients with creatinine clearances (CrCl) <30 mL/min, warranting real-world analysis of daratumumab use in MM patients with renal insufficiency. **Methods**: Following IRB approval, we performed a retrospective chart review of relapsed MM patients at our institution who had reduced CrCl and received at least one dose of either daratumumab between October 2018 and January 2022. All subjects received IV daratumumab, 52% went on to receive SQ. Outcomes included change in CrCl during treatment, adverse events, and survival. Survival was estimated using product-limit estimates. CrCl groups at daratumumab initiation of more or less than 30 were compared using the chi-square test or Fisher's exact test, as deemed appropriate, for categorical variables and the two-sample t-test or Mann-Whitney test for continuous data (SAS Institute Inc., Cary, NC). **Results**: 101 MM patients were included, with median age of 74 (54-92); 46 (45.5%) were female. 14% were on hemodialysis. Patients had a median of 2 prior lines of therapy. Distribution of R-ISS stages were I (20%), II (35%), and III (45%). High-risk cytogenetics were present in 20%. A median of 23 daratumumab infusions (1-60) were delivered over a median of 18 months (median IV=16, SQ=10). Daratumumab regimens included DRD (32%), DPD (35%), DKD (13%), and DVD (35%). Median CrCl at MM diagnosis and at daratumumab initiation was 45 (7.3-101) and 40 (5.3-107), respectively, with 33% having CrCl <30. Following 3, 6, and 12 months (n = 95, 89, 69) on daratumumab-based regimens, median CrCl were 45, 43, and 41, respectively. There were no differences in renal function in patients who went on to receive SQ daratumumab. 16 patients had died at the time of data collection, and the median survival was 63 months. Of the 101 patients, 16 subjects were deceased at the time of data collection, and 23% of subjects had gone on to subsequent treatments. Analysis showed that there was a progression-free survival of 54% at 5 years. The most common adverse events reported were anemia (37%) and neutropenia (15%). Infusion-related reactions were reported in 19% of patients. **Conclusions**: This is the largest real-world assessment of outcome for MM patients treated with daratumumab-containing regimens in the setting of renal insufficiency. There was no significant impact of the treatment on renal function at 12 months. Compared to published data on patients treated with CrCl>30, there does not appear to be a detriment to survival or an increase in adverse events when using daratumumab regimens in patients with more advanced renal insufficiency. Research Sponsor: None.

8027 **Poster Session**

Characteristics of long-surviving patients with multiple myeloma: Over 12 years of follow-up in the Connect MM Registry.

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Background: The Connect MM Registry is a large, US, multicenter, prospective observational cohort study of pts with newly diagnosed multiple myeloma (NDMM) and one of the largest, longest running MM registries. Long-term survivors (LTS), defined as patients (pts) who have ≥ 8 years of follow-up, comprise a large portion of the Connect MM Registry. The purpose of this analysis was to assess LTS demographic and clinical characteristics. **Methods**: Adult pts with NDMM (N = 3011) were enrolled from 250 community, academic, and government sites: Cohort 1 from 2009 – 2011 and Cohort 2 from 2012 – 2016. As 99% of LTS were enrolled in Cohort 1, only pts from Cohort 1 were included in this analysis. Pt data were unevaluable if there were missing treatments, disease assessments, or large gaps in activity during follow-up (n = 28). Baseline characteristics, treatment patterns, and quality of life (QoL) form completion rates were examined. **Results**: At data cutoff (5/17/21), of the 1493 pts in Cohort 1 with evaluable data, 279 were LTS and 1186 were non-LTS. LTS were generally younger and had better performance status at enrollment (Table). Most (66%) LTS received stem cell transplants and few experienced progression within the first 6 months (3%). Top first-line (1L) regimen for LTS was lenalidomide/bortezomib/dexamethasone (31%) vs bortezomib/dexamethasone (22%) in non-LTS. At data cutoff, 73% of LTS were still on treatment at their most recent visit. LTS underwent disease assessments more frequently (2.0 vs 1.3 per year) and had a higher QoL completion rate by year 5 (58% vs 46%). This analysis showed an estimated 8-year survival of 36% vs an observed 8-year survival of 39% from the SEER database. Additional analyses are ongoing. **Conclusions**: LTS were younger and healthier than non-LTS. Most LTS received triplets at induction, stem cell transplants in 1L, and were less likely to relapse within the first 6 months of treatment than non-LTS. These findings are consistent with what has been observed in MM clinical trials. Further, this analysis demonstrates the value of longitudinal data in the CONNECT MM Registry and provides insights on long surviving pts with MM. Clinical trial information: NCT01081028. Research Sponsor: Bristol Myers Squibb.

Characteristic*	Long-Term Survivors (n=279)	Non-Long Term Survivors (n=1186)
Age at informed consent, yr	62	68
Received SCT, n (%)	185 (66.3)	361 (30.4)
ECOG PS < 2, %	66.3	56.9
Fast progression, n (%)†	8 (2.9)	84 (7.1)
Visits/yr, n	3.5	3.0
Disease assessments/yr, n	2.0	1.3
New lines of therapy/yr, n	0.2	0.6
QoL questionnaire completion rate at baseline, %	96.7	94.2
QoL questionnaire completion rate at 5 yrs, %	58.4	45.6
No evidence of treatment in most recent yr of follow-up, n (%)	5 (1.8)	—

ECOG PS, Eastern Cooperative Oncology Group performance status; QoL, quality of life; SCT, stem cell transplant.*All continuous variables reported as medians. †Defined as having progressed ≤ 6 months of start of 1L. Among patients with at least one line of therapy.

8028 **Poster Session**

Phase 1b/2 study of ciltacabtagene autoleucel, a BCMA-directed CAR-T cell therapy, in patients with relapsed/refractory multiple myeloma (CARTITUDE-1): Two years post-LPI.

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Background: Ciltacabtagene autoleucel (cilta-cel), a chimeric antigen receptor T (CAR-T) cell therapy with 2 B-cell maturation antigen (BCMA)–targeting single-domain antibodies, led to early, deep, and durable responses in the phase 1b/2 CARTITUDE-1 study (NCT03548207) in heavily pretreated patients (pts) with relapsed/refractory multiple myeloma (RRMM). At ~1-year (y) median follow-up (MFU), overall response rate (ORR) was 97%; 67% of pts achieved stringent complete response (sCR). 1-y progression-free survival (PFS) and overall survival (OS) rates were 77% and 89%, respectively (Berdeja 2021). Updated results 2-y post last patient in (LPI) will be presented (~30-month total MFU). Here, we report CARTITUDE-1 results at 21.7-month MFU. **Methods:** Eligible pts with RRMM received ≥3 prior lines of therapy (LOT) or were refractory to a proteasome inhibitor (PI) and immunomodulatory drug (IMiD) and had received a PI, IMiD, and anti-CD38 antibody. Bridging therapy was permitted after apheresis. Pts received a single cilta-cel infusion (target dose 0.75×10^6 CAR+ viable T cells/kg) 5–7 days after lymphodepletion. Primary objectives were to evaluate cilta-cel safety and efficacy. Response was assessed per International Myeloma Working Group criteria by independent review committee and minimal residual disease (MRD) negativity at 10^{-5} by next-generation sequencing. **Results:** As of July 22, 2021, 97 pts (59% male; median age 61 y) received cilta-cel. Pts had a median of 6 (range 3–18) prior LOT; 84% were penta-drug exposed, 88% were triple-class refractory, 42% were penta-drug refractory, and 99% were refractory to last LOT. ORR was 97.9% (95% CI 92.7–99.7), 94.9% achieved very good partial response, and 82.5% achieved sCR. Median times to first response, best response, and ≥CR were 1.0, 2.6, and 2.9 months (m), respectively; median duration of response was not reached (NR). Of 61 pts evaluable for MRD, 92% were MRD negative (10^{-5}), sustained for ≥6 m in 44% (27/61) and ≥12 m in 18% (11/61). 2-y PFS was 60.5% (95% CI 48.5–70.4). Median PFS and OS were NR. 2-y PFS rates in pts with sustained MRD negativity for ≥6 m and ≥12 m were 91% and 100%, respectively. There were no new safety signals or new events of CAR-T cell neurotoxicity, movement and neurocognitive treatment-emergent adverse events, or treatment-related deaths since 1-y MFU. 15 second primary malignancies were reported in 11 pts over ~2-y MFU. **Conclusions:** At ~2-y MFU, a single cilta-cel infusion led to deepening and durable responses in heavily pretreated pts with RRMM with a manageable safety profile. Follow-up is ongoing, and landmark 2-y post LPI data (~8 m additional follow-up; ~30 m total MFU) will be presented. Further investigations of cilta-cel are ongoing in earlier LOT and outpatient settings across the CARTITUDE program (NCT04133636, NCT04181827, NCT04923893). Clinical trial information: NCT03548207. Research Sponsor: Janssen Research & Development, LLC, Pharmaceutical/Biotech Company.

8029 **Poster Session**

Biological correlative analyses and updated clinical data of ciltacabtagene autoleucel (cilta-cel), a BCMA-directed CAR-T cell therapy, in patients with multiple myeloma (MM) and early relapse after initial therapy: CARTITUDE-2, cohort B.

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Background: In cohort B of the multicohort phase 2 CARTITUDE-2 (NCT04133636) study, the efficacy and safety of cilta-cel are being evaluated in patients (pts) with MM who had early relapse after initial therapy. These pts have functionally high-risk disease, with early relapse post autologous stem cell transplantation (ASCT) being a poor prognostic factor and representing an unmet medical need. We present updated results. **Methods:** Eligible pts had MM, received 1 prior LOT (PI and IMiD required), had disease progression per IMWG (either ≤12 mo after ASCT or ≤12 mo after start of anti-myeloma therapy for pts who did not undergo ASCT), and were tx-naive to CAR-T/anti-BCMA therapies. A single cilta-cel infusion (target dose 0.75×10^6 CAR+ viable T cells/kg) was given post lymphodepletion. Safety and efficacy were assessed, and the primary endpoint was MRD negativity at 10^{-5}. Management strategies were implemented to minimize risk of movement/neurocognitive AEs (MNTs). Pharmacokinetic (PK) analyses (C_{max} and T_{max} of CAR+ T-cell transgene levels in blood) are being conducted, as well as analyses of levels of CRS-related cytokines (eg, IL-6) over time, peak levels of cytokines by response and CRS, association of cytokine levels with ICANS, and CAR+ T cell CD4/CD8 ratio by response, CRS, and ICANS. **Results:** As of January 2022, 19 pts (median age 58.0 y [range 44–67]; 74% male; median follow-up 13.4 mo [range 5.2–21.7]) received cilta-cel. 79% of pts received prior ASCT. ORR was 100.0%, 90% achieved CR or better, and 95% achieved ≥VGPR. Median time to first response and best response were 0.95 mo (range 0.9–9.7) and 5.1 mo (range 0.9–11.8), respectively. Of pts who were MRD-evaluable (n = 15), 14 (93%) achieved MRD 10^{-5} negativity during this study. Median DOR was not reached and 12-mo event-free rate was 88.9%. The 12-mo PFS rate was 90%. Median time to onset of CRS was 8 d (range 5–11) and occurred in 16 (84.2%) pts (1 gr 4). CRS resolved in all pts. ICANS (gr 1) occurred in 1 pt; MNT (gr 3) occurred in 1 pt, previously reported. 1 pt died post cilta-cel due to PD at d 158. Preliminary PK analyses indicate that peak expansion of CAR-T cells occurred on d 13.1 (range 8.96–209.9) and median persistence was 76.9 d (range 40.99–221.8). **Conclusions:** A single cilta-cel infusion led to deep and durable responses in a functionally high-risk pt population who experienced early clinical relapse/tx failure to initial therapy, with a manageable safety profile. In this pt population with ineffective or insufficient response to ASCT, cilta-cel led to responses. Responses continue to deepen, and follow-up is ongoing. Updated and in-depth PK, cytokine, and CAR-T subset analyses and clinical correlation will be presented and provide novel insights into biological correlates of efficacy and safety in this pt population. Clinical trial information: NCT04133636. Research Sponsor: Janssen Research & Development, LLC, Pharmaceutical/Biotech Company.

8030 **Poster Session**

Health-related quality of life (HRQoL) in patients with relapsed/refractory multiple myeloma (RRMM) receiving real-life current standard of care (SOC) in the LocoMMotion study.

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Background: Evaluation of patient (pt)-reported outcomes provides insight into how real-life SOC treatments (tx) affect HRQoL for pts with RRMM. LocoMMotion (NCT04035226) is the first prospective, multinational study of real-life SOC in triple-class exposed pts with RRMM. Here, we present measures of symptoms, functioning, and overall HRQoL. **Methods:** LocoMMotion is a prospective, noninterventional study across 76 sites (63 European; 13 US). Pts had received ≥3 prior lines of therapy (LOT) or were refractory to PI and IMiD; received PI, IMiD, and anti-CD38 mAb; and had disease progression during/after last LOT. Real-life SOC tx were defined as those used in local clinical practice. The questionnaires were EORTC QLQ-C30, 4 single items from EORTC QLQ-MY20, and EQ 5D-5L. HRQoL was assessed at baseline (BL), day 1 of each tx cycle, end of tx visit, and during the follow-up period (every 4 weeks). Improvement compared to BL health status was evaluated using established thresholds. Within-group change was assessed using mixed models for repeated measures. **Results:** Questionnaire completion for pts in the LocoMMotion study (N=248; 54.4% male; median age 68 yrs; median 4.0 [range, 1–20] cycles of SOC) was 75.6% during SOC tx. Most pts did not achieve meaningful improvement in PRO scores, defined by a literature-based minimally important difference of 10 points in mean score. This was most pronounced in pain symptoms (62% of pts had no meaningful improvement during the first 3 months of tx; 55% had no improvement during full tx duration). For the overall population, the least square (LS) mean changes from BL during SOC tx and subsequent LOT are described (Table). Pts who achieved very good partial response and better during SOC tx had greater improvement in PRO scores, including in LS mean change for pain score (-14.9 [95% confidence interval (CI): -22.9, -7.0]). **Conclusions:** In this first prospective study of real-life current SOC in triple-class exposed pts, limited gains in HRQoL were reported, most notably in pain symptoms. There is an urgent need for effective therapies that can help pts achieve deep responses and delay disease progression, as these are associated with improved HRQoL. Clinical trial information: NCT04035226. Research Sponsor: Janssen Research & Development, LLC, Pharmaceutical/Biotech Company.

LS mean changes from BL.

LS mean change from BL (95% CI)	During SOC tx N=172	During subsequent tx N=87
Physical functioning[a]	2.5 (–0.5, 5.5)	–11.8 (–17.7, –5.9)
Global health status[a]	1.9 (–1.4, 5.1)	–2.0 (–7.1, 3.2)
Pain score[b]	–1.4 (–5.8, 2.9)	1.8 (–4.7, 8.3)
Fatigue symptoms[b]	–5.3 (–8.7, –1.8)	6.1 (0.3, 12.0)
Restless or agitated[b]	–2.6 (–6.8, 1.6)	9.3 (2.1, 16.4)
Thinking about illness[a]	9.4 (4.9, 13.9)	–7.5 (–14.5, –0.5)
Worried about dying[a]	6.1 (1.9, 10.3)	–14.4 (–22.5, –6.4)
Worried about health[a]	7.9 (3.5, 12.4)	–9.7 (–16.6, –2.8)
Visual analog scale[a]	2.4 (–0.2, 5.1)	–0.6 (–5.5, 4.3)

[a]Higher score indicates better outcome. [b]Higher score indicates worse outcome.

8031 **Poster Session**

Subgroup analyses in patients with relapsed/refractory multiple myeloma (RRMM) receiving real-life current standard of care (SOC) in the LocoMMotion study.

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Background: Patients (pts) with RRMM who are triple-class exposed (proteasome inhibitor [PI], immunomodulatory drug [IMiD], and anti-CD38 monoclonal antibody [mAb]) have an urgent and currently unmet clinical need. LocoMMotion (NCT04035226) is the first prospective multinational study of real-life SOC in triple-class exposed pts with RRMM. Here we present efficacy in subgroups of pts treated with SOC therapies in the LocoMMotion study. **Methods:** LocoMMotion is a noninterventional study across 76 sites (63 European; 13 US). Eligible pts had received ≥3 prior lines of therapy (LOT) or were double refractory to a PI and an IMiD; received a PI, an IMiD, and anti-CD38 mAb; and had disease progression during/after their last LOT. Real-life SOC treatments were defined as those used in local clinical practice. Responses and disease progression were assessed by response review committee, per IMWG criteria. Subgroups were defined by baseline (BL) characteristics: age, Eastern Cooperative Oncology Group performance status (ECOG PS), renal function, ISS stage, presence of extramedullary plasmacytoma, LDH level, % of bone marrow plasma cells, number of prior LOT, triple-class or penta-drug exposure, and refractoriness. **Results:** As of May 21, 2021 (median follow-up 11.0 mo), 248 pts were enrolled and treated with median 4.0 (range, 1–20) cycles of SOC therapy. Evaluation of efficacy outcomes in subgroups demonstrated that refractoriness to 3 classes of antimyeloma therapy, presence of extramedullary plasmacytomas, high LDH, and ECOG PS ≥1 were associated with generally worse outcomes, compared with pts who did not have these characteristics (Table). Overall response rate (ORR) ranged from 20.0–43.1% across all subgroups. Age and number of prior LOT did not have an impact on efficacy outcomes. **Conclusions:** Subgroup analyses of this first prospective study of real-life SOC tx in triple-class exposed pts with RRMM indicate that specific pt and disease characteristics were associated with poor outcomes. Triple-class refractory and non-triple-class refractory pts had poor outcomes, although the latter had longer median progression-free survival (PFS). These findings should be considered when planning bridging strategy for CAR-T therapy. Clinical trial information: NCT04035226. Research Sponsor: Janssen Research & Development, LLC, Pharmaceutical/Biotech Company.

Efficacy in select subgroups of pts in LocoMMotion.

Pts	N	Median OS, months	Median PFS, months	ORR, n, %	Median DOR,[a] months
Overall	248	12.4	4.6	74 (29.8)	7.4
Triple-class refractory	183	11.1	3.9	46 (25.1)	4.5
Non-triple-class refractory	65	NE	8.2	28 (43.1)	9.1
BL ECOG PS of 0	63	NE	5.4	19 (30.2)	5.7
BL ECOG PS of ≥1	184	10.8	4.4	55 (29.9)	7.7
Extramedullary plasmacytomas, yes	33	8.2	3.4	9 (27.3)	4.1
Extramedullary plasmacytomas, no	215	13.0	5.1	65 (30.2)	7.7
LDH (U/L) of ≤245	114	13.8	5.7	39 (34.2)	5.1
LDH (U/L) of >245	72	7.4	3.3	19 (26.4)	8.5

[a]In responders (partial response or better). DOR, duration of response; OS, overall survival.

8032 **Poster Session**

A novel, immunotherapy-based approach for the treatment of relapsed/refractory multiple myeloma (RRMM): Updated phase 1b results for daratumumab in combination with teclistamab (a BCMA x CD3 bispecific antibody).

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Background: Teclistamab (tec; JNJ-64007957) is a BCMA × CD3 T-cell redirecting bispecific antibody under investigation in patients (pts) with RRMM. Daratumumab (dara) is a CD38 mAb with direct on-tumor and immunomodulatory actions. Initial clinical data from the phase 1b multicohort TRIMM-2 study support the combination of tec + dara for the treatment of RRMM, with tolerable safety, no overlapping toxicities, and promising efficacy. We present updated results with additional pts and longer follow-up. **Methods:** Eligible MM pts aged ≥18 y had received ≥3 prior lines of therapy (LOT; including a proteosome inhibitor [PI] and immunomodulatory drug [IMiD]) or were double-refractory to a PI and IMiD. Pts treated with anti-CD38 therapy ≤90 d prior were excluded. Pts received dara SC 1800 mg per approved schedule and tec SC 1.5–3 mg/kg QW or Q2W. Primary objectives were to identify the recommended phase 2 dose of tec for combination therapy and evaluate safety of the combination. Responses were assessed by IMWG criteria. AEs were graded per CTCAE v5.0; cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) were graded per ASTCT guidelines. **Results:** At data cutoff (Jan 13, 2022; safety population: N=46), median follow-up was 7.2 mo (range 0.1–16.6; median age 67 y [range 50–79]; 52% female). Pts received a median of 6 prior LOT (range 2–17; 74% triple-class exposed; 63% penta-drug exposed; 15% anti-BCMA exposed). 91% of pts had ≥1 AE (grade 3/4 78%), most commonly CRS (61%; all grade 1/2; median time to onset 2 d; median duration 2 d), neutropenia (54%; grade 3/4 50%), anemia (46%; grade 3/4 28%), thrombocytopenia (33%; grade 3/4 28%), and diarrhea (33%; grade 3/4 2%). Infections occurred in 29 pts (63%; grade 3/4 28%). One pt had grade 1 ICANS that fully resolved. Among 37 response-evaluable pts, ORR was 78% (29/37); 27 pts (73%) had very good partial response (VGPR) or better (Table). Median time to first response across dosing cohorts was 1.0 mo (range 0.9–2.8); median duration of response was not reached. Upregulation of $CD38^+/CD8^+$ T cells and proinflammatory cytokines was observed with tec + dara, supporting potential synergy of the combination in pts with prior anti-CD38 exposure. Updated results will be presented. **Conclusions:** Tec + dara provides a novel immunotherapy approach for the treatment of RRMM that may yield improved clinical efficacy in heavily pretreated pts. Clinical trial information: NCT04108195. Research Sponsor: Janssen Research & Development, LLC.

Responses in evaluable pts[a] in tec + dara cohorts.

	Dara 1800 mg + Tec 1.5 mg/kg QW (n=20)[b]	Dara 1800 mg + Tec 3 mg/kg QW (n=4)	Dara 1800 mg + Tec 3 mg/kg Q2W (n=13)
Overall response, n	15	4	10
VGPR or better, n	14	4	9
Complete response or better, n	6	2	1

[a]Pts who received ≥1 study treatment and had ≥1 postbaseline response evaluation. [b]8 pts switched to tec 3 mg/kg Q2W (3 at cycle [C] 4, 3 at C5, 1 at C7, and 1 at C9).

8033 **Poster Session**

Health-related quality of life in patients with relapsed/refractory multiple myeloma (RRMM) treated with teclistamab, a B-cell maturation antigen (BCMA) x CD3 bispecific antibody: Patient-reported outcomes in MajesTEC-1.

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Background: As multiple myeloma (MM) negatively affects patients' (pts) health-related quality of life (HRQoL), assessment of patient-reported outcomes (PROs) in addition to clinical outcomes is important. Teclistamab (tec; JNJ-64007957) is an off-the-shelf bispecific antibody that redirects CD3+ T cells to mediate T-cell activation and subsequent lysis of BCMA-expressing MM cells. Initial results from the pivotal cohort of the phase 1/2 MajesTEC-1 study demonstrated that tec was well tolerated with encouraging efficacy in pts who received ≥3 prior lines of treatment (LOT; including a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 antibody). Here we report PROs from this cohort. **Methods:** Pts (aged ≥18 years) had documented RRMM (International Myeloma Working Group criteria), progressive/measurable disease, and had previously received ≥3 prior LOT; prior anti-BCMA treatment (tx) was not allowed. Pts received weekly subcutaneous tec at the recommended phase 2 dose (1.5 mg/kg with step-up doses of 0.06 and 0.3 mg/kg). PROs were assessed at screening and every even cycle (cycles 2–8 reported here) using the EORTC QLQ-C30 (range: 0–100; higher scores indicate better global health status [GHS] but greater symptom severity [symptom scales]) and the EuroQol 5-dimensional descriptive system (visual analog scale [VAS] range: 0 [worst imaginable health state] to 100 [best imaginable]). Tx effect was assessed by a mixed-effects model with repeated measures; the proportion of pts with meaningful improvement was defined as a change ≥10 points. Time to worsening was determined using the Kaplan-Meier estimate. **Results:** A total of 110 pts were included (median follow-up: 7.8 mos). Overall PRO compliance rates were high (baseline [BL]: 85–90%; cycles 2–8: 80–94%). Tec improved overall HRQoL as evidenced by improvements in GHS scores (cycles 2–8) and reduction in pain (-4.2 [cycle 2] to -15.1 [cycle 8]; Table), with no overall change in physical functioning and fatigue. The proportions of pts with meaningful improvements from BL at cycle 8 were GHS: 50%; physical functioning: 35%; pain: 65%; fatigue: 73%; 50% of pts reported meaningful improvement in their overall health (VAS). Median time to improvement from baseline was ~1.5 months (with nausea/vomiting and fatigue taking longer to improve), while median time to worsening (all symptoms) ranged from 2 months to not estimable. **Conclusions:** Consistent with clinical outcomes, pts treated with tec reported rapid, clinically meaningful improvements in HRQoL. Clinical trial information: NCT04557098. Research Sponsor: Janssen Research & Development, LLC.

BL and least squares (LS) mean change from baseline in PRO measures.

	GHS	Physical functioning	Pain	Fatigue	VAS
BL (mean)	58.0	71.3	43.6	39.6	61.2
LS mean change					
Cycle 2	0.6	–6.7	–4.2	6.9	0
Cycle 4	6.6	0.4	–9.6	–0.6	7.9
Cycle 6	6.8	0.6	–10.7	0.8	8.9
Cycle 8	11.3	5.3	–15.1	–0.4	10.7

8034 **Poster Session**

Indirect treatment (tx) comparison of teclistamab (tec) in MajesTEC-1 versus physician's choice of therapy in the long-term follow-up of the CASTOR, POLLUX, EQUULEUS, and APOLLO trials in patients (pts) with triple-class exposed (TCE), relapsed/refractory multiple myeloma (RRMM).

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Background: Tec is a B-cell maturation antigen × CD3 bispecific antibody currently being evaluated in the single-arm, phase 1/2 MajesTEC-1 trial (NCT04557098) in pts with RRMM who had received ≥3 prior lines of therapy (LOT) and were TCE to an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. The aim of this study is to evaluate the comparative efficacy of tec versus physician's choice of therapy, as no head-to-head trials have been conducted. **Methods**: An external control arm for MajesTEC-1 was created from pts in the long-term follow-up of 4 clinical trials of daratumumab (CASTOR, POLLUX, EQUULEUS, and APOLLO) who met the eligibility criteria for MajesTEC-1. These pts (N = 427) were subsequently treated with physician's choice of therapy after discontinuing trial txs, and disease progression and best tx response were based on the investigator's assessment. Individual pt-level data from MajesTEC-1 pts who received tec (1.5 mg/kg weekly) at a clinical cutoff of Sep 7, 2021 were included. Inverse probability of tx weighting (IPTW) with average tx effect on the treated population was used to adjust for imbalances in baseline covariates of prognostic significance: refractory status, progression on last LOT, cytogenetic risk, International Staging System stage, number of prior LOT, extramedullary plasmacytoma, time since diagnosis, age, and hemoglobin. Overall response rate (ORR), rate of complete response or better (≥CR), rate of very good partial response or better (≥VGPR), progression-free survival (PFS), time to next tx (TTNT), and overall survival (OS) were assessed. For binary endpoints (ORR, ≥CR rate, ≥VGPR rate), the relative effect of tec vs physician's choice of therapy was estimated with an odds ratio (OR) and 95% confidence interval (CI) derived from a weighted logistic regression analysis. A weighted Cox proportional hazards model was used to compute hazard ratios (HRs) and 95% CIs for time-to-event endpoints (PFS, OS, and TTNT). Several sensitivity analyses were conducted. **Results**: After IPTW, baseline characteristics were comparable between the 2 cohorts. Pts treated with tec had improved outcomes vs physician's choice of therapy: ORR (OR 4.58; 95% CI 2.83–7.53; $P < 0.0001$); ≥CR rate (OR 12.62; 95% CI 5.20–38.55; $P < 0.0001$); ≥VGPR rate (OR 11.64; 95% CI 6.49–21.98; $P < 0.0001$); PFS (HR 0.62; 95%CI 0.45–0.84; $P = 0.0024$); TTNT (HR 0.38; 95% CI 0.27–0.52; $P < 0.0001$); and OS (HR 0.47; 95% CI 0.32–0.69; $P = 0.0001$). Results were similar for all sensitivity analyses. **Conclusions**: Tec showed improved efficacy versus physician's choice of therapy in all clinical outcomes, highlighting its therapeutic potential to address unmet needs in pts with TCE RRMM who received ≥3 prior LOT. Research Sponsor: Janssen Global Services, LLC.

8035 **Poster Session**

Matching-adjusted indirect treatment comparison (MAIC) of teclistamab (tec) versus belantamab mafodotin (belamaf) for the treatment of patients (pts) with triple-class exposed (TCE), relapsed/refractory multiple myeloma (RRMM).

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Background: Pts with RRMM who are TCE to immunomodulatory drugs, proteasome inhibitors, and anti-CD38 antibodies have limited treatment options. While there is no standard of care for treatment of pts with TCE RRMM, belamaf is a recently approved, novel therapeutic option. MajesTEC-1 (NCT04557098) is a single-arm phase 1/2 study evaluating tec, a B-cell maturation antigen × CD3 bispecific antibody in pts with TCE RRMM who received ≥3 prior lines of therapy (LOT). Given the absence of a control arm in MajesTEC-1, we compared efficacy outcomes of pts who received tec at the recommended phase 2 dose in MajesTEC-1 with those of pts treated with belamaf in the phase 2 DREAMM-2 trial (NCT03525678). **Methods:** An unanchored MAIC was performed using individual pt-level data (IPD) from MajesTEC-1 (tec 1.5 mg/kg weekly; N = 150) at a clinical cutoff of Sep 7, 2021, and published summary-level data from pts who received the approved dose of belamaf in DREAMM-2 (2.5 mg/kg every 3 weeks; N = 97). The DREAMM-2 eligibility criteria were applied to pts from the intent-to-treat population of MajesTEC-1. IPD from MajesTEC-1 were weighted to match the aggregated DREAMM-2 baseline pt characteristics. Baseline characteristics of prognostic significance (refractory status, cytogenetic profile, International Staging System stage, presence of extramedullary disease, and number of prior LOT) were adjusted for in the analysis. Comparative efficacy of tec vs belamaf was estimated for overall response rate (ORR), complete response or better (≥CR) rate, progression-free survival (PFS), overall survival (OS), and duration of response (DOR). For binary endpoints (ORR and ≥CR rate), the relative effects of tec vs belamaf were quantified using an odds ratio (OR) and 95% CI derived from a weighted logistic regression analysis, while time-to-event endpoints (DOR, PFS, OS) were estimated using a weighted Cox proportional hazards model. **Results:** After adjustment, the effective sample size (ESS) of the MajesTEC-1 cohort was 33 and baseline characteristics for the reweighted MajesTEC-1 population were balanced with the DREAMM-2 population. Pts treated with tec had an improved ORR (OR 2.05; 95% CI 0.92–4.57; *P*= 0.0786), ≥CR rate (OR 2.13; 95% CI 0.80–5.65; *P*= 0.1283), PFS (HR 0.63; 95% CI 0.34–1.15; *P*= 0.1338), OS (HR 0.95; 95% CI 0.47–1.92; *P*= 0.8897), and DOR (hazard ratio [HR] 0.19; 95% CI 0.05–0.73; *P*= 0.0149) compared with belamaf. The reduced ESS following adjustment may account for the lack of statistical significance for most outcomes. **Conclusions:** These analyses demonstrated statistically improved DOR for tec vs belamaf and numerically favorable results for other outcomes, highlighting its potential as a treatment for pts with TCE RRMM who received ≥3 prior LOT. Research Sponsor: Janssen Global Services, LLC.

8036 **Poster Session**

Comparative effectiveness of teclistamab versus real-world treatments for patients with triple-class exposed (TCE), relapsed/refractory multiple myeloma (RRMM).

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Background: Teclistamab is a B-cell maturation antigen × CD3 bispecific antibody currently being evaluated in MajesTEC-1 (NCT04557098), an open-label, single-arm, phase 1/2 trial in patients with RRMM who had received ≥3 prior lines of therapy (LOT) and were TCE to an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. Given the absence of a control arm in MajesTEC-1, we assessed the comparative effectiveness of teclistamab versus treatment regimens using an external control arm from a real-world database. **Methods**: An external control arm for MajesTEC-1 was created from eligible patients in the nationwide de-identified electronic health record-derived Flatiron Health multiple myeloma cohort database who started a new line of therapy (physician's choice) following triple-class exposure between January 2011 and August 2021, received ≥3 prior LOT, and satisfied key MajesTEC-1 eligibility criteria. Individual patient data from MajesTEC-1 included patients who received teclistamab (1.5 mg/kg weekly) at a clinical cutoff of Sep 7, 2021. Inverse probability of treatment weighting (IPTW) was used to adjust for imbalances in baseline covariates of prognostic significance: refractory status, progression on last LOT, cytogenetic risk, International Staging System stage, number of prior LOT, time since diagnosis, age, and hemoglobin. Outcomes of interest included progression-free survival (PFS), time to next treatment (TTNT), and overall survival (OS); these outcomes were analyzed as time-to-event data using IPTW adjusted Kaplan-Meier estimates and a weighted Cox proportional hazards model. Several sensitivity analyses were conducted. **Results**: After IPTW, baseline characteristics were comparable between the 2 cohorts. Patients treated with teclistamab had improved PFS (hazard ratio [HR] 0.43; 95% confidence interval [CI] 0.32–0.59; $P<$ 0.0001), TTNT (HR 0.42; 95% CI 0.31–0.58; $P<$ 0.0001), and OS (HR 0.73; 95% CI 0.48–1.09; $P=$ 0.13) versus assessed real-world treatments. Results were similar for all sensitivity analyses. **Conclusions**: Teclistamab showed improved effectiveness for PFS, TTNT, and OS, compared with real-world treatments used in patients with TCE RRMM who received ≥3 prior LOT. These findings highlight the therapeutic potential of teclistamab in patients with RRMM who have limited treatment options. Research Sponsor: Janssen Global Services, LLC.

8037 **Poster Session**

Circulating tumor DNA analysis and association with relapse in patients with primary refractory multiple myeloma receiving secondary salvage therapy.

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Background: Multiple myeloma (MM) is an incurable plasma cell malignancy with a 5 year-median overall survival (OS) in newly diagnosed (ND) patients. Real-world data reveals that 23% of transplant eligible (TE) ND MM patients relapse within 12 months of starting first-line bortezomib (1LB) based therapy and of these ~50% will fail secondary therapy and die within 18 months. It is currently impossible to identify these high-risk patients and genomic studies could potentially inform alternative secondary therapeutic options. We propose that circulating tumour DNA (ctDNA) analysis could provide a more holistic approach to determine genomics of high-risk patients than bone marrow (BM) tumour DNA analysis in this genetically heterogenous multi-site malignancy. **Methods:** Peripheral blood plasma and BM samples (n = 186) were obtained at baseline, cycle 3 day 1 (C3D1), end of the study (EOS) and/or relapse, whichever appeared earlier, from a Phase II multicentre single arm study of carfilzomib-thalidomide-dexamethasone (KTd) in 50 TE ND MM patients who were refractory or registered suboptimal response to 1LB (Australasian Leukaemia and Lymphoma Group - MM17 trial). Somatic variants were identified in BM or ctDNA with ultra-sensitive targeted amplicon sequencing of 22-genes known to be mutated in MM. Mutational spectrum was correlated to standard MM risk factors including International Staging System (ISS), response to 1LB and KTd, cytogenetics/FISH, lactate dehydrogenase (LDH) levels, progression-free survival (PFS) and OS. **Results:** Our initial analysis of ctDNA mutational proportions between patients who did not or did experience relapse on KTd revealed a significantly higher proportion of *RAS/RAF* (3% vs 25%), or *ATM/ATR/TP53* (17% vs 41%; $p < 0.0001$), respectively, in relapse patients. Subsequently, we correlated ctDNA *RAS/RAF* and/or *ATM/ATR/TP53* mutational presence to standard MM risk factors. We identified a shorter PFS and OS for ISS Stage 2 and 3 compared to Stage 1 patients ($p = 0.002$ and $p = 0.02$, respectively) and a significantly higher proportion of *RAS/RAF* or *ATM/ATR/TP53* mutations in patients with refractory as compared to sub-optimal response to 1LB therapy ($p = 0.0002$). Patients with *RAS/RAF* or *ATM/ATR/TP53* mutations in ctDNA at the time of starting salvage therapy also had a shorter PFS and OS on KTd ($p = 0.003$ and $p = 0.02$, respectively). Sequential ctDNA analysis discovered that in 87.5% of patients, one or more of the dominant mutations present at the time of relapse were already present at the start of salvage therapy. **Conclusions:** Our analysis reveals that *RAS/RAF* and *ATM/ATR/TP53* mutations in ctDNA could be prognostic biomarkers of response to secondary salvage therapy in primary refractory patients thus providing the opportunity to design targeted salvage treatment paradigms in high-risk MM patients. Research Sponsor: Black Swan Research Initiative, International Myeloma Foundation.

8038 **Poster Session**

Prevalence of ocular comorbidities in patients with multiple myeloma: An analysis of U.S. claims data.

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Background: Multiple myeloma (MM) predominantly affects older patients (pts) (median age at diagnosis 69 yrs) in whom comorbidities must be considered to manage the disease appropriately. Some anti-MM therapies can be associated with ocular toxicities and require careful attention when used among pts with pre-existing ocular comorbidities (OC). In 2018, 41% of Medicare enrollees had OC. Despite the potential implication on treatment decisions, information on pre-existing OC (e.g., disorders of lens, glaucoma) in MM pts is limited. This study aims to describe the prevalence of OCs among real-world pts with MM in 2011-2020 in the US. **Methods:** Adults with newly diagnosed MM (NDMM) with or without treatment, with 1L systemic therapy, and with relapsed/refractory MM (RRMM) who received up to 4 lines of systemic therapies (LOT) for MM were identified in the IQVIA PharMetrics Plus data. The index date was the date of initial MM diagnosis or a LOT initiation date. The prevalence of OC in each group was defined as the presence of any OC ICD 9/10 diagnosis codes in the 12 months prior to the index date. OCs (e.g., disorders of conjunctiva, lens, choroid, retina, glaucoma) were considered a potentially MM-related disease manifestation or MM treatment-related toxicity based on published literature and clinical expert opinion. **Results:** The median age at initial MM diagnosis was 64 yrs overall (N=49,814), and 63 yrs among treated pts (N=22,963). The median age was 63 yrs at 1L initiation and 64 yrs at 2L, 3L, and 4L initiation. The prevalence of OC at initial MM diagnosis was 39.0% overall and 35.2% among treated pts (Table). The OC prevalence was 35.8% prior to 1L initiation and higher in RRMM pts (42.1%, 44.9%, and 45.7% prior to 2L, 3L, and 4L initiation, respectively). This trend was observed across all OC categories, among MM-related OCs, and across all age groups. The prevalence of OC by MM stage was stable over the years. **Conclusions:** Approximately 40% of NDMM pts have a pre-existing OC, and the prevalence increases with the number of LOT in RRMM. While some OC may be due to aging, the impact of OC on treatment decisions for MM should be explored. Research Sponsor: Regeneron Pharmaceuticals, Inc.

Prevalence of pre-existing ocular comorbidities during 12-month baseline by cohort.

Index date	All pts *First MM dx* N = 49,814	Treated pts *First MM dx* N = 22,963	1L initiator *1L initiation* N = 22,963	2L initiator *2L initiation* N = 8,860	3L initiator *3L initiation* N = 3,667	4L initiator *4L initiation* N = 1,709
Any OCs (%) (range, 2011-2020)	39.0 (35.2–41.4)	35.2 (29.4–38.3)	35.8 (31.2–38.8)	42.1 (37.5–47.5)	44.9 (40.2–48.6)	45.7 (41.5–52.5)
By OC type						
Related to MM or MM tx*	31.7	28.1	28.6	33.3	35.6	36.9
Unrelated to MM or MM tx	13.1	12.1	12.2	15.8	18.3	17.8
By age group						
18–54	23.2	19.6	19.8	25.7	27.1	30.0
55–64	29.7	26.7	27.1	34.9	34.6	36.8
65–74	45.8	43.8	44.3	49.0	52.7	53.2
75–84	57.5	57.4	56.7	59.7	65.9	59.6
≥ 85	57.9	58.9	59.0	60.6	63.1	64.1

* Pts may have both MM related and non-MM related OCs and counted in both categories.

8039 **Poster Session**

Factors associated with dose adjustment for the bortezomib, lenalidomide, dexamethasone regimen among patients with newly diagnosed multiple myeloma.

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Background: VRd (bortezomib/lenalidomide/dexamethasone) has become one of the established treatment regimens in the US for multiple myeloma (MM). Due to toxicities, dose adjustments are often required for VRd. This real-world study described the patient characteristics and factors associated with dose adjustment among MM patients treated with VRd as first line (1L) therapy. **Methods:** Adult MM patients treated with 1L VRd were selected from the Optum Clinformatics database (Nov 1, 2015-Sep 30, 2020). Patient characteristics were evaluated during a 6-month baseline period. Dose adjustments were defined based on lenalidomide (len) dose received during 1L. Receipt of > 15mg len was categorized as VRd regular, ≤15mg len as VRd lite, and initial len dose > 15mg reduced to ≤15 mg over treatment period as VRd reduced. Baseline factors associated with different VRd dose categories were studied using multinomial logistic regression. **Results:** Among the 1497 patients identified, the mean (SD) age was 69 (9.5) years (52% ≥70), 51% were male, 59% were White, 37% were frail, and 67% with Medicare. Baseline Charlson Comorbidity Index was 4.2, with hypertension (70%), hyperlipidemia (56%), renal impairment (26%), and CVD (25%) being the most prevalent comorbidities. Over half of the patients received an adjusted dose, VRd lite (33%) and VRd reduced (22%). Overall, for patients treated with 1L VRd, median follow-up was 16.2 months; median duration of 1L was 4.9 months (among those with confirmed end of therapy); and median TTNT was 14.5 months. Compared to VRd regular, use of VRd lite was over 6 times more likely to be associated with patients ≥75 years of age, about 2 times more likely to be associated with females, and about 40% less likely to be associated with commercial insurance vs. Medicare; VRd reduced was 1.3 times more likely to be associated with females, and 1.5 times more likely to be associated with frail patients (table). No differences were observed among different races. **Conclusions:** Over half of the MM patients treated with 1L VRd in the real-world were > 70 years of age and over one-third were frail. A large proportion of patients received a modified dose of VRd. Receipt of VRd lite dose was highly associated with older age (≥75 years), and receipt of VRd reduced dose was associated with frailty. These dose adjustments may potentially result in reduced efficacy of the VRd regimen in the real-world relative to controlled clinical trials, which needs to be assessed in future studies. Research Sponsor: Janssen Scientific Affairs, LLC.

Patient factors	VRd lite vs. VRd regular (ref.) Odds ratio (95% CI)	VRd reduced vs. VRd regular (ref.) Odds ratio (95% CI)
65 to < 70 vs. < 65	1.0 (0.6–1.7)	0.9 (0.6–1.5)
70 to < 75 vs. < 65	2.2 (1.3–3.8)	1.2 (0.7–2.0)
≥75 vs. < 65	6.2 (3.6–10.5)	1.6 (0.9–2.8)
Female vs. male	1.8 (1.4–2.4)	1.3 (1.0–1.8)
Commercial vs. Medicare	0.6 (0.4–0.9)	0.8 (0.5–1.3)
Frailty index > 0.2 vs. ≤0.2	1.3 (0.9–1.8)	1.5 (1.1–2.2)

8040 **Poster Session**

B-PRISM (Precision Intervention Smoldering Myeloma): A phase II trial of combination of daratumumab, bortezomib, lenalidomide, and dexamethasone in high-risk smoldering multiple myeloma.

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Background: Early therapeutic intervention with lenalidomide has shown to be effective in delaying progression in patients with high-risk smoldering multiple myeloma (HR-SMM) (Lonial J Clin Oncol 2020). Quadruplet regimen of daratumumab, bortezomib, lenalidomide and dexamethasone (D-RVD) has demonstrated significant activity in multiple myeloma, achieving high rates of minimal residual disease (MRD) negativity (Voorhees Blood 2020). Thus, we proposed to examine the activity and safety of D-RVD in patients with HR-SMM. **Methods:** This is a phase II single center, single-arm, open label study evaluating the combination of D-RVD in HR-SMM. Eligibility included high risk per Mayo 2018 "20-2-20" model and other previously established criteria including Mayo 2008 criteria, presence of immunoparesis, evolving type of SMM, and high risk FISH. Primary objective is rate of sustained MRD negativity at 2 years. Secondary objectives include PFS, response rates and safety. Treatment duration with modified D-RVD is for total of 2 years (24 cycles). Daratumumab is administered subcutaneously (SQ) per standard dose and schedule, bortezomib given weekly on days 1, 8, 15 for cycles 1-6 and then biweekly until completion of cycle 24. Lenalidomide is administered on days 1-21 and dexamethasone is administered weekly. All eligible patients will undergo stem cell collection after 6 cycles of therapy. **Results:** At the time of data cut off, 20 patients have been enrolled with a median follow up of 6 months. The median age is 58 years old (range 40-73). Sixteen out of 20 (80%) patients met high risk criteria per Mayo 2018 model with median plasmacytosis of 20%, median M protein value of 2.6 g/dl and median FLC ratio of 28.2. Seven patients had high-risk FISH: 5 with 1q duplication, 2 with t(4;14). Most common toxicities of any grade included neutropenia (65%), WBC decreased (55%) insomnia (50%), constipation (45%) and hypophosphatemia (45%). Most common grade 3 toxicities included neutropenia (15%), ALT increased (5%), thrombocytopenia (5%), hyperglycemia (5%), hypertension (5%), diarrhea (5%), syncope (5%). No patients discontinued therapy due to toxicity. The overall response rate is 90% with 40% PR, 25% VGPR and 25% CR. All patients have achieved at least a MR and 50% achieved VGPR or greater with responses deepening over time. No patients have progressed on treatment. MRD was evaluable in 16 patients and 8 patients have undergone MRD testing, with MRD negativity rate of 50% (4/8) and 25% (2/8) at thresholds of 10^{-5} and 10^{-6}, respectively. Stem cells were successfully collected in all patients with mean stem cell yield of 5.78 x 10^{6} CD34+/kg cells. **Conclusions:** D-RVD is well tolerated in patients with HR-SMM demonstrating significant early activity. Responses continue to deepen over time with patients achieving MRD negative disease. Clinical trial information: NCT04775550. Research Sponsor: Janssen.

8041 **Poster Session**

Phase II study of the combination of daratumumab, ixazomib, pomalidomide, and dexamethasone as salvage therapy in relapsed/refractory multiple myeloma: Stage 2 interim results.

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Background: The combination of daratumumab (Dara), pomalidomide (POM), and dexamethasone (dex) (DPd) has previously demonstrated deep and durable responses including high rates of minimal residual disease (MRD) negativity, in patients with relapsed/refractory (R/R) MM. Quadruplet regimens may further improve results. We report updated findings from a phase 2 multicenter trial of the addition of ixazomib to DPd (DIPd) in patients with early R/R MM. **Methods:** This is a prospective, multicenter, open-label, single arm phase II trial with a primary objective to evaluate the overall response rate (ORR), safety, and efficacy of DIPd. Secondary endpoints include progression-free survival (PFS), overall survival (OS), and MRD-negativity rate. A Simon's optimal 2-stage design was used, with 14 subjects in stage 1 to assess response and 32 patients for stage 2. Eligible patients may not have had exposure Dara or ixazomib, may not have progressed on POM, and may have received $\geq$1 and $\leq$3 prior lines of therapy. The first six patients in the safety run-in received Dara 16mg/kg IV weekly x 8 doses, biweekly x 8 doses, then monthly, POM 4mg orally on days 1-21 of a 28-day cycle, ixazomib 4mg orally on days 1,8,15 every 28 days, and dex 20-40mg weekly. Grade 3-4 neutropenia was observed in 100% of patients, prompting dose reduction to ixazomib 3 mg and POM 3 mg by the DSMB. An amendment allowed subcutaneous Dara administration. MRD assessments are being performed by EuroFlow for patients in VGPR or suspected CR. Pharmacodynamic changes in patients' tumor microenvironments were established by custom panel mass cytometry to include T-cell memory and activated subpopulations, B-cell content, NK-cell subpopulations as well as MDSCs, Tregs and T-exhaustive markers, monocytes and dendritic cells. **Results:** To date, 14 subjects have been treated in stage 1, and 18 patients in stage 2. Median age was 61.5 (range 41-87) years, 50% were female and 72% white. Median number of prior regimens was 1 (range 1-3), all patients were lenalidomide-exposed, and 47% (11/23) had high-risk cytogenetic features. The most common grade 3-4 treatment emergent adverse events included neutropenia (78%), infection (30%), leukopenia (11%), respiratory conditions (7%), psychiatric disturbance (4%), and thrombosis (4%). Median time on treatment was 4 months (1-29), with 11 patients remaining on DIPd and 5 deaths (4 due to progressive disease and 1 due to sepsis). ORR to date was 84% (16/19), and the best responses included: 5 (26%) sCR; 4 (21%) VGPR; 7 (37%) PR. After a median follow up of 12 months, the median OS was 39 months and PFS was 9.5 months. **Conclusions:** The quadruplet regimen DIPd is a well-tolerated combination that has shown early safety, efficacy, and ORR in early R/R myeloma, including patients with high-risk genetic abnormalities. Clinical trial information: NCT03590652. Research Sponsor: Takeda Pharmaceutical Company, Janssen Pharmaceuticals, Bristol Myers Squibb.

8042 **Poster Session**

Idecabtagene vicleucel (Ide-cel) chimeric antigen receptor (CAR) T-cell therapy for relapsed/refractory multiple myeloma (RRMM): Real-world experience.

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Background: Ide-cel, a BCMA directed CAR T-cell therapy, was FDA approved 3/26/2021 for the treatment of RRMM after 4 prior lines of therapy. We evaluated the real-world outcomes of patients treated with standard of care ide-cel under the commercial FDA label. **Methods:** Ten US academic centers contributed data to this effort independent of the manufacturer. As of 1/10/2022, 138 patients were leukapheresed with overall manufacturing failure in 6 (4%). 108 patients were infused ≥ 30 days prior to data-cut off and constitute the study population for this retrospective analysis. **Results:** Table describes the study population compared to the pivotal KarMMa-1 trial (Munshi et al, NEJM 2021). Patients in our study were less likely to have ECOG PS of 0/1 (77%) and more likely to be penta-refractory (41%). 67% of patients would not have met eligibility criteria for KarMMa. Common reasons for ineligibility (> 1 reason in 22% patients) were co-morbidities (28%), cytopenias (22%), prior therapy with alloSCT/CAR-T/other BCMA therapy (19%), CNS myeloma/non-measurable disease/plasma cell leukemia (13%), and fitness (12%). 81% of patients received bridging therapy. Toxicity was comparable to that seen in KarMMa-1. Cytokine release syndrome (CRS) was seen in 82% (> grade 3: 4%) and immune effector cell-associated neurotoxicity syndrome (ICANS) in 15% (> grade 3: 5%) of patients, respectively. Tocilizumab and steroids were used in 72% and 25% of patients, respectively. Infections were seen in 34% of patients. Day 30 response was evaluable in 104 patients. Response rates were: ≥ partial response, 83%; ≥ very good partial response, 64%; and ≥ complete response (CR), 34%. 11% of patients have died by data cut-off, 7 due to disease progression and 5 due to other causes (1 grade 5 CRS, 1 hemophagocytic lymphohistiocytosis, 1 progressive neurological weakness, 2 COVID-19). **Conclusions:** This multicenter retrospective study delineates the real-world outcomes of ide-cel CAR T-cell therapy for RRMM. Despite more patients being penta-refractory and less fit compared to the pivotal KarMMa trial, safety and 30-day responses in the real-world setting (overall response rate: 83%, CR: 34%) are comparable to the clinical trial population. Follow-up is ongoing and updated data will be presented. Research Sponsor: None.

Patient characteristics and outcomes: Comparison between KarMMa-1 (Munshi et al. NEJM 2021) and commercial standard of care ide-cel treatment at 10 U.S. centers.

	KarMMa-1, N=128	Real world, N=108
Median age, yrs	61 (33-78)	64 (36-78)
ECOG PS 0 or 1	98%	77%
Extramedullary disease	39%	53%
High-risk cytogenetics	35%	33%
Median prior regimens	6	6
Prior autologous transplant	94%	85%
Penta-refractory disease	26%	41%
ORR/CR	73%/33% (Best response)	83%/34% (Day 30)
Grade ≥ 3 CRS and ICANS	5%, 3%	5%, 5%

8043 **Poster Session**

Demographic disparities in genomic data and clinical trials for multiple myeloma.

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Background: There are considerable outcome disparities among patients with multiple myeloma (MM). African-Americans have higher risk of developing MM, earlier age at diagnosis, and higher mortality compared to Whites. While outcomes have multifactorial socioeconomic etiologies, race and ethnicity (R&E) correlate with genomic ancestry, and any role of genetics should be explored. This requires equitable representation in biological databases like The Cancer Genome Atlas (TCGA). Here, we characterize disparities in MM cases of TCGA and clinical trials (CT). **Methods:** MM incidence was obtained from North American Association of Central Cancer Registries (NAACCR) for R&E, sex and age (< 50, 50-64, 65+ years). Race includes White, Black, and Asian, along with Hispanic ethnicity, as TCGA MM is limited to these groups. Genes with oncogenic potential and > 5% mutation were stratified by R&E and age. TCGA MM cases are from USA, Canada, Italy, and Spain. On ClinicalTrials.gov, completed MM CT limited to these countries were identified. Student's t-test and chi-square test were used to analyze disparities and gene mutations. Kaplan-Meier curve was generated to evaluate survival. **Results:** TCGA MM representation is in Table, calculated as (demographic TCGA cases divided by total TCGA cases) divided by (demographic incidence divided by total incidence). Race was not reported in 20% of TCGA, 4% of CT, and 3% of NAACCR. Of cases reporting R&E, Hispanics are underrepresented by 26% in TCGA and 47% in CT relative to incidence, Blacks by 22% in TCGA and 41% in CT, and Asians by 40% in TCGA and 10% in CT. Whites are overrepresented, by 8% in TCGA and 7% in CT. More men are in TCGA than women, in all R&E. Less than 25% of patients age < 50 relative to incidence are in TCGA, in all R&E. *BCL7A* is mutated more in Blacks age < 50 (n = 20, 50%) than Whites (n = 39, 10%) ($p < 0.01$). *FAT4* is mutated in Whites age 65+ (n = 31, 10%) but not Blacks. In all ages, *KRAS* is mutated more in Blacks than Whites (31-35% vs. 20-25%, $p < 0.05$). Black patients have lower survival than Whites ($p < 0.02$). In patients age 65+, *KRAS* mutation is associated with 10% lower 4.5-year survival. **Conclusions:** Substantial disparities in Black, Hispanic, women, and age representation exist for MM cases in TCGA and CT. This stratification by R&E and age offers new insight on BCL7A, FAT4, and KRAS mutation in MM. Mutation status is associated with survival in older patients. Equitable demographic representation should be pursued to improve quality of available data and access to medical resources for all populations. Research Sponsor: None.

Percent of All Demographic Incidence Represented in TCGA	All Ages (TCGA n=1065, NAACCR n=26843)	Age <50 (TCGA n=94, NAACCR n=1723)	Age 50-64 (TCGA n=441, NAACCR n=7749)	Age 65+ (TCGA n=418, NAACCR n=17371)
Asian Women	32%	2%	19%	43%
Asian Men	63%	6%	106%	18%
Black Women	54%	20%	53%	52%
Black Men	74%	9%	51%	114%
White Women	82%	21%	77%	93%
White Men	93%	25%	92%	107%
Hispanic Women	49%	2%	30%	92%
Hispanic Men	74%	2%	69%	112%

8044 **Poster Session**

Time to response, duration of response, and patient-reported outcomes (PROs) with daratumumab (DARA) plus lenalidomide and dexamethasone (D-Rd) versus lenalidomide and dexamethasone (Rd) alone in transplant-ineligible patients with newly diagnosed multiple myeloma (NDMM): Subgroup analysis of the phase 3 MAIA study.

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Background: In the phase 3 MAIA study, adding DARA to Rd improved progression-free survival (primary endpoint), overall survival, duration of response, and PROs in transplant-ineligible pts with NDMM. We report a MAIA subgroup analysis of time to response, duration of response, and PROs. **Methods:** Transplant-ineligible pts with NDMM received 28-day cycles of Rd (R 25 mg PO on Days 1-21; d 40 mg PO QW) ± DARA (16 mg/kg IV QW in Cycles 1-2, Q2W in Cycles 3-6, and Q4W thereafter) until disease progression or unacceptable toxicity. Secondary endpoints included time to response and duration of response. PROs were measured using the EORTC QLQ-C30, with treatment effects assessed via mixed-effects model with repeated measures. **Results:** In total, 368 pts were assigned to the D-Rd group and 369 pts to the Rd group; 162 (44%) D-Rd pts and 142 (38%) Rd pts had renal impairment (defined as baseline CrCl ≤60 mL/min). At a 56.2-mo median follow-up, median times to very good partial response or better (≥VGPR) and complete response or better (≥CR) were shorter with D-Rd vs Rd in the overall study population and in the subgroups of pts with and without renal impairment (Table). Among pts who achieved ≥CR or partial response or better (≥PR), higher proportions of D-Rd vs Rd pts had not experienced disease progression at 48 mo (Table). Among pts with renal impairment, greater improvements from baseline in pt-reported pain, fatigue, and nausea and vomiting symptom scores were observed with D-Rd vs Rd across most timepoints; a notably greater meaningful reduction in pain symptom score was seen with D-Rd vs Rd as early as Cycle 6 Day 1 (least squares mean change from baseline, −14.9 vs −7.0; *P*=0.0241). Analyses for additional pt subgroups will be presented. **Conclusions:** In transplant-ineligible pts with NDMM, D-Rd showed more rapid deep responses as well as more durable responses vs Rd, regardless of renal function. Improvements in pt-reported symptoms were generally greater with D-Rd vs Rd in pts with renal impairment. Our results support the use of D-Rd in transplant-ineligible pts with NDMM. Clinical trial information: NCT02252172. Research Sponsor: Janssen Research & Development, LLC.

	All Responders (≥PR)		Responders with Baseline CrCl >60 mL/min		Responders with Baseline CrCl≤60 mL/min	
	D-Rd	Rd	D-Rd	Rd	D-Rd	Rd
Time to response						
Median (range), mo						
≥CR	10.7 (1.0-46.7)	13.2 (2.8-54.6)	11.0 (1.0-41.9)	13.0 (2.8-47.9)	10.4 (3.0-46.7)	13.6 (5.6-54.6)
≥VGPR	3.0 (0.9-55.1)	4.7 (0.9-43.3)	3.0 (0.9-28.9)	4.7 (0.9-43.3)	2.9 (0.9-55.1)	4.9 (1.0-41.7)
Duration of response						
Estimated 48-mo event-free rate, % (95% CI)						
≥CR	81.8 (74.3-87.2)	57.8 (43.4-69.7)	82.2 (72.9-88.5)	55.3 (37.4-70.0)	81.0 (66.5-89.7)	61.5 (34.8-79.9)
≥PR	68.7 (63.1-73.5)	47.2 (40.8-53.3)	69.8 (62.4-76.0)	48.9 (40.8-56.5)	67.2 (58.5-74.5)	44.4 (34.1-54.3)

8045 **Poster Session**

African American patients with smoldering multiple myeloma may have a lower risk of progression compared to White patients.

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Background: The incidence of multiple myeloma (MM) is two to threefold higher in African Americans (AAs) compared to whites when adjusted for socioeconomics, age, and sex. However, there is limited information on whether racial background affects the risk of progression from smoldering MM (SMM) to MM. **Methods:** Patients with SMM presenting to Memorial Sloan Kettering Cancer Center between the years 2000 and 2019 and who identified as either AA or white were included in the study. Baseline characteristics were collected at the time of diagnosis including laboratory, imaging, and pathology reports. Differences in distributions of continuous and discrete characteristics were assessed by Kruskal-Wallis and chi-square tests. Time to progression (TTP) was assessed using the Kaplan-Meier method with log-rank test for comparisons. Univariate and multivariate Cox proportional hazard models were used to estimate effects of risk factors on TTP with hazard ratios (HR) and 95% confidence intervals (CI). **Results:** A total of 576 patients were included (70 were AA, 12%). Median follow-up time was 3 years in AAs and 4 years in whites. Differences in baseline characteristics between AAs and whites included median age (60 years in AAs vs 64 years in whites, $p = 0.01$), median hemoglobin level (12.3g/dL in AA vs 12.8g/dL in whites, $p = 0.02$), and immunoparesis including 1 or 2 uninvolved immunoglobulins (31% and 10% in AAs vs 56% and 27% in whites, $p = 0.002$). There was no difference in bone marrow plasma cells, M-spike, free light chain ratio, or Mayo-2018 SMM risk score. AA race was associated with a significantly decreased risk of progression in the univariate model (HR 0.57, CI 0.34-0.94). In the multivariate model adjusting for age, sex, and variables associated with an increased risk of progression in the univariate model (bone marrow plasma cells, M-spike, free light chain ratio, immunoparesis and low albumin), AA race remained associated with a decreased risk of progression (HR 0.39, CI 0.16-0.95). Overall, AA patients with SMM had a significantly ($p = 0.027$) longer median TTP (9.7 vs 6.2 years), and a lower 2-year (12.6% vs 20.1%) and 5-year (34% vs 44.6%) progression rate than whites. Because AA patients were younger at diagnosis, we stratified patients by age group, < 65 vs ≥ 65 years. In patients < 65 years, there was no difference in progression rate. In patients aged ≥ 65 years, AA patients continued to have a longer TTP than whites (9.8 vs 5.2 years, $p = 0.02$). **Conclusions:** In our retrospective single institution experience, AA patients with SMM had a lower risk of progression to MM compared to whites. Both groups had similar Mayo-2018 risk scores, however, AA patients had a lower degree of immunoparesis at baseline. Future studies are needed to better understand if these differences are explained by differences in disease biology including genomic mechanisms, immune microenvironment, and systemic immune response. Research Sponsor: None.

8046 **Poster Session**

A patient perspective on cure in multiple myeloma: A survey of over 1,500 patients.

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Background: As treatments advance in multiple myeloma (MM) and increasingly deeper and longer responses are achieved, the definition of what a cure is becomes increasingly relevant. While many physicians quote that patients may achieve a "functional cure", understanding the patient perspective on the concept of cure has yet to be explored. **Methods:** HealthTree Cure Hub by the HealthTree Foundation represents an online portal for patients with plasma cell dyscrasias to help navigate their disease. It is the largest single database of patients with multiple myeloma with over 10,200 patients as of January 2022. Using this platform, we surveyed patients online from November 11th 2021 to Feb 7th 2022. Varying scenarios incorporating toxicity, disease status, and being on/off treatment were presented, and participants were asked to rate them from 1-5, with 5 being an ideal cure. Patient awareness of the term functional or operational cure was also. **Results:** A total of 1525 participants completed the survey. Table lists characteristics of the patients who completed this survey. The majority of the patients were female (55.5%), college educated (88.5%) and non-Hispanic White (70.7%). Most patients rated being off treatment permanently and having no evidence of disease as a cure (1116/1469, 75.5%), with a median score of 5 amongst respondents, indicating an ideal version of cure. Continuing to take the same pill or injection with significant toxicity and no evidence of disease had a median score of 1, a score lower than either "continuing to take same pill or injection without significant toxicity even in the evidence of disease" (median score 2) or "stopping treatment permanently even with some detectable disease" (median score 2). The majority of patients (76.3%) reported being unfamiliar with the term functional or operational cure. **Conclusions:** In the first study of patients with plasma cell dyscrasias in which patients were asked about their perceptions of what a cure is, our results highlight that drug toxicity and being on treatment profoundly impacts patient's perception of cure. Furthermore, most patients are not familiar with the term functional or operational cure. Future efforts should recruit more diverse patient populations and incorporate patient preferences in approaches to defining cure in myeloma, as well as explaining cure in easily comprehensible terms to patients. Research Sponsor: None.

Participant characteristics.

		Number/Percentage of patients for which information available
Gender		1480, 97.0%
Female	821,55.5%	
Age, years, median (range)	66 (33–90)	1477, 96.9%
Race/ethnicity, no of patients (%)		1045, 68.5%
Non-Hispanic White	739,70.7%	
Hispanic	159, 15.2%	
Black	53, 5.1%	
Other	94,9.0%	
Education Status		1023, 67.1%
College degree or higher	905, 88.5%	
Disease Status		1351, 88.6%
Monoclonal gammopathy of undetermined significance	68, 5.0%	
Smoldering Myeloma	169, 11%	
Multiple Myeloma	1074, 79.5%	
Other	40, 3.0%	

8047 **Poster Session**

Evaluating serum-free light chain ratio as a biomarker for multiple myeloma.

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Background: In 2014, the definition of multiple myeloma was updated to include serum free light chain (FLC) ratio ≥100 as a myeloma defining biomarker, based on retrospective data indicating a 2-year progression rate of 80% and a median time to progression (TTP) of 12 months associated with this marker. However, two recent studies have reported lower 2-year progression rates, 30-44%, and longer median TTP of 40 months in patients with FLC ratio ≥100. Because of the disparity in risk prediction by FLC ratio across studies, we were motivated to assess the risk of progression in patients with SMM and a FLC ratio ≥100. **Methods:** We performed a retrospective analysis of patients diagnosed with SMM at Memorial Sloan Kettering Cancer Center between January 2000 and December 2017. Diagnosis of SMM and progression to MM was defined according to the International Myeloma Working Group (IMWG) criteria at the time of diagnosis. Kaplan-Meier method was used to assess TTP and generate survival curves, with log-rank test for comparison between groups. **Results:** A total of 438 patients were included in the study, with a median follow-up time of 52 months. While all patients with a FLC ratio ≥100 (n = 66) had elevated involved FLC levels, 35 (53%) had an involved FLC concentration > 100 mg/L. Per current diagnostic criteria, we only included patients with an involved FLC concentration > 100 mg/L in the FLC ratio ≥100 group, and found a median TTP of 31 months (95% confidence interval [CI] 16-59 months) and a 2-year progression rate of 49% (CI 28-63%). In a sensitivity analysis including all 66 cases with FLC ratio ≥100 (independent of involved FLC concentration), we found the median TTP to be 41 months (CI 30-72 months), compared to 101 months for those with a FLC ratio < 100 (CI 78-127 months; $p < 0.0001$). The risk of progression within 2 years was 35% (CI 22-46%) compared to 18% (CI 14-23%; $p < 0.0001$). Of note, 22 patients with a FLC ratio ≥100 were monitored expectantly for > 4 years, among whom 12 patients had an involved FLC level > 100 mg/L. Ten patients (7 with involved FLC level > 100 mg/L) were followed over a period ranging from 4 to 8.5 years before eventually progressing, and 12 patients (5 with involved FLC level > 100 mg/L) were followed between 4 and 8 years and did not progress during the study period. **Conclusions:** While FLC ratio ≥100 is associated with a high risk of progression in patients with SMM, it does not infer an imminent risk of progression, defined by the IMWG as median TTP of 12 months and 2-year progression rate of at least 80%. On the contrary, select patients with FLC ratio ≥100 can be followed for many years without progressing and some may never progress despite long-term follow-up. These findings suggest that in patients where FLC ratio ≥100 is the only myeloma-defining event, other high-risk features as well as the evolution of FLCs over time should be considered in the decision to start a patient on treatment. Research Sponsor: None.

8048 **Poster Session**

Retrospective review of outcomes of patients with multiple myeloma with COVID-19 infection (two-center study).

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Background: Coronavirus-2 has profound effects on patients (pts) with Multiple myeloma (MM). At the beginning of the pandemic, COVID-19 infection resulted an overall mortality around 54% (cook et al. BMJ 2020). Here, we report an updated morbidity and fatality for MM. **Methods:** After obtaining IRB approvals from each participating institute, retrospectively, between January 1, 2021 and August 30, 2021, we identified pts with MM and COVID-19 in two myeloma centers (Levine Cancer Institute (LCI) & the University of Kansas medical center (KUMC). **Results:** We identified 162 MM pts who had COVID-19 (LCI n=132, UKMC n=30), including 57% males, with median age of 64 years. Current or former smoking reported in 40% of pts. Most pts have associated comorbid conditions: hypertension (45%), hypogammaglobulinemia (32%), CKD (30%), DM (22%), obesity (16.6%), CHF (14%), and CAD (13.5%). Within 3 months prior to infection, treatment included immunomodulatory combinations in 35%, proteasome inhibitors in 28 %, and Daratumumab in 26.5%. Symptoms are summarized in table. 69% had Mild symptoms (no need for hospitalization), 20 % had moderate symptoms (requiring hospitalization), and 9.8% had severe symptoms (ICU level of care). The 18% of pts required oxygen: 6 pts required invasive oxygenation and 3 pts needed vasopressors. The 32% of pts had RRMM, 29.5% on maintenance, and 12% was getting induction. Regarding MM response: >VGPR in 45% and PD in 18%. The 78 pts had ASCT prior to COVID-19 infection: only 3 pts < 1 year and 3 pts < 6 months. MM response or ASCT did not affect hospitalization or mortality.The case fatality rate (CFR) was 6%. In the univariate analysis, CKD, DM, HTN and hepatic dysfunction were associated with an increased risk of hospitalization. However, in multivariate analysis, only CKD, hepatic dysfunction, and Hypogammaglobulinemia significantly increased the risk of admission with only age and lymphopenia were associated with increased COVID-19 related fatatlity. **Conclusions:** With implementation of center-specific disease control measures and universal screening, pts might have lower case severity and fatality rate than was initially reported. Research Sponsor: None.

Symptoms	Number	Frequency
Fatigue	90	56%
Cough	86	53%
Fever	65	40%
Shortness of breath	61	38%
Myalgias	48	30%
Headache	40	25%
Rhinorrhea	29	18%
Diarrhea	25	15%
Nausea	20	12%
Anosmia	14	9%
Abdominal pain	12	7%
Confusion	11	7%
Diaphoresis	11	7%
Weight loss	5	3%
Asymptomatic	46	28%

8049 **Poster Session**

Kinetics of humoral immunodeficiency with bispecific antibody therapy in multiple myeloma.

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Background: Bispecific antibodies (bsAb) are a promising class of therapeutics in RRMM. While hypogammaglobinemia (HGG) is anticipated due to plasma cell depletion, there is a lack of information about the degree of secondary immunodeficiency and resultant infectious complications. We investigated the kinetics of HGG in patients with RRMM on bsAb therapy. **Methods:** We identified and followed 42 patients treated on early clinical trials of bsAb at our institution between 2019 and 2021. Serial immunoglobulin levels and infections were obtained from the start of therapy until last follow up or 3 months after study exit. **Results:** 49 treatment courses were included from 42 individual patients. All patients were triple class exposed with a median of 5 prior lines of therapy. The median age was 67 (44-85) years, with 49% females. African Americans accounted for 18% of patients. 96% of patients had at least one prior ASCT. 90% of patients received bsAb targeting BCMA including 7 patients who received more than one line of BCMA targeting therapies. At a median follow up 9.5 (0.9-28.6) months, 40.8% of patients remained on bsAb therapy. At the start of therapy, the median IgG, IgA, and IgM levels were 560 (44-9436), 15 (5-3886) and 6 (5-64) mg/dL, respectively and 50% of patients had severe HGG (≤400mg/dl). Serum IgG levels reached a nadir at 3 months while, IgA and IgM at 1 month, from the start of therapy. The median nadir levels of IgG were 159 (40-2996) mg/dL, while it was < 5 mg/dL for both IgA and IgM. IgG levels were below the detectable range (< 40 mg/dl) in 28% of patients at some point during therapy. IgA and IgM were also below the detectable range (< 5 mg/dl) in 50% and 60% of patients, respectively. At last follow-up, the median IgG levels were 444 (40-1860) mg/dL and IgA 5 (5-254) mg/dL and IgM 5 (5-44) mg/dL. Additionally, 38% of patients remained severely hypogammaglobinemic. 57% (24/42) of patients received IVIG supplements in the current series. About 71% of patients had at least one infectious event and the cumulative incidence of infections progressively increased with increasing duration of therapy with risk at 3, 6, 9 12, 15 months being 41%, 57%, 64%, 67% and 70%, respectively. Among these, 54% of infection were bacterial. Viral infection accounted for 41% of infections. A third of patients had new infectious events during the first 90 days following stopping bsAb treatment. 57% (8/14) of patients did not mount a response to the primary COVID19 immunization series. Among the five patients with repeat antibody titers after the booster dose, 50% were still not able to mount an antibody response. **Conclusions:** bsAb therapy in RRMM can be associated with profound and prolonged HGG. The cumulative risk of infection correlated with the degree of HGG and progressively increases with treatment and persisted months after being off therapy. Additionally, an impaired antibody response to the COVID-19 immunization series was also noted. Research Sponsor: None.

8050 **Poster Session**

The association of agent orange (AO) exposure with monoclonal gammopathy of undetermined significance (MGUS) to multiple myeloma (MM) progression: A population-based study.

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Background: With limited evidence from a single center study [n=211 (11 with AO exposure)] reporting AO exposure as a risk factor for transformation, whether or not AO exposure increases the rate of transformation from MGUS to MM is unclear. Thus, we aimed to conduct a nation-wide study to determine the association between AO exposure and the risk of MGUS to MM progression. **Methods:** A retrospective, matched cohort study using data from the U.S. Veterans Health Administration system was conducted. Based on a power calculation, a random sample of MGUS patients with AO exposure was selected and 1:1 matched to those with MGUS without AO exposure (matching factors: age at MGUS diagnosis, race, body mass index categories). Data abstraction confirmed MGUS and MM diagnoses. In addition, information on date of diagnosis, MGUS subtype, and monoclonal protein (M-protein) values was performed. Patients were considered to have MGUS if they had M-protein detected on serum protein electrophoresis (SPEP) with immunofixation confirmation. The association of AO exposure with progression from MGUS to MM was examined using a multivariable Fine-Gray subdistribution hazard model with death as the competing event. The covariates included M-protein at MGUS diagnosis (>1.5, ≤1.5 g/dL [reference]), MGUS subtype (Immunoglobulin A, light chain, and Immunoglobulin G [reference]), and Charlson comorbidity score at MGUS diagnosis. A sensitivity analysis was conducted using inverse probability treatment weighted survival analysis to evaluate the robustness of the conclusion. **Results:** After excluding individuals with no confirmed MGUS or M MGUS subtype, a total of 563 MGUS patients with AO exposure and 563 matched controls were included. No statistically significant difference was observed in the progression of MGUS to MM between the AO exposed group and control group (adjusted hazard ratio (aHR) 0.78, 95% confidence interval (CI) 0.53 to 1.17). The sensitivity analysis demonstrated consistent results. **Conclusions:** Our carefully designed study does not show an association between AO exposure and progression of MGUS to MM in a national cohort of Veterans. Research Sponsor: U.S. National Institutes of Health.

Multivariable analysis of progression of MGUS to MM.

Parameter	Hazard Ratio	95% Confidence Interval	P-value
AO Exposure	0.78	0.53-1.17	0.23
M-protein >1.5 g/dL	16.29	5.86-45.27	<0.0001
Immunoglobulin A MGUS	1.09	0.58-2.06	0.79
Light Chain MGUS	5.57	1.45-21.41	0.01
Comorbidity	0.99	0.91-1.08	0.78

8052 **Poster Session**

Daratumumab (DARA) in combination with bortezomib plus dexamethasone (D-Vd) or lenalidomide plus dexamethasone (D-Rd) in relapsed or refractory multiple myeloma (RRMM): Subgroup analysis of the phase 3 CASTOR and POLLUX studies in patients (pts) with early or late relapse after initial therapy.

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Background: High-risk multiple myeloma (MM) is often defined based on cytogenetic abnormalities (ie, t[4;14], t[14;16], and/or del17p); however, pts who relapse early (12-18 months) after initial therapy are considered a functional high-risk group that is also associated with poor prognosis. DARA, a human IgGκ monoclonal antibody targeting CD38, is approved in combination with standard-of-care regimens for MM. In the phase 3 CASTOR and POLLUX studies, D-Vd and D-Rd significantly improved progression-free survival (PFS), regardless of cytogenetic risk, and achieved higher rates of complete response or better (≥CR) and minimal residual disease (MRD)–negativity vs Vd or Rd alone in pts with RRMM. Post hoc analyses of CASTOR and POLLUX evaluated D-Vd vs Vd and D-Rd vs Rd in pt subgroups with 1 prior line of therapy based on timing of relapse (early or late) after initiation of the first line of therapy. **Methods:** In CASTOR and POLLUX, pts with RRMM and ≥1 prior line of therapy were randomized to D-Vd/Vd or D-Rd/Rd, respectively. The primary endpoint was PFS. In this analysis, the early relapse subgroup included pts with 1 prior line of therapy who relapsed <18 months after initiating their first line of therapy; pts with 1 prior line of therapy who relapsed ≥18 months after initiating their first line of therapy were included in the late relapse subgroup. **Results:** 49 and 186 pts from CASTOR and 99 and 196 pts from POLLUX were included in the early relapse and late relapse subgroups, respectively. Median follow-up was 72.6 months (CASTOR) and 79.7 months (POLLUX). PFS consistently favored the DARA-containing regimens across subgroups (Table). In CASTOR, ≥CR rates were higher with D-Vd vs Vd in the early relapse (21% vs 17%; $P = 0.7360$) and late relapse (51% vs 14%; $P < 0.0001$) subgroups. In POLLUX, ≥CR rates were higher with D-Rd vs Rd in the early relapse (53% vs 12%; $P < 0.0001$) and late relapse (62% vs 38%; $P = 0.0012$) subgroups. MRD-negativity rates (10^{-5}) were higher with D-Vd/D-Rd vs Vd/Rd regardless of relapse timing (CASTOR: early, 13% vs 0%; $P = 0.1476$; late, 23% vs 3%; $P < 0.0001$; POLLUX: early, 30% vs 4%; $P = 0.0006$; late, 34% vs 14%; $P = 0.0009$). **Conclusions:** These post hoc analyses of CASTOR and POLLUX showed PFS and depth of response benefits of DARA-containing regimens in patients with 1 prior line of therapy, regardless of relapse timing (early or late). Our results support the use of D-Vd and D-Rd in RRMM, including in pts who are considered functional high risk. Clinical trial information: NCT02136134 and NCT02076009. Research Sponsor: Janssen Research & Development, LLC.

Median PFS, months	D-Vd	Vd	HR (95% CI); *P* value	D-Rd	Rd	HR (95% CI); *P* value
Early relapse	15.4	9.0	0.51 (0.26-1.00); $P = 0.0488$	36.9	11.7	0.41 (0.26-0.65); $P = 0.0002$
Late relapse	27.7	7.9	0.20 (0.14-0.29); $P < 0.0001$	69.3	29.7	0.53 (0.37-0.77); $P = 0.0007$

8053 **Poster Session**

Outcomes for transplant-eligible, newly diagnosed Black patients (Pts) with multiple myeloma (MM): The Levine Cancer Institute (LCI) experience.

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Background: Studies have revealed disparities for Black (B) pts with MM, including more advanced disease at presentation, delayed therapy with novel agents such as immunomodulatory drugs (IMIDs) and proteasome inhibitors (PIs), reduced access to autologous stem cell transplant (ASCT), and under-representation in clinical trials. However, B pts tend to be younger at diagnosis and less likely to harbor high risk disease biology, suggesting outcomes could be better relative to their White (W) counterparts. To better understand outcomes by race in the setting of more optimal treatment access, we pursued a retrospective analysis of pts treated at LCI undergoing ASCT as part of first line therapy. **Methods:** 255 pts (181 W pts, 74 B pts) transplanted between 3/2014 – 12/2018 were included. Analysis was restricted to pts with MM who underwent a single ASCT as part of first line therapy. Pts with < 1 year of follow-up and no overall survival (OS) events were excluded. Proportions were compared between groups with Fisher's exact tests; OS and progression free survival (PFS) were evaluated with Kaplan Meier methods and compared between groups with log-rank tests. **Results:** Median follow-up for B and W pts was 5.0 yrs (0.9 – 7.8 yrs) and 4.1 yrs (0.5 – 8.0 yrs). At initial presentation, median age was 59 yrs (24 – 76 yrs) and 61 yrs (35 – 78 yrs, P= 0.038), anemia was present in 81.3% and 64.6% (P= 0.020), renal impairment in 41.3% and 33.1% (P= 0.335), and high-risk cytogenetics [gain 1q21, t(4;14), t(14;16) or del(17p)] in 25.4% and 35.9% (P= 0.162) of B and W pts, respectively. Median time from diagnosis to ASCT was 0.6 yrs (0.3 – 2.4 yrs) and 0.5 yrs (0.3 – 2.0 yrs) for B and W pts. 35.2% of all B pts and 43.9% of all W pts treated at LCI during the study period underwent ASCT (48.3% and 64.4% of pts ≤70 yrs of age, P= 0.002), while 63.5% and 80.1% received PI/IMID-based induction therapy (P= 0.009) and 90.5% and 93.4% received maintenance therapy post-ASCT (P= 0.438), respectively. Although ≥very good partial responses were achieved in fewer B pts than W pts after induction (65.8% and 80.7%,(P= 0.014), there was no difference after ASCT (95.8% and 93.9%, P= 0.759). Median PFS was 5.9 yrs (95% CI 3.4 – 6.6) and 3.6 yrs (95% CI 3.0 – 4.5) for B and W pts (P= 0.039). Median OS trended in favor of B pts (P= 0.163) with 5-year OS of 83.0% (95% CI 71.2% - 90.3%) and 74.2% (95% CI 65.8% - 80.9%), respectively. **Conclusions:** Despite disparities in optimal induction therapy, Black pts with MM who underwent frontline ASCT enjoyed better PFS relative to W pts. Optimizing access to PI/IMID-based induction therapy and ASCT will be necessary to further improve OS. Research Sponsor: None.

8054 **Poster Session**

Randomized phase II trial of bortezomib, lenalidomide, dexamthasone with/without elotuzumab for newly diagnosed, high risk multiple myeloma (SWOG-1211).

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Background: The introduction of immunomodulatory agents, proteasome inhibitors, and autologous stem cell transplantation (ASCT) has improved outcomes for patients with multiple myeloma (MM), but those with high risk MM (HRMM) have a poor long-term prognosis. Herein we provide survival outcomes on the first randomized trial in newly diagnosed HRMM, S1211, to follow-up on the previously reported progression-free survival (PFS) (NCT01668719, Usmani SZ et al, Lancet Haem 2021). **Methods:** S1211 is a randomized phase II trial comparing 8 cycles of lenalidomide, bortezomib and dexamethasone (RVd) induction followed by dose-attenuated RVd maintenance until disease progression with or without elotuzumab (RVd-Elo). Stem cell collection was allowed, but ASCT was deferred until progression. HRMM was defined by one of the following: gene expression profiling high-risk (GEP^{hi}), t(14;16), t(14;20), del(17p), amplification 1q21, primary plasma cell leukemia (pPCL), or elevated serum LDH (> 2X ULN). Median PFS was the primary endpoint, using a one-sided stratified log-rank test at a one-sided significance level of 0.1. Secondary endpoints included overall response rate (ORR), adverse events (AE), serious adverse events (SAE) and OS. Response was assessed using the IMWG 2009 criteria. **Results:** S1211 enrolled 103 evaluable patients, RVd n=54, RVd-Elo n=49. 74% had ISS II/III, 48% amp1q21, 38% del(17p), 11% t(14;16), 9% GEP^{hi}, 7% pPCL, 5% t(14;20) and 4% elevated LDH (17% >1 feature). With median follow-up of 72 months (mos.), no difference in median PFS was observed [RVd-Elo=29 mos., RVd= 34 mos., HR = 1.11 (80% CI=0.82, 1.49, p=0.66]. No difference in OS was observed [RVd-Elo = median not reached (NR), RVd= 68 mos., HR = 0.85 (80% CI: 0.59, 1.23), p-value = 0.58]. 76% pts had >Grade 3 AEs, no differences in the safety profile were observed. Amongst patients with gain/amp 1q21, median PFS was [RVd-Elo=31 mos., RVd= 37 mos., HR = 1.48 (80% CI= 0.95, 2.31), p=0.25], median OS was [RVd-Elo = 61 mos., RVd= 68 mos., HR = 1.23 (80% CI: 0.72, 2.10), p-value = 0.63]. In patients with del(17p), median PFS was RVd-Elo=41 mos., RVd= 30 mos.[HR = 0.98 (80% CI= 0.60, 1.58), p=0.95], median OS RVd-Elo = NR, RVd= 72 mos., [HR = 0.77 (80% CI: 0.40, 1.48), p-value = 0.61]. **Conclusions:** In the first randomized HRMM study reported to date, the addition of Elo to RVd induction and maintenance did not improve PFS and OS with a median follow-up of 6 years. Although the median PFS for Del17p subgroup on RVd-Elo arm is higher than RVd, it did not achieve statistical significance. The PFS and OS observed for gain/amp 1q21 and del17p in the RVd control arm may serve as important benchmarks for future enrichment design HRMM clinical trials. The PFS and OS in both arms of the study exceeded the original statistical assumptions and support the role for PI/IMiD combination induction/ maintenance therapy for this population. Clinical trial information: NCT01668719. Research Sponsor: U.S. National Institutes of Health.

8055 **Poster Session**

Myeloma developing regimens using genomics (MyDRUG) trial: Results from the RAS mutation targeting arm.

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Background: Multiple myeloma (MM) is characterized by somatic mutations involving cancer-associated genes. The most commonly mutated genes are N- and K-Ras, which increase in prevalence as the disease progresses. Case reports and retrospective data suggest efficacy of targeting the MAPK pathway in N/K-Ras mutated MM. The MyDRUG trial was initiated to explore the efficacy of specific molecularly-targeted therapies in combination with standard therapies in MM. **Methods:** MyDRUG (NCT03732703) is a genomically-guided umbrella trial for patients with functional high-risk MM, defined as early relapse following primary therapy (3 years for transplant with maintenance, 18 months without), with specific genetic abnormalities. Subjects undergo molecular profiling of their MM cells and are assigned to a targeted arm if a variant allele frequency (VAF) over 25% is identified. The targeted mutated genes and respective agents (approved for non-MM indications and with a known phase 2 dose) are: KRAS/NRAS/BRAF (cobimetinib), FGFR3 (enasidenib), IDH (erdafitinib), CDKN2C (abemaciclib), *t*(11;14) (venetoclax). Patients receive the investigational drug for 2 cycles as a single agent followed by addition of an active MM combination (ixazomib, pomalidomide and dexamethasone, IPd). Limited dose escalation was performed with the single agent followed by dose assessment in combination with IPd. Here we present the results of the dose escalation portion of C1 arm exploring cobimetinib in patients with N/K-RAS or BRAF mutations. Cobimetinib was administered at 40 mg daily in combination with standard doses of IPd. **Results:** Eleven subjects with BRAF/RAS mutations were screened between August 2019 and October 2020, with 4 screen failures. Seven were enrolled, 5 males, median age 65 years, and median time from diagnosis of 30 months. N-RAS, K-RAS or BRAF mutations were seen in 4, 2, and 1 subject(s), respectively, with VAF ranging from 33-93%. Median number of prior lines of therapy was 1 (1-3), 3 patients had extramedullary disease, and 1 patient had high risk cytogenetics. Median duration of therapy was 12 months. One patient was not evaluable for dose limiting toxicity. All but 1 patient had at least one cycle delayed due to adverse events (AEs), but no dose reductions were required. No dose limiting toxicities were observed across the cycles, either during single agent therapy (Cycles 1-2) or in combination with IPd (Cycles 3 and 4). Six patients responded to therapy (4 PR, 2 VGPR). One patient was not response evaluable. Fatigue was the most common non-hematological AE followed by diarrhea. **Conclusions:** Here we report on the feasibility of genomically-guided, precision medicine therapy in K/N-RAS/BRAF-mutated MM. The MEK inhibitor cobimetinib in combination with IPd appears safe in functionally high-risk patients. Ongoing study will provide more information regarding the efficacy of this approach. Clinical trial information: NCT03732703. Research Sponsor: The Multiple Myeloma Research Foundation.

8056 **Poster Session**

Clinicopathological characteristics of high-risk multiple myeloma in Hispanic versus non-Hispanic patients in central California.

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Background: Roughly 37% of Multiple Myeloma (MM) patients in the U.S. are non-white minorities. Advanced stage at diagnosis and specific cytogenetic abnormalities are associated with high-risk disease and poor prognosis. Few studies evaluated these risk factors in ethnic minorities. To further investigate, we analyzed ethnic variations in characteristics and outcomes of high-risk MM patients who were treated at our institution in Fresno, CA (49.6% Hispanic population). **Methods:** Patients diagnosed with high-risk MM at Community Medical Centers from 1-1-2011 to 12-31-2020 were included. High risk was defined by Mayo Clinic mSMART 3.0 classification. Demographic and disease-relevant information were collected. Cytogenetics, R ISS stage, 1st line treatment (doublet vs triplet), and treatment response (IMWG response criteria) were evaluated. Hispanic and non Hispanic comparisons were made by Fisher's exact test where appropriate. Progression Free Survival (PFS) and Overall Survival (OS) were evaluated by Kaplan-Meier estimates and compared via log-rank test. Univariate cox proportional hazard model for survival was used to examine the association of variables with mortality risk after 1st line therapy. **Results:** 147 MM patients were screened. 42 high risk patients were identified: 11 (26%) Hispanic, 31 (74%) non Hispanic (22 white, 8 African American, 1 East Indian). Median age at diagnosis was 65. 26 (61%) were females. 25 (59%) were R ISS stage 3. Hispanic vs non Hispanic median income was $46119 vs $65080 (p=0.035). 6 Hispanics had Medi-Cal insurance vs 2 non-Hispanics (54.6% vs 6.5%, p=0.003). More Hispanics had Lambda light chain disease (73% vs 26%; p=0.01). 13 non Hispanics had del 17p vs 0 Hispanics (p=0.009). 40/42 patients (95%) received triplet therapy. 4 Hispanics received ASCT vs 9 non Hispanics (40% vs 33.3%, p=0.716). Hispanics and non Hispanics did not have significantly different treatment responses per IMWG criteria (p=0.799). No significant difference in PFS was seen between Hispanics and non Hispanics (805 vs 793 days; p=0.089); OS was better in Hispanics (1062 days vs 453 days; p=0.008). Per univariate cox proportional Hazard model, female sex (HR 4.34) and age (HR 1.05) were associated with higher mortality while Hispanic ethnicity was associated with lower mortality (HR 0.19). **Conclusions:** Hispanic and non Hispanic high risk MM patients differed significantly in median income, insurance, and del 17p incidence. These did not translate to a difference in 1st line therapy or treatment response. OS in our study is higher in Hispanic high-risk MM patients compared to other ethnicities and warrants further investigation. Research Sponsor: None.

	Total*	Hispanic	Non Hispanic	Fisher's Exact
t(4;14)	8	3	5	0.412
t(14;16)	3	1	2	0.999
t(14;20)	0	0	0	-
1q gain	19	6	13	0.504
p53 Mutation	6	1	5	0.999
Del 17p	13	0	13	**0.009**
R ISS				0.280
Stage 1	4	2	2	
Stage 2	13	2	11	
Stage 3	25	7	18	

*Includes patients with >1 abnormality.

8057 **Poster Session**

Impact of second primary malignancy post-autologous hematopoietic stem cell transplantation on outcomes of multiple myeloma: A CIBMTR analysis.

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Background: Following autologous hematopoietic stem cell transplant (auto HCT), maintenance therapies improve survival, reduce relapse risk in multiple myeloma (MM), and are the *de facto* standard-of-care. However, clinical trials have shown an increased risk of second primary malignancies (SPM) with maintenance therapy, including second hematological malignancies (SHM). We examined data from the Center for International Blood and Marrow Transplant Research (CIBMTR) registry to evaluate the impact of SPM on progression-free (PFS) and overall survival (OS) and the utilization of allogeneic HCT in patients with therapy-related myeloid neoplasms (t-MN). **Methods:** Adult patients (pts) with MM who underwent first auto HCT in the United States with a melphalan conditioning regimen from 2011-2018 and subsequently received maintenance therapy were included (N=3948). The primary endpoint of interest was the impact of SPM and SHM on OS. Multivariate analytic (MVA) modelling was applied, accounting for competing risks while integrating significant covariates to determine the impact of SPM on PFS and OS. Finally, we studied the utilization and survival following allogeneic HCT for SHM. **Results:** Baseline characteristics were similar between the two groups. Maintenance regimens used were lenalidomide (2836, 72%), bortezomib (370,9 %) or lenalidomide + bortezomib (372, 9%) based combinations. At a median follow up of 37 months, 175 (5%) pts developed SPM, including 112 (64%) solid 36 (21%) myeloid, and 27 (15%) lymphoid cancers. In MVA, the development of SPM and SHM was associated with an inferior PFS (HR 2.62, $P<0.001$ and HR 5.01, $P<0.001$, respectively) and OS (HR 3.85, $P<0.001$ and 8.13, $P<0.001$, respectively). The two commonest causes of death were MM (42%) and SPM (30%) for those developing SPM. Similarly, MM (53%) and SHM (18%) were the two commonest causes of death for those developing SHM. Nine (14%,5 t-MDS and 4 t-AML) of 63 patients with SHM underwent an allogeneic HCT. Patients undergoing allogeneic HCT were more likely to have Karnofsky score ≥90 (100% *vs.* 50%, $P=0.02$) compared to those who did not. One year survival from allo SCT was 66.7% (CI 34.6-92%). **Conclusions:** The three-year cumulative incidence of SPM was 3.3 (2.6-4)% in this large contemporaneous CIBMTR cohort. Disease relapse remains the primary cause of death in MM patients who develop SPM or SHM. Given the median OS for MM is now > 10 years, longer follow-up is needed to assess the SPM and SHM risks with maintenance therapy post-auto HCT. Research Sponsor: U.S. National Institutes of Health.

8058 **Poster Session**

Early intervention for high-risk and low-risk of progression for patients with smoldering multiple myeloma.

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Background: Previous studies have observed smoldering multiple myeloma (SMM) patients with a biomarker criteria of > 20% bone marrow plasma cells, > 2 g/dL M protein spike, and > 20 free light chain ratio, also known as 20/2/20, are at a higher risk of progressing to multiple myeloma (MM) than others. These findings have ignited interest in pursuing early intervention for these high-risk patients. However, we asked if early intervention would be beneficial for all SMM patients regardless of the progression risk level. **Methods:** We utilized real-world data from HealthTree Cure Hub for Multiple Myeloma to first, determine whether 20/2/20 resulted in a higher risk of progression and second, analyze whether early intervention delayed progression from SMM to MM. A 2-sample t-test was used to compare 20/2/20 to non-20/2/20 patients, as well as in the comparison between SMM patients who received early intervention with treatment to without early intervention. **Results:** We found that patients who met at least two of the criteria of 20/2/20 had a tendency to progress to MM 35% faster than patients who did not meet the criteria ($n = 36$, p-value < 0.10). While not significant, it's still worth noting that there is a difference in the mean time to progression for these patients. Next, we found SMM patients who do not receive early intervention with treatment develop MM two times faster than those who do receive early intervention with treatment, regardless of progression risk level ($n = 129$, p-value < 0.001). **Conclusions:** Our results revealed that at least two of the biomarker criteria could aid in the identification of patients with a higher risk of progression. However, a casual approach of "sit and wait" for patients to develop 20/2/20 is not warranted since our findings revealed that all SMM patients benefited from treatment intervention regardless of the progression risk level. Research Sponsor: None.

8059 **Poster Session**

Analysis of long-term outcomes in R-ISS stage 2 multiple myeloma with and without the presence of high-risk cytogenetics.

Nisha Joseph, Craig C. Hofmeister, Leonard T. Heffner, Vikas Anand Gupta, Lawrence Boise, Jonathan L. Kaufman, Madhav V. Dhodapkar, Sagar Lonial, Ajay K. Nooka; Emory University, Winship Cancer Institute, Atlanta, GA; Winship Cancer Institute of Emory University, Atlanta, GA; Winship Cancer Institute, Emory University, Atlanta, GA; Yale School of Medicine, New Haven, CT

Background: The Revised International Staging System (R-ISS) is the current standard for risk-stratification of newly diagnosed myeloma (NDMM), incorporating albumin and β2M with high-risk cytogenetics and/or elevated LDH. (Palumbo et al, JCO 2015) R-ISS stage 2 represents a heterogeneous cohort including myeloma with and without high-risk cytogenetics, a known poor prognosticator. Here, we present a retrospective analysis on outcomes of R-ISS stage 2 NDMM utilizing our institutional database of patients treated at the Winship Cancer Institute of Emory University. **Methods:** From January 2007 to August 2016, 1,000 consecutive newly diagnosed myeloma patients treated with RVD induction therapy were identified. Demographics, clinical characteristics, and outcomes data for the patients were obtained from our institutional review board-approved myeloma database. Responses were evaluated per IMWG Uniform Response Criteria. **Results:** The median age of this cohort was 61 years (range 16-83). Other notable patient characteristics include: M/F 54.6%/45.4%, W/AA 61.8%/35.9%; ISS I/II/III 45.8%/30.8%/23.4%. R-ISS I/II/III 39.9%/48.7%/11.5%; Isotype IgG/IgA/FLC 59.2%/19.0%/15.7%; standard risk (SR)/high risk (HR) 71.2%/15.8%. ISS data was available for 75% of patients; R-ISS was available for 41% of patients. HR disease was defined as the presence of t(4;14), t(14;16), del(17p), and/or complex karyotype by conventional metaphase cytogenetics. Frequency of specific CTG abnormalities were 2.8% with t(14;16), 10% with del(17p), and 4.8% with t(4;14). With a median follow up of 88.4 months, the median PFS (mPFS) for the entire cohort was 68.7 months (95% CI 61.8-75.5) and the median OS was 128.9 months. The median PFS for HR vs SR patients was 42.4 months (95% CI 35.7-48.9) vs 80.3 months (95% CI 72.8-87.8). The median OS for SR patients was not reached, and for HR patients was 86.6 months (95% CI 70.1-103.1). The mPFS for R-ISS 1,2 and 3 was 95.4 months (95% CI 73.4-117.5), 56.6 months (95% CI 44.4-68.7), and 31.1 months (95% CI 16.3-45.9). When the R-ISS 2 cohort was divided into those without HR CTG and with HR CTG, the mPFS was 67.1 months (95% CI 53.3-80.8) versus 40.2 months (95% CI 30.1-50.3), respectively. The mOS for R-ISS I/II/III was NR, 122.7 months (95% CI 101.6-143.9), and 60.6 months (95% CI 11.6-109.5). For R-ISS 2 without and with HR CTG, the mOS was 129.1 months and 94.8 months (95% CI 61.3-128.3), respectively. **Conclusions:** The R-ISS is a validated risk model clearly defining three distinct groups in terms of long-term outcomes. However, these data suggest R-ISS stage 2 can further be characterized into two distinct groups based on the presence or absence of high risk cytogenetics. R-ISS 2 with HR-CTG portends both inferior mPFS and increased risk of death when compared to R-ISS 2 without HR-CTG (HR 2.63 versus HR 1.65), and behaves more similarly to R-ISS 3 disease. Research Sponsor: None.

8060 **Poster Session**

Retrospective, single-center, real-world experience of belantamab mafodotin in relapsed/refractory multiple myeloma.

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Background: Belantamab mafodotin (belamaf) is a BCMA antibody drug conjugate approved for the treatment of relapsed refractory multiple myeloma (RRMM) patients (pts) based on the pivotal phase 2 DREAMM-2 study (Lonial et al, *Lancet Oncology*, 2019), which demonstrated an overall response rate (ORR) of 32%, median progression free survival (PFS) of 2.8 months, and overall survival (OS) of 13.7 months in triple class (proteasome inhibitor, IMiD, and anti-CD38) refractory (TCR) MM. In this single-center retrospective study, we report the efficacy and safety of belamaf in RRMM pts administered in a real-world, standard of care (SOC) setting. **Methods**: All MM pts who initiated therapy with SOC belamaf, either as monotherapy or in combination, between 11/1/2020 and 11/30/2021 at MD Anderson were included in this study. Response and progression were evaluated using International Myeloma Working Group standard criteria. Keratopathy and best corrected visual acuity (BCVA) adverse events (AEs) were graded per the Keratopathy and Visual Acuity (KVA) scale. The Kaplan-Meier method was used to estimate time to event endpoints. **Results**: A total of 39 consecutive pts with a median of 7 prior lines of therapy were included in the analysis, of whom 37 pts (95%) received single agent belamaf. Median age was 66 years (range 39-89), 14 of 37 (38%) pts with available FISH had high risk disease (del 17p, t(4;14, and/or t(14;16)), 14 pts (36%) had extramedullary disease, 37 (95%) pts were TCR, 32 (82%) pts were TCR and alkylator-refractory, and 8 pts (21%) were BCMA-refractory. Notably, the majority (69%) of pts in this analysis would have been ineligible for the DREAMM-2 trial based on key eligibility criteria. Median number of belamaf doses administered was 2 (range 1-9). Among 37 pts with measurable, response evaluable baseline disease, the best ORR (≥ PR) was 27% with ≥ VGPR of 3%. The clinical benefit rate (≥ MR) was 35%. Among 8 BCMA-refractory pts, there was 1 PR and 1 MR. Median PFS was 1.8 months and median OS was 9.2 months with a median follow-up of 10.1 months. Median duration of response has not been reached among 10 responding pts. Among 33 pts with a post-treatment ocular exam, 25 pts (76%) developed any grade keratopathy (Grade 1/2/3/4, 9%/55%/12%/0%, respectively) and BCVA changes (Grade 1/2/3/4, 42%/27%/6%/0%, respectively). Median time to first keratopathy or BCVA AE was 1.3 months. The most common reasons for treatment discontinuation were disease progression (75%) and AEs (9%). **Conclusions**: Our current study in heavily pretreated RRMM pts, of whom the majority would have been ineligible for the DREAMM-2 study, demonstrates an ORR, PFS, and ocular AE profile with SOC belamaf therapy comparable to outcomes reported in the pivotal registration study. Future studies are needed to further define the optimal use and sequencing of belamaf in MM pts, particularly in context of other BCMA-targeting modalities. Research Sponsor: None.

8061 **Poster Session**

Updated survival with extended follow-up on patients with newly diagnosed multiple myeloma treated with lenalidomide, bortezomib, and dexamethasone (RVD) induction therapy and a risk-stratified maintenance approach.

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Background: Lenalidomide, bortezomib, and dexamethasone (RVD) has been established as an effective and well-tolerated induction regimen in patients with newly diagnosed myeloma (NDMM). We have previously published a retrospective analysis of 1000 patients treated with RVD and risk-stratified maintenance therapy showing a median PFS of 65 months and median OS of 126 months for the entire cohort (Joseph et al, *JCO* 2020). This data has served as an important benchmark for evaluating upfront treatment strategies in NDMM. Here, we present updated survival data with extended follow up on this patient population treated at the Winship Cancer Institute of Emory University. **Methods:** From January 2007 to August 2016, 1000 consecutive newly diagnosed myeloma patients treated with RVD induction therapy (R-25 mg/day on days 1-14, V-1.3 mg/m2 on days 1,4,8,11 and D-40 mg once/twice weekly as tolerated) were identified. Demographics, clinical characteristics, and outcomes data for the patients were obtained from our institutional review board-approved myeloma database. Responses were evaluated per IMWG Uniform Response Criteria. **Results:** The median age of this cohort was 61 (range 16-83). Other notable patient characteristics include: M/F 54.6%/45.4%, W/AA 61.8%/35.9%; ISS I/II/III 45.8%/30.8%/23.4%. R-ISS I/II/III 39.9%/48.7%/11.5%; Isotype IgG/IgA/FLC 59.2%/19.0%/15.7%; standard risk(SR)/high risk (HR) 71.2%/15.8%.. High risk disease was defined as the presence of t(4;14), t(14;16), del(17p), and/or complex karyotype by conventional metaphase cytogenetics. 81.8% of patients underwent ASCT, with 16.8% having deferred ASCT. 75.3% of patients were initiated on maintenance therapy. With a median follow up of 88.4 months, the median PFS for the entire cohort was 68.7 months (95% CI 61.8-75.5) and the median OS was 128.9 months. The median PFS for HR patients was 42.4 months (95% CI 35.7-48.9), and the median PFS for SR patients was 80.3 months (95% CI 72.8-87.8). The median OS for SR patients was not reached, and for HR patients was 86.6 months (95% CI 70.1-103.1). **Conclusions:** Updated analysis with long-term follow up of this database of 1000 NDMM patients treated with RVD continues to demonstrate that, in combination with a risk-stratified maintenance strategy, RVD delivers durable remissions and impressive long-term outcomes. This study remains the largest cohort of patients treated with RVD reported to date, and continues to show the efficacy of this upfront treatment approach in newly diagnosed myeloma. Research Sponsor: None.

8062 **Poster Session**

Clinical features of patients with multiple myeloma harboring t(4;14) and impact on long-term survival.

Nisha Joseph, Craig C. Hofmeister, Leonard T. Heffner, Vikas Anand Gupta, Jonathan L. Kaufman, Madhav V. Dhodapkar, Sagar Lonial, Ajay K. Nooka, Lawrence Boise; Emory University, Winship Cancer Institute, Atlanta, GA; Winship Cancer Institute of Emory University, Atlanta, GA; Winship Cancer Institute, Emory University, Atlanta, GA; Yale School of Medicine, New Haven, CT

Background: Translocation (4;14) is a known adverse prognostic factor in myeloma. However, utilization of proteasome inhibitors (PIs) in myeloma has abrogated the negative impact of t(4;14) in myeloma, and some investigators question whether t(4;14) still needs to be considered a high-risk marker. Here, we present a retrospective analysis of 142 patients with t(4;14) and describe disease characteristics, treatment patterns, and long-term outcomes. **Methods:** From January 2007 to August 2016, 42 patients with newly diagnosed myeloma and t(4;14) were identified. Demographics, clinical characteristics, and outcomes data for the patients were obtained from our institutional review board-approved myeloma database. Responses were evaluated per IMWG Uniform Response Criteria. **Results:** The median age of this cohort was 59.6 years (range 33-78). Notable patient characteristics include: W/AA/Asian 25.9%/23.6%/50%; ISS I/II/III 36.4%/22.9%/24.1%; R-ISS I/II/III 0%/27.8%/25.8%. Median lab values at diagnosis include: Hgb 10.4 g/dL, Hct 30.8%, Cr 1.01, and Ca 9.4, Frequency of concurrent cytogenetic abnormalities include del(17p): 19.7%; del(13): 44.4%, and +1q21: 46.5%. A majority of patients (86.7%) were induced with either triplet or quadruplet regimens, with 88% of these regimens including a proteasome inhibitor. 78.9% of patients underwent ASCT. Of those responses captured, 75.3% achieved ≥VGPR (sCR 4.8%, CR 30.5%, VGPR 40%, PR 20%). Post-transplant, 88% achieved ≥VGPR (sCR 35.1%, CR 30.9%, VGPR 22.3%), and 82% received maintenance therapy. The most common maintenance regimens included revlimid (34.8%), bortezomib (16.5%), and RVD (11.3%); one-third of patients received triplet maintenance regimens. With a median follow up of 99.5 months, the overall mPFS and mOS for this cohort of t(4;14) patients was 47.6 m (95% CI 32.3-62.8) and 108.5 months (95% CI 87.9-129.2). In patients with both t(4;14) and del(17p), the mPFS was 20.8 months and mOS was 89.6 months; for concurrent t(4;14) and +1q21, the mPFS was 32.0 months and 89.6 months. In patients that received maintenance therapy versus no maintenance, the mPFS and mOS was 54.9 months (95% CI 47.4-62.4) and 115.3 months (95% CI 96.3-134.3) versus 14.7 months (95% CI 13.1-16.3) and 34.3 months (95% CI 10.1-58.5), respectively. **Conclusions:** Overall, the prognosis of t(4;14) myeloma patients significantly improved compared to the pre-proteasome inhibitor era. In particular, maintenance therapies (predominantly PI- based) have made a clear survival impact (doubling of mPFS to 4.5 years and mOS to 9.5 years) compared to patients that did not receive maintenance therapy. However, presence of other concomitant cytogenetic abnormalities such as +1q21 and del(17p) continues to confer poorer outcomes, and innovative approaches are needed to obtain better outcomes for this subgroup of patients. Research Sponsor: None.

8063 **Poster Session**

The impact of complex karyotype identified by conventional cytogenetics on survival outcomes of 1,000 patients with newly diagnosed myeloma (NDMM).

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Background: Complex karyotype (CK), defined as two or more cytogenetic abnormalities on conventional metaphase cytogenetics, is not routinely used for the risk-stratification or treatment determination in patients with newly diagnosed myeloma (NDMM). Here, we present a retrospective analysis utilizing our institutional data of NDMM patients treated with RVD and a risk-adapted maintenance strategy at the Winship Cancer Institute of Emory University to assess the impact of CK on long-term outcomes. **Methods**:1000 consecutive NDMM patients treated with RVD induction therapy (R25mg/day, days 1-14; V1.3 mg/m^2, days 1,4,8,11 and D40mg once/twice weekly as tolerated) were identified from January 2007 to August 2016. Demographics, clinical characteristics and outcome data for patients were obtained from our institutional review board-approved myeloma database. Responses were evaluated per IMWG Uniform Response Criteria. **Results**: The median age of this cohort was 61 (range 16-83). Notable patient characteristics include: M/F 54.6%/45.4%, W/AA 61.8%/35.9%; ISS I/II/III 45.8%/30.8%/23.4%. R-ISS I/II/III 39.9%/48.7%/11.5%; Isotype IgG/IgA/FLC 59.2%/19.0%/15.7%; standard risk(SR)/high risk(HR) 71.2%/15.8%. ISS data was available for 75% of patients; R-ISS was available for 41% of patients. HR disease defined as the presence of t(4;14), t(14;16), del(17p) and/or CK. Frequency of specific CTG abnormalities were:14.9% with +1q21, 8.3% with del(1p),12.1% with t(11;14), 25.7% with del(13), 13.9% with CK, 2.8% with t(14;16), 10% with del(17p), and 4.8% with t(4;14). 11.9% of patients were classified high risk by FISH alone, 10.0% of patients were classified as high risk by complex karyotype(CK), and 3.9% of patients were classified as high risk by the presence of both high-risk FISH and CK. With a median follow up of 88.4 months, the median PFS (mPFS) for patients HR by FISH alone was 47.6 months (95% CI 35.2-59.9), for HR by CK alone was 46.9 months (95% CI 28.1-65.7) and for HR by both was 24.0 months (95% CI 8.3-39.7). The mOS for HR by FISH alone was 94.7 months (95% CI 74.4-115.1),HR by CK alone was 105.9 months (95% CI 60.8-151.0) and HR by both was 41.0 months (95% CI 24.2-57.8). **Conclusions:** CK by conventional metaphase cytogenetics is not currently included in the risk-stratification or risk stratification models of NDMM patients. In patients with a complex karyotype at time of diagnosis, mPFS and mOS is essentially the same as patients classified HR by FISH abnormalities. When compared to SR patients, prognosis is significantly worse, therefore the standard treatment approach is likely insufficient. As many centers do not routinely perform chromosome analysis, this highlights a gap in providing appropriate risk-stratified care. Moreover, NDMM with HR features by FISH and CK portends a poor prognosis for which alternative treatment strategies may need to be explored. Research Sponsor: None.

8064 **Poster Session**

Prognostic impact of t(11;14) on PFS1 among patients with myeloma receiving triplet induction therapy.

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Background: Presence of t(11;14) on plasma cells by FISH or metaphase cytogenetics is considered a standard-risk prognostic factor per IMWG risk-stratification. However, recent studies suggest inferior PFS and OS observed among t(11;14) patients relative to the standard-risk myeloma patients. In the context of the ongoing trials of BCL-2 inhibitors (venetoclax) among t(11;14) relapse/refractory myeloma patients yielding response rates closer to 90%, we review the prognostic impact of t(11;14) on PFS. These results may have implications for earlier incorporation of BCL-2 inhibitors among t(11;14) myeloma patients. **Methods:** Among the 1000 consecutive newly diagnosed myeloma patients uniformly treated with RVD induction therapy from January 2008 until August 2016, we have information on FISH probes for t(11;14) tested for 869 patients [121 - t(11;14) and 748 – no t(11;14)]. First, we explore the frequency of IMWG defined concomitant high-risk cytogenetic characteristics [del 17p, t(4;14), t (14;16)]. Next, we create a synthetic control cohort that received maintenance, and excluded patients exhibiting high-risk features to evaluate the relative prognostication conferred by presence of t(11;14). Median follow up was 91 months. Demographic and outcomes data were collected from IRB approved myeloma database and responses were evaluated per IMWG Uniform Response Criteria. **Results:** Median age is 61.2 years (range 16.3-79.83). 34% of the patients are above the age of 65. Men (14.1% vs 11.7%, p = NS) and blacks had higher rates of t(11;14) (16.1% vs 11.1%, p = 0.028). 17 (14%) had concomitant high-risk features – 4 (3.3%) had t(4;14), 3 (2.5%) had t(14;16) and 11 (9.1%) had del17p. Interestingly, the rates of amplification of 1q (26.1% vs 14.9%, p = 0.002), and del13 (34.7% vs 24.4%, p = 0.015) were higher among t(11;14) patients. Compared to the synthetic cohort, the post-induction and post-transplant responses were lower for t(11;14) patients as summarized in table 1. ≥VGPR for t(11;14) vs no t(11;14) post-induction were 48.2% vs 71.5% p < 0.001 and post-transplant were 83.1% vs 92.8% p = 0.001, respectively. The median progression-free survival for the t(11;14) and non-t(11;14) groups were 61.4 months (95% confidence interval (CI), 49.13-73.67) and 82.56 months (95% CI, 70.47-94.65) months, respectively (p = 0.002). **Conclusions:** Even with the use of modern day induction regimens and transplant, patients with t(11;14) seem to have inferior response rates compared to the other standard-risk myelomas. The lower rates of ≥VGPR post-induction and the shorter median PFS suggests BCL-2 inhibitors such as venetoclax may be incorporated earlier in myeloma treatments to improve the outcomes of t(11;14) patients on par with the other standard-risk myeloma patients. Research Sponsor: None.

8065 **Poster Session**

Immune cell differences between patients in different stages of monoclonal plasma cell disorders.

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Background: Multiple myeloma (MM) is an incurable plasma cell malignancy. Precursor conditions include monoclonal gammopathy of unknown significance (MGUS) and smoldering multiple myeloma (SMM). Immune surveillance is paramount for keeping the malignancy in check, whereas a dysfunctional immune system is suspected to promote disease progression. **Methods:** We performed flow cytometric immune panel analyses including T-cell, B-cell, natural killer (NK) cell and dendritic cell (DC) subsets in MGUS, SMM, and MM patients between 2018-2021. Immune panels were analyzed on fresh peripheral blood samples drawn at diagnosis. The patient population were MGUS (n=28), SMM (n=19) and MM (n=94). Samples from MGUS and SMM patients were combined into a single group (asymptomatic) and were compared to MM patients (symptomatic). Lymphocytes were identified by CD45+ expression resolving against side-scattered light on a bivariate plot. B cell and NK cell antigen expression profiles were assessed from this lymphocyte population. T cell subsets were further determined by CD3+. The percent gated for each marker was summarized by cohort using the appropriate descriptive statistics and compared using the Mann-Whitney U exact test. Analyses were performed in SAS v9.4 (Cary, NC) using a two-sided α=0.05. **Results:** Compared to MGUS/SMM patients, MM patients had a significant lower proportion of naive B cells, NK cells, and cytolytic NK cells, and a significant higher proportion of cytolytic T cells at diagnosis (Table). Consistent with prior studies, we demonstrated an increase in exhaustion markers. There was a trend toward a higher population of CD8+ exhausted T cells in MM patients compared to MGUS/SMM patients. Since the follow up for this study was short, survival data is not mature. **Conclusions:** This study demonstrates the immune imbalance that occurs between myeloma precursor conditions and MM. There is a shift in certain cell subsets in the immune microenvironment that alters tumor immunosurveillance and tumor cell killing favoring disease progression. In data not shown, we are currently analyzing the bone marrow microenvironment and its relation to disease progression. Follow up studies could assess if therapeutic intervention could reverse the imbalance, restore homeostatic equilibrium with the goal of controlling disease long-term. Research Sponsor: None.

Summary of the baseline immune markers by disease group for blood sample.

Population	MGUS/SMM (Median %)	MM (Median %)	p_value
Naïve B cells CD19+ CD27- IgD+	4.85	3.13	0.010
Natural Killer cells CD3- CD16- CD56+	11.46	9.20	0.027
Cytolytic Natural Killer cells CD3- CD16- CD56+ CD57+	6.14	3.71	0.001
Cytolytic T cells CD3+CD16- CD56- CD57+	3.62	7.25	0.025
CD8 Exhausted T cells CD3+ CD8+ TIM3- LAG3- TIGIT+ PD1+	0.01	0.03	0.050

8066 **Poster Session**

Determinants of overall survival (OS) of primary plasma cell leukemia (pPCL): A National Cancer Database (NCDB) analysis of years 2004 to 2009.

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Background: Outcome data for pPCL is limited due to the rare & aggressive nature of the disease. In this retrospective analysis, we utilized NCDB to identify factors contributing to 1 & 5-year OS of pPCL patients treated at CoC-accredited facilities across USA. **Methods:** Using the NCDB, we identified N= 325 pPCL patients diagnosed between 2004-2009 after excluding entries missing relevant values. Univariate analysis was used to summarize & assess the potential survival factors individually & multivariate Cox regression analysis with backward elimination (using significance level of $p<0.05$) was utilized to identify the independent survival factors. Kaplan-Meier (KM) survival curves of patient cohort were also produced. SAS version 9.4 was used to analyze the data. **Results:** Multivariate Cox regression analysis with backward elimination method revealed that there were 4 significant independent survival factors including sex, Charlson-Deyo Comorbidity Index (CCI), facility type, and insurance, while age & year-of-diagnosis were not independent survival factors (Table). Male patients were more likely to die compared to female patients (HR=1.40, p=0.005); patients with CCI ≥ 1 had higher chance to suffer death compared to patients with CCI= 0 (HR=1.52, p=0.002); patients not treated at an academic center (AC) had lower survival compared to those treated at ACs (HR=1.35, p=0.001); and patients without private insurance (PI) were more likely to suffer death compared to those with PI (HR=1.54, p=0.001). The 1 & 5-year survival rates for whole cohort were 51.3% (95%CI: 45.8%-56.8%), and 18.9% (95%CI: 14.6%-23.2%) using KM estimate, respectively. Only 6/325 =1.8% patients underwent autologous hematopoietic stem cell transplant (HSCT). Detailed analysis will be presented. **Conclusions:** In this large analysis of pPCL patients, we identified that being female, having less comorbidities, getting treatment at ACs, and having PI had significantly greater OS. Overall, pPCL is associated with low survival rates both at 1 & 5-years and HSCT may be enormously under-utilized for pPCL patients in the real world setting. Research Sponsor: Internal hematologic malignancy research fund, Cleveland Clinic Florida.

Multivariate Cox regression model analysis for overall survivorship.

Variable	HR (95%CI)	p-value
Sex (male vs. female)	1.40 (1.11-1.78)	0.005
Charlson-score (≥1 vs. 0)	1.52 (1.16-1.99)	0.002
Facility type (other vs. Academic center)	1.35 (1.13-1.62)	0.001
Insurance (other vs. Private program)	1.54 (1.21-1.96)	0.001

Six significant variables (age, sex, CCI, facility type, insurance, and year-of-diagnosis) being identified by univariate analysis were included in the Cox model as explanatory variables, and finally age (p=0.9146) and year-of-diagnosis (p=0.0910) were eliminated by backward elimination method.

8067 **Poster Session**

COVID vaccine immune response in patients with plasma cell dyscrasia: A systematic review.

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Background: The defective immune system in plasma cell dyscrasia places patients at a higher risk of developing a severe infection, which is one of the leading causes of death in such patients. In an era of a global pandemic, it is essential to protect them against COVID-19, but fewer effective plasma cells lead to a suboptimal response to vaccines. There is still a lack of evidence whether the seroconversion is truly clinically relevant and if patients with plasma cell disorders would benefit from frequent boosters to maintain antibody levels. **Methods:** Online databases including PubMed, CINAHL, Ovid, and Cochrane were searched (January 11th, 2022), following the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) guidelines. Only articles published in the English language were included. Abstracts, case reports, and case series were excluded. Out of 40 studies, 5 articles were selected for a systematic review. **Results:** In all 5 studies (N=654), seroconversion post-vaccination was used as a positive response to COVID-19 vaccination. Although patients with plasma cell disorders had a lower seroconversion rate compared to controls, the overall percentage was substantial and ranged between 23-95.5%. Amongst patients on active therapy, lower seroconversion rates were seen in patients on a CD-38 inhibitor, ranging from 20.2-92.1% (N=174). Also, a significantly lower percentage was recorded in patients above 65 years and those who have been treated with multiple therapies previously. Better seroconversion rates were seen in mRNA vaccines compared to J&J. **Conclusions:** Variable seropositive rates are seen in patients with plasma cell dyscrasias, lower rates are reported in patients on active therapy, CD-38 targeting therapy, and elderly patients. Hence, these patients should receive a 4 shot series. Research Sponsor: None.

Efficacy of COVID-19 vaccines in patients with plasma cell dyscrasia.

Author	Study, Year	Study Population	n/N	Vaccine	Overall Seropositive %	On Therapy Seropositive %	Not on Therapy Seropositive %	CD-38 Therapy Seropositive %	SMM Seropositive %	Age Seropositive %
Avivi et. al	Case Control, 2021	MM vs Control	171 /171 vs 64	mRNA	78 vs 98	76	79	69	100 (N=12)	<65y 87, >65y 71
Gandhili et. al	Prospective, 2021	B cell neoplasm	82/82 (78 MM)	mRNA- and vector-based (N=63 vs 19)	23	40.5	35	6.5	NA	<70y 34, >70y 6.7
Greenberg et. al	Prospective, 2021	MM	44/44	mRNA	93	93	94	100	NA	<65y 65, >65y 35
Shah et. al	RS, 2021	PCD	89/89 (41 MM)	mRNA or Ad26.COV.S (N=78 vs 11)	95.5	100	94.4	92.1	NA	NA
Terpos et. al	Case control, 2021	PCD vs Control	276/ 276	mRNA or the AZD1222 (N=215 vs 61)	42.4 vs 64.2 (D22), 71 vs 90.3 (D50)* 57.3 vs 81 (D50)**	79.8 **	20.2	25.2**	60.5** (N 38)	NA

n/N=number of participants evaluated/number of participants enrolled, SMM=Smoldering multiple myeloma, y=years, RS=retrospective study, MM=multiple myeloma, PCD=plasma cell dyscrasia, *=antibody titer >30%, **=antibody titer >50%, NA=Not available, D=Day.

TPS8068 **Poster Session**

MagnetisMM-9: An open-label, multicenter, non-randomized phase 1/2 study of elranatamab in patients with relapsed/refractory multiple myeloma.

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Background: Elranatamab (PF-06863135) is a humanized bispecific antibody that targets both B cell maturation antigen (BCMA) on multiple myeloma (MM) cells and CD3 on T cells resulting in T cell-mediated cytotoxicity. In preclinical studies, elranatamab has demonstrated anti-myeloma activity and delayed disease progression. In the ongoing phase 1 MagnetisMM-1 study, elranatamab has demonstrated clinical efficacy and a manageable safety profile in patients with relapsed/refractory MM (Bahlis et al, J Clin Oncol 2021). Elranatamab maximum tolerated dose has not yet been reached. Subcutaneous (SC) elranatamab at the recommended dose of 76 mg QW on a 28-d cycle with a 2 step-up priming dose regimen administered during the first week is currently being evaluated in a phase 2 study, MagnetisMM-3 (Lesokhin et al, Blood, 2021). **Methods:** MagnetisMM-9 (start date: Oct 2021; estimated completion date: Apr 2025) is an open-label, multicenter, non-randomized phase 1/2 study evaluating an alternative priming regimen to further mitigate cytokine release syndrome (CRS) incidence and severity and to evaluate SC elranatamab Q2W and Q4W dosing regimens in patients with relapsed/refractory MM. In part 1 of the study, patients will receive premedications and 2 step-up priming doses on cycle 1 D1 (4 mg) and D4 (20 mg), followed by elranatamab 76 mg QW for 6 cycles, and a dose Q2W thereafter if partial response or better is achieved and maintained. In part 2, higher doses of elranatamab (> 76 mg) at increased intervals between doses will be evaluated. The primary endpoint is grade ≥2 CRS rate during cycle 1. Secondary endpoints include dose-limiting toxicities (part 2 only), objective response rate, duration of response, progression-free survival, overall survival, minimal residual disease negativity rate, safety, and pharmacokinetics. Eligible patients should be ≥18 years of age with a MM diagnosis and measurable disease according to IMWG criteria, refractory to at least one proteasome inhibitor, one immunomodulatory drug, and one anti-CD38 antibody, relapsed/refractory to their last treatment regimen, and have an ECOG performance status ≤1. Key exclusion criteria are smoldering MM, active plasma cell leukemia, amyloidosis, POEMS syndrome, stem cell transplant within 12 weeks of enrollment, active, uncontrolled bacterial, fungal, or viral infections, or any other active malignancy within 3 years prior to enrollment (except for adequately treated basal cell or squamous cell skin cancer, or carcinoma in situ), or previous treatment with an anti-BCMA bispecific antibody. The study is open at centers in the USA, UK, Japan, and Taiwan. Clinical trial information: NCT05014412. Research Sponsor: Pfizer.

TPS8069 **Poster Session**

CAMMA 1: A multicenter phase Ib trial evaluating the safety, pharmacokinetics, and activity of cevostamab-containing regimens in patients with relapsed or refractory multiple myeloma.

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Background: Treatment of relapsed/refractory (R/R) multiple myeloma (MM) is challenging, especially in later lines where drug resistance reduces therapeutic options and remission duration. Prognosis is poor (estimated survival: < 1 year) for patients with MM who have received > 3 prior lines of therapy and are triple refractory to immunomodulatory drugs (IMiDs), proteasome inhibitors (PIs) and anti-CD38 agents (Gandhi et al. 2019). Thus R/R MM constitutes a significant unmet medical need. Fragment crystallizable receptor-like 5 (FcRH5) is expressed on myeloma cells with near 100% prevalence (Li et al. 2017), constituting a novel therapeutic target. Cevostamab is an IgG1-based T-cell-engaging bispecific antibody engineered to target the most membrane-proximal domain of FcRH5 on myeloma cells and cluster of differentiation 3 (CD3) on T-cells, resulting in T-cell killing of myeloma cells. Clinical data from the first-in-human Phase I study (GO39775) suggest that cevostamab monotherapy is highly active in heavily pretreated patients with R/R MM, with an overall response rate of 56.7% at the 132–198mg dose level (Trudel et al. ASH 2021 Oral presentation). Thus, cevostamab's activity and safety profile support further development. Due to their stimulatory effects on T-cell activity, combination of cevostamab with anti-myeloma agents (pomalidomide [P] or daratumumab [D]) may be synergistic, offering the potential to further improve efficacy. CAMMA 1 (NCT04910568) is an open-label, multicenter Phase Ib trial evaluating the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics of cevostamab-containing combination regimens (Arm B: cevostamab plus P and dexamethasone [d] [Pd]; Arm C: cevostamab plus Dd) in patients with R/R MM. A modified weekly schedule for cevostamab is also under investigation (Arm A: cevostamab monotherapy). **Methods:** Patients must be aged ≥18 years, have an ECOG performance status of 0 or 1 and a life expectancy of > 12 weeks. Patients in all arms have R/R MM; Arms B and C include patients with prior IMiD and PI exposure. Patients with prior CAR-T therapy may enroll with a washout period of 12 weeks post-CAR-T infusion. Cevostamab is administered by intravenous infusion q1w (C1–2)/q2w (C3–6)/q4w (C7–13) in Arm A, q2w (C1–6)/q4w (C7+) in Arm B, and q3w (C1–8)/q4w (C9+) in Arm C. Each arm consists of a safety run-in and an expansion cohort. Enrolment for Arm A is ongoing, with patients receiving up to 13 treatment cycles. Arms B and C are planned; patients will receive treatment until disease progression or unacceptable toxicity. The primary objective is to evaluate the safety and tolerability of cevostamab plus Pd, cevostamab plus Dd and cevostamab monotherapy. Secondary objectives include assessment of activity, PK, immunogenicity, and pharmacodynamic biomarkers. Clinical trial information: NCT04910568. Research Sponsor: CAMMA 1 is a Genentech, Inc. sponsored study. Third-party medical writing assistance, under the direction of the authors, was provided by Rachel Dobb of Ashfield MedComms, an Ashfield Health company, and was funded by F. Hoffmann-La Roche Ltd, Collaborator: F. Hoffman-La Roche Ltd.

TPS8070 **Poster Session**

CAMMA 3: A multicenter phase Ib trial evaluating the safety, pharmacokinetics, and activity of subcutaneous cevostamab monotherapy in patients with relapsed or refractory multiple myeloma.

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Background: Multiple myeloma (MM) remains an incurable disease. Although new treatment paradigms have increased survival, most patients relapse and treatment in later lines remains a challenge. Prognosis for patients refractory to immunomodulatory drugs, proteasome inhibitors and anti-CD38 antibodies is extremely poor, with an estimated survival of < 1 year (Gandhi et al. 2019). Therefore, patients with relapsed/refractory (R/R) disease represent a high unmet need, and new targets and treatment modalities are needed. Cevostamab is an IgG1-based T-cell-dependent bispecific antibody engineered to target the most membrane-proximal domain of fragment crystallizable receptor-like 5 (FcRH5) on myeloma cells, and cluster of differentiation 3 (CD3) on T cells. This dual binding results in efficient immunological synapse formation and T-cell-mediated killing of myeloma cells. In the ongoing first-in-human Phase I GO39775 study, intravenous (IV) administration of cevostamab monotherapy continues to show clinically meaningful activity and durable responses in patients with heavily pre-treated R/R MM (Trudel et al. ASH 2021), and uses Cycle (C) 1 step-up dosing for the mitigation of cytokine release syndrome (CRS). Subcutaneous (SC) delivery of antibody therapies has been shown to be effective and well tolerated and offers several advantages over IV administration in regards to improved healthcare utilization, including ease of administration, reduced treatment burden and reduced hospitalization. The slower absorption rate observed with SC versus IV antibody therapies may also support the potential for SC cevostamab to provide a further improved CRS profile (Bartlett et al. ASH 2021). CAMMA 3 (GO43227; ISRCTN26168155) is an open-label, multicenter, Phase Ib dose-escalation and dose-expansion trial evaluating the safety, tolerability, pharmacokinetics (PK) and preliminary activity of SC cevostamab monotherapy in patients with R/R MM. **Methods:** For inclusion, patients must be aged ≥18 years and must have R/R MM for which no established therapies are available or appropriate. Cevostamab is administered by SC injection in 28-day cycles, with step-up dosing in C1, q2w dosing in C2–6, and q4w dosing in C7–13. Patients may receive up to 13 cycles unless there is disease progression or unacceptable toxicity. Patients who respond to cevostamab but develop recurrent or progressive disease after 13 cycles may be eligible for cevostamab re-treatment. Primary objectives are to evaluate the safety and tolerability (including the maximum tolerated dose and dose-limiting toxicities) of SC cevostamab and to identify a recommended Phase II dose. Secondary objectives include assessment of PK, activity, and immunogenicity, and identification of biomarkers associated with response and resistance. Clinical trial information: 26168155. Research Sponsor: CAMMA 3 is a Genentech, Inc. sponsored study. Third-party medical writing assistance, under the direction of the authors, was provided by Rachel Dobb of Ashfield MedComms, an Ashfield Health company, and was funded by F. Hoffmann-La Roche Ltd, Collaborator: F. Hoffman-La Roche Ltd.

TPS8071 **Poster Session**

TTI-622-01: A phase 1a/1b dose-escalation and expansion trial of TTI-622 in patients with advanced hematologic malignancies, including multiple myeloma.

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Background: CD47 is an innate immune checkpoint that binds signal regulatory protein alpha (SIRPα) and delivers a "don't eat me" signal to suppress macrophage phagocytosis. TTI-622 is a fusion protein consisting of the CD47-binding domain of human SIRPα linked to the Fc region of human IgG4. It is designed to enhance phagocytosis and antitumor activity by preventing CD47 from delivering its inhibitory signal as well as generating a moderate pro-phagocytic signal via IgG4 Fc. CD47 is significantly increased in multiple myeloma (MM) bone marrow mononuclear cells and expression inversely correlates with survival in patients. Relapsed/Refractory (R/R) MM shows particularly high expression of CD47. Preclinical studies demonstrate that the addition of proteasome inhibitors to CD47 blockade significantly increases phagocytosis of MM cells in vitro and anti-myeloma activity in vivo. The ongoing phase 1a part of this study has been previously described. The phase 1b part of the study will determine the safety and efficacy of TTI-622 when given as monotherapy or in combination with selected approved anticancer treatments in patients with hematological malignancies where new treatments with novel mechanism of action are needed. Here we describe 5 RRMM cohorts within phase 1b of the study. **Methods:** TTI-622-01 is a multi-center Phase 1a/1b study. Phase 1a was designed to determine the MTD, pharmacokinetics (PK), pharmacodynamics, and preliminary antitumor activity of QW, Q2W, and Q3W single-agent TTI-622 in R/R lymphoma using a 3+3 dose escalation schema. Phase 1b, ongoing, will determine the safety and recommended dose of TTI-622 to be given as single agent and in combination with carfilzomib + dexamethasone (Kd) in RRMM and will evaluate the preliminary efficacy. Secondary objectives are to further characterize the safety, PK and immunogenicity of TTI-622 when combined with Kd. Patients will be enrolled in 5 separate cohorts: 3 cohorts will explore different doses and administration schedules of TTI-622 combined with the approved dose of Kd; 2 cohorts will explore different doses of TTI-622 monotherapy. Cohorts will be opened in a staggered manner. In each cohort 3 patients will be dosed and followed for 28 days (21 days in the monotherapy) before expanding enrolment to approximately an additional 27 patients. Key eligibility criteria include: relapse or progression following $\geq$3 prior lines of therapy (including a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 antibody), carfilzomib-refractory progressive and measurable disease per IMWG at study entry; age $\geq$18 years; ECOG performance status $\leq$2; adequate organ functions; no known CNS involvement; no prior anti-CD47 or anti-SIRPα therapy. Patient recruitment is planned or ongoing at 40 sites worldwide. Clinical trial information: NCT03530683. Research Sponsor: Trillium Therapeutics Inc., which was acquired by Pfizer, Inc. in November 2021.

TPS8072 **Poster Session**

MajesTEC-3: Randomized, phase 3 study of teclistamab plus daratumumab versus investigator's choice of daratumumab, pomalidomide, and dexamethasone or daratumumab, bortezomib, and dexamethasone in patients with relapsed/refractory multiple myeloma.

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Background: Patients (pts) with relapsed/refractory multiple myeloma (RRMM) after prior therapy with a proteasome inhibitor (PI) and lenalidomide are challenging to treat. Daratumumab in combination with pomalidomide and dexamethasone (DPd) or bortezomib and dexamethasone (DVd) are approved for pts with RRMM; however, disease control could be further improved. There is an unmet need for new therapeutic options with different modes of action. Teclistamab (tec; JNJ-64007957) is a B-cell maturation antigen (BCMA) $\times$ CD3 bispecific antibody that redirects CD3+ T cells to mediate T-cell activation and subsequent lysis of BCMA-expressing myeloma cells. In the phase 1, MajesTEC-1 study (NCT03145181), tec monotherapy was well-tolerated and showed encouraging efficacy in heavily pretreated pts with RRMM. The combination of tec and daratumumab (tec-dara) in the phase 1b TRIMM-2 study (NCT04108195) was also well-tolerated with promising efficacy. MajesTEC-3 (NCT05083169) is a multicenter, open-label, randomized phase 3 study that will compare the efficacy of tec-dara versus investigator's choice of DPd or DVd in pts with RRMM. **Methods:** Pts ($\geq$18 years old) must have documented MM per International Myeloma Working Group (IMWG) criteria; measurable disease; Eastern Cooperative Oncology Group performance status 0–2; received 1–3 prior treatment (tx) lines, including a PI and lenalidomide (pts with 1 prior tx line must be lenalidomide-refractory); with progressive disease on or after their last tx (or within 60 days of completing lenalidomide). Pts who received prior BCMA-directed tx or who are refractory to an anti-CD38 monoclonal antibody will be excluded. ~560 pts will be randomized 1:1 to receive 28-day cycles of tec-dara or investigator's choice of DPd or DVd (stratified by investigator's choice of DPd or DVd, ISS stage, and number of lines of prior tx). Step-up doses of tec will be given prior to the first tx dose. Dara, DPd and DVd will be administered per approved schedules. Pts will be treated until disease progression, death, intolerable toxicity, withdrawal of consent or end of study, whichever occurs first. Response will be assessed per 2016 IMWG criteria. The primary endpoint will be progression-free survival (PFS). Secondary endpoints include overall response rate, complete response or better, MRD negativity, PFS on next-line tx (PFS2), overall survival, and incidence and severity of AEs. Adverse events (AEs) will be graded by Common Terminology Criteria for AEs v5.0, except for cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome, which will be graded by American Society for Transplantation and Cellular Therapy guidelines. The study opened in October 2021 and enrollment is ongoing. Clinical trial information: NCT05083169. Research Sponsor: Janssen Research & Development, LLC.

TPS8073 **Poster Session**

Exploring alternative dosing regimens of single-agent belantamab mafodotin on safety and efficacy in patients with relapsed or refractory multiple myeloma: DREAMM-14.

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Background: Belantamab mafodotin (belamaf: BLENREP) is a first-in-class, monomethyl auristatin F (MMAF)-containing, B-cell maturation antigen (BCMA)-directed antibody–drug conjugate (ADC). In the DREAMM-2 study, belamaf showed deep responses with a manageable safety profile in patients with relapsed/refractory multiple myeloma (RRMM). At 13 months of follow-up, the median duration of response was 11 months and overall survival was 13.7 months at the 2.5 mg/kg Q3W dose. Corneal events are common and expected with belamaf and other MMAF-containing ADCs. In DREAMM-2, corneal events were managed with dose modifications. Clinical responses were observed even with prolonged dose holds, suggesting alternative dosing regimens may lower corneal event rates without compromising efficacy. The DREAMM-14 study (NCT05064358) will investigate if an improved benefit/risk profile of single-agent belamaf can be achieved by modifying the dose, schedule, or both, relative to the approved dosing regimen (2.5 mg/kg Q3W). **Methods:** This Phase II, randomized, open-label study will include adults with RRMM who had ≥3 prior lines of therapy (LOT), including an anti-CD38 monoclonal antibody, an immunomodulatory agent, and a proteasome inhibitor. Patients with corneal epithelial disease (except nonconfluent superficial punctate keratitis) or with prior exposure to BCMA-targeted therapies, or ADCs will be excluded. Patients will be randomized into Arms A–D (n=40 each) and Arm E (n=20) in parallel and stratified by the International Staging System (I vs II vs III) and prior LOT (3 vs ≥4). Belamaf will be administered as follows—Arm A: 2.5 mg/kg Q3W; Arm B: 1.9 mg/kg Q3W; Arm C: 2.5 mg/kg Q6W; Arm D: 1.9 mg/kg Q6W; Arm E: 1.9 mg/kg Q6W with ocular event-related dose modifications based on oncology staff assessment of ocular symptoms (patient-reported symptoms using the Ocular Surface Disease Index), and visual acuity (Snellen chart or equivalent) in addition to corneal findings assessed by an eye care specialist. Patients in all Arms will have response assessments, safety assessments, and ophthalmic exams performed by an eye care specialist Q3W regardless of dosing schedule. Ocular event-related dose modifications (except in Arm E) will be guided by a modified Keratopathy and Visual Acuity scale. The primary endpoint will be incidence of ocular events. Key secondary endpoints include ocular safety and tolerability, overall safety and tolerability, pharmacokinetics, and efficacy outcomes. Follow-up for progression-free survival will be Q3W until progressive disease, start of new anticancer therapy, withdrawal of consent, end of study, or death. Status: Recruitment is ongoing. Funding: GSK (Study 209628); drug linker technology licensed from Seagen Inc.; mAb produced using POTELLIGENT Technology licensed from BioWa. Clinical trial information: NCT05064358. Research Sponsor: GlaxoSmithKline.

TPS8074 **Poster Session**

MagnetisMM-5: An open-label, multicenter, randomized phase 3 study of elranatamab as monotherapy and in combination with daratumumab in patients with relapsed/refractory multiple myeloma.

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Background: Elranatamab (PF-06863135) is a humanized bispecific antibody that targets both B cell maturation antigen (BCMA)-expressing multiple myeloma (MM) cells and CD3-expressing T cells, with binding resulting in T cell-mediated cytotoxicity. Elranatamab has demonstrated antitumor activity and delayed tumor progression in preclinical studies, as well as promising efficacy and manageable safety in the ongoing phase 1 MagnetisMM-1 study in patients (pts) with relapsed/refractory MM (Bahlis et al, J Clin Oncol 2021). **Methods:** MagnetisMM-5 is an open-label, multicenter, randomized phase 3 study designed to evaluate the efficacy and safety of subcutaneous (SC) elranatamab monotherapy and SC elranatamab + SC daratumumab in pts with relapsed/refractory MM who have received prior therapy, including lenalidomide and a proteasome inhibitor (PI). The study consists of 2 parts. In part 1, a minimum of 20 pts will be enrolled to assess the safety of an elranatamab priming regimen and identify the recommended combination dose for SC elranatamab + SC daratumumab for part 2. The primary endpoint of part 1 is dose-limiting toxicities encompassing the elranatamab monotherapy priming duration (14 d) and the first cycle of SC elranatamab + SC daratumumab dosing (28 d). In part 2, ~450 pts will be stratified by prior lines of therapy (1 vs 2–3 vs ≥4) and prior treatment with anti-CD38 therapy (yes vs no) and enrolled in a 1:1:1 ratio to receive SC elranatamab or SC elranatamab + SC daratumumab or SC daratumumab + oral pomalidomide + oral dexamethasone. The primary endpoint of part 2 is progression-free survival (PFS), according to International Myeloma Working Group (IMWG) response criteria and blinded independent review. Secondary endpoints include PFS and PFS on next-line treatment by investigator per IMWG, overall survival, objective response rate, duration of response, complete response (CR) rate, duration of CR, time to response, overall and sustained minimal residual disease negativity rates, safety, quality of life, immunogenicity, and PK. Key inclusion criteria are age ≥18 y, MM diagnosis with measurable disease according to IMWG criteria, ECOG performance status 0–2, and clinical laboratory values within specified ranges. For part 2, pts should have received ≥1 prior line of anti-myeloma therapy, including treatment with lenalidomide and a PI. Key exclusion criteria include smoldering MM, plasma cell leukemia, amyloidosis, POEMS syndrome, stem cell transplant within 12 wk of enrollment, primary refractory MM, active, uncontrolled bacterial, fungal, or viral infections, previous treatment with BCMA-targeted therapy, anti-CD38 therapy within 6 mo of the first dose of study treatment, and previous pomalidomide therapy. MagnestisMM-5 will include sites in 28 countries. Clinical trial information: NCT05020236. Research Sponsor: Pfizer.

TPS8075 **Poster Session**

Subcutaneous daratumumab (DARA SC) versus active monitoring in patients (pts) with high-risk smoldering multiple myeloma (SMM): Randomized, open-label, phase 3 AQUILA study.

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Background: Standard of care for SMM includes active monitoring until progression to multiple myeloma (MM); however, recent evidence suggests pts with high-risk features may benefit from early treatment. DARA is a human IgGκ monoclonal antibody targeting CD38 that is approved as monotherapy for relapsed/refractory MM (RRMM) or in combination with standard of care for RRMM or newly diagnosed MM. Results from the phase 3 COLUMBA study showed that DARA SC demonstrated similar efficacy to intravenous (IV) DARA but with a lower rate of infusion-related reactions and shorter administration time. Based on the promising single-agent activity observed with IV DARA in intermediate- or high-risk SMM pts during the phase 2 CENTAURUS study, we hypothesized that DARA SC may delay progression to MM versus active monitoring in pts with high-risk SMM. **Methods:** AQUILA is an ongoing, randomized, open-label, multicenter phase 3 study of DARA SC versus active monitoring in pts with high-risk SMM. DARA SC (DARA 1,800 mg + recombinant human hyaluronidase PH20 [rHuPH20; 2,000 U/mL; Halozyme]) is administered by manual injection over approximately 5 minutes at alternating locations on the abdomen weekly in Cycles 1 and 2, every 2 weeks in Cycles 3-6, and every 4 weeks thereafter until 39 cycles (28 days/cycle), up to 36 months, or until disease progression. Eligibility criteria include confirmed diagnosis of SMM for ≤5 years, factors indicating high risk of progression to MM (clonal bone marrow plasma cells [BMPCs] ≥10% and ≥1 of the following: serum M protein ≥30 g/L, IgA SMM, immunoparesis with reduction of 2 uninvolved Ig isotypes, serum involved:uninvolved free light chain ratio ≥8 to < 100, or clonal BMPCs > 50% to < 60% with measurable disease), and ECOG performance status ≤1. The primary endpoint is progression-free survival (PFS), assessed by an independent review committee, with disease progression defined according to International Myeloma Working Group diagnostic criteria for MM. Secondary endpoints include time to biochemical or diagnostic (SLiM-CRAB) progression, overall response rate, complete response rate, duration of response, time to response, time to first-line treatment for MM, PFS on first-line treatment for MM (PFS2), overall survival, and incidence of MM with adverse prognostic features. The study completed enrollment on May 6, 2019; 390 pts have been randomly assigned to DARA SC or active monitoring. The primary efficacy analysis will be performed after approximately 165 PFS events have been observed. Clinical trial information: NCT03301220. Research Sponsor: Janssen Research & Development, LLC.

TPS8076 **Poster Session**

Birtamimab in patients with Mayo stage IV AL amyloidosis: Rationale for confirmatory affirm-AL phase 3 study.

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Background: Light chain (AL) amyloidosis is a progressive and typically fatal disorder caused by misfolded AL protein produced by plasma cells. Birtamimab is a monoclonal antibody designed to neutralize circulating soluble and deposited insoluble amyloid, thus promoting phagocytic clearance. In 2018, the phase 3 VITAL study in newly diagnosed, treatment-naive patients was terminated based on futility analysis of the primary endpoint (time to all-cause mortality [ACM] or time to cardiac hospitalization > 90 days after first study drug infusion); the final hazard ratio (HR) numerically favored birtamimab + standard of care (SOC) over placebo + SOC (0.835 [95% CI: 0.5799, 1.2011]; p = 0.330). Post-hoc analysis of ACM over 9 months revealed a substantial survival benefit (HR = 0.413 [95% CI: 0.191, 0.895]; p = 0.025) in patients at high risk for early death (Mayo Stage IV). Post-hoc analyses of secondary endpoints in this subgroup indicated meaningful improvements in health-related quality of life (assessed with 36-Item Short Form Health Survey version 2; SF-36v2) and 6-minute walk test (6MWT) distance with birtamimab + SOC ($p < 0.05$) at 9 months. **Methods:** The phase 3, double-blind, placebo-controlled AFFIRM-AL study (NCT04973137) will enroll up to 150 Mayo Stage IV patients with newly diagnosed, untreated AL amyloidosis. Patients will be randomized (2:1) to 24 mg/kg intravenous birtamimab or placebo every 28 days. Both arms will receive concomitant chemotherapy with a first-line bortezomib-containing regimen, with or without daratumumab (D), at the discretion of the investigator. Patients will be stratified at randomization based on their 6MWT distance (< 300 vs ≥300 meters) and initiation of D. The primary efficacy endpoint is time to ACM. Secondary endpoints are change from baseline to month 9 in the physical component summary of the SF-36v2 and 6MWT distance. This trial is powered at a significance level of 0.1 under a Special Protocol Assessment (SPA) with the U.S. Food and Drug Administration (FDA). Given the > 50% relative risk reduction for ACM observed in the post-hoc analysis of VITAL for patients with Mayo Stage IV disease, the AFFIRM-AL study is designed to confirm this effect of birtamimab. Approximately 130 global sites are planned; site initiation and patient randomization are underway. Conclusion: Treatments that improve survival in AL amyloidosis are needed, particularly for patients with advanced cardiac involvement, as median overall survival for those with Mayo Stage IV disease is ~6–9 months. The AFFIRM-AL study is designed to confirm the survival benefit observed in the VITAL study in patients with Mayo Stage IV AL amyloidosis. Clinical trial information: NCT04973137. Research Sponsor: Prothena Biosciences Ltd.