Phase 3 study results of isatuximab, bortezomib, lenalidomide, and dexamethasone (Isa-VRd) versus VRd for transplant-ineligible patients with newly diagnosed multiple myeloma (IMROZ).

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Background: The first line of treatment (tx) is important for patients (pts) with newly diagnosed multiple myeloma (NDMM) as pts may not have a chance for subsequent therapy. VRd is currently a standard of care (SOC) in NDMM. Isa is an approved anti-CD38 monoclonal antibody (mAb) inducing myeloma cell death through multiple mechanisms. In the Phase 3 IMROZ study (NCT03319667), we investigate the efficacy and safety of Isa-VRd vs VRd in transplant-ineligible NDMM pts. **Methods:** IMROZ is a global, prospective, randomized, open-label study done at 102 study sites in 21 countries. Included pts had active, measurable NDMM not considered for transplant due to elderly age or comorbidities. Pts aged ≥80 were excluded. Pts were randomized 3:2 and stratified by age, R-ISS stage and China vs non-China, to receive Isa-VRd or VRd. Isa-VRd arm pts received Isa (10 mg/kg IV); both arms received V (1.3 mg/m^2 SC), R (25 mg PO) and d (20 mg IV/PO). The primary endpoint was progression-free survival (PFS). Key secondary endpoints were complete response (CR), minimal residual disease negativity (MRD-) (10^{-5} by NGS) in pts with CR, very good partial response or better and overall survival. Adverse events (AEs) and laboratory parameters were graded with NCI CTCAE v4.03. **Results:** 446 pts (265 Isa-VRd, 181 VRd) were randomized; pt characteristics were well balanced. At data cutoff (26 Sep 2023), 125 (47.2%) and 44 (24.3%) pts in Isa-VRd and VRd arms were still on tx, respectively. Median (mdn) tx duration was 53.2 (Isa-VRd) vs 31.3 (VRd) mo; addition of Isa did not significantly affect relative dose intensity of VRd. At mdn follow-up of 59.7 mo, mdn PFS was not reached (Isa-VRd) vs 54.3 mo (VRd); HR 0.596 (98.5% CI 0.406–0.876), log-rank p=0.0005. From the current trend, projected Isa-VRd mdn PFS will reach ~90 mo. PFS benefit was consistent across subgroups and maintained through subsequent line of therapy (PFS2 HR 0.697; 95% CI: 0.51-0.952). Isa-VRd led to deep and sustained responses and was well-tolerated (Table). Exposure-adjusted Grade 5 TEAE rate was 0.03 (Isa-VRd) vs 0.02 (VRd). **Conclusions:** IMROZ is the first Phase 3 study of an anti-CD38 mAb with SOC VRd in this pt population to show a significantly reduced risk of progression or death by 40.4% vs VRd while providing deep and sustained responses. The safety profile was consistent with addition of Isa to VRd. Numerical differences in TEAEs are largely explained by longer exposure in the Isa-VRd arm. These results support Isa-VRd as a potential new SOC in pts not intended for transplant. Clinical trial information: NCT03319667. Research Sponsor: Sanofi.

% pts	Isa-VRd (n=265)	VRd (n=181)	Stratified Odds Ratio (95% CI)	1-Sided p-value
CR	74.7	64.1	1.656 (1.097–2.500)	0.008
MRD- CR	55.5	40.9	1.803 (1.229–2.646)	0.0013
Sustained MRD- for at least 12 mo	46.8	24.3	2.729 (1.799–4.141)	<0.0001
Grade ≥3 TEAE	91.6	84.0	-	
Grade 5 TEAE	11.0	5.5		
Any TEAE leading to definitive tx discontinuation	22.8	26.0		

Phase 3 randomized study of isatuximab (Isa) plus lenalidomide and dexamethasone (Rd) with bortezomib versus isard in patients with newly diagnosed transplant ineligible multiple myeloma (NDMM TI).

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Background: CD38 targeting immunotherapy is approved in combination with lenalidomide and dexamethasone in NDMM TI and considered the current standard of care (SOC). The best treatment combinations are important in NDMM TI, as outcomes worsen with successive line of therapy. To improve current SOC, we evaluated the added value of prolonged use of bortezomib for 18 months with reduced intensity weekly schedule to IsaRd, with the intent to demonstrate the impact of a PI in a quadruplet regimen to improve depth of response. In BENEFIT/IFM2020-05 study (NCT04751877), we investigated efficacy and safety of IsaRd vs Isa-VRd in NDMM TI. **Methods:** BENEFIT is a prospective, multicenter, randomized, parallel trial. Patients aged 65-79, non-frail, with NDMM TI were randomized 1:1 and stratified by age, high-risk cytogenetic and center. Isa-VRd arm received V (1.3 mg/m^2 SC weekly up to c12 (c), bimonthly up to c18); both arms received Isa (10 mg/kg IV weekly and bimonthly up to c12, then monthly), R (25 mg), and d (20 mg up to c12). The primary endpoint was minimal residual disease (MRD) 10^{-5} negative rate (NGS) at 18 months from treatment start analyzed in ITT. Key secondary endpoints included survival times (OS, PFS, EFS, TTNT), response rates and durations, MRD endpoints, and safety (using NCI CTCAE v5.0). **Results:** At data cutoff date (02 Feb 2024), 270 patients (135 per arm) were recruited. Patients baseline characteristics were well balanced across arms, overall median age was 73.2 years [IQR. 71;76], 90 patients (33%) were >75 years, 23 (9%) had high-risk cytogenetic (IFM score >1), 181 (76%) had R-ISS2+3, and 47 (17%) had impaired renal function (eGFR <60 mL/min). MRD negativity rates at 10^{-5} at 18 months were significantly higher in Isa-VRd arm compared to IsaRd arm (47% vs 24%, OR for negative MRD =2.96 [95%CI. 1.73 – 5.07, p<0.001]. The MRD benefit was consistent across subgroups. At 21.2 months median follow-up, 33 (12%) patients had relapsed and 20 (7%) had died, and no significant difference were observed across arms, yet. The addition of weekly "light" schedule of bortezomib did not significantly affect relative dose intensity of IsaRd. Forty-four (33%) patients presented with neurological adverse events grade ≥2 in the Isa-VRd vs 27 (20%) in IsaRd arm. **Conclusions:** Isa-VRd significantly deepened responses including a significant increase of the MRD negative rate at 10^{-5} vs IsaRd. The safety profile is consistent with addition of bortezomib. This study supports Isa-VRd as a new standard of care for NDMM TI non-frail patients. Clinical trial information: NCT04751877. Research Sponsor: Sanofi.

N (%) (ITT Population) [95%CI] at 18 Months	IsaRd(n=135)	Isa-VRd (n=135)	p-value
≥CR	24 (18) [12 – 25]	54 (40) [32 – 49]	0.0001
≥CR- MRD- 10-5	16 (12) [7 – 19]	29 (21) [15 – 29]	0.04
MRD- 10^{-6}	20 (15) [9 – 22]	46 (34) [26 – 43]	0.0004
PFS at 18 months	86% [80 – 92]	87.2% [82 – 93]	0.47
OS at 18 months	93.6% [90 – 98]	92.4% [88 – 97]	0.77

Daratumumab (DARA) + bortezomib/lenalidomide/dexamethasone (VRd) in transplant-eligible (TE) patients (pts) with newly diagnosed multiple myeloma (NDMM): Analysis of minimal residual disease (MRD) in the PERSEUS trial.

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Background: In the primary analysis of the phase 3 PERSEUS study, subcutaneous DARA (DARA SC) + VRd (D-VRd) induction/consolidation (ind/consol) and D-R maintenance improved progression-free survival (PFS) and increased depth of response (complete response or better [≥CR] and MRD negativity [neg]) compared to VRd ind/consol and R maintenance for TE NDMM. Here, we report further results on deepening of response and MRD neg during maintenance. **Methods:** TE pts with NDMM were randomized 1:1 to D-VRd or VRd. Pts in both arms received up to six 28-day cycles (4 pre-ASCT ind, 2 post-ASCT consol) of VRd (V 1.3 mg/m^2 SC on Days [D] 1, 4, 8, 11; R 25 mg PO on D 1-21; d 40 mg PO/IV on D 1-4, 9-12) followed by R maintenance (10 mg PO on D 1-28 until progressive disease [PD]). Pts in the D-VRd arm also received DARA SC (DARA 1,800 mg + recombinant human hyaluronidase PH20 [rHuPH20; 2,000 U/mL; Halozyme]) QW in Cycles 1-2, Q2W in Cycles 3-6, and Q4W during maintenance until PD. MRD-neg rate (clonoSEQ) was defined as the proportion of ITT pts who achieved both ≥CR and MRD neg. **Results:** In the 709 pts randomized (D-VRd, n=355; VRd, n=354), responses deepened over time with D-VRd vs VRd, including rates of ≥CR (end of consol: 44.5% vs 34.7%; *P*= 0.0078 and overall: 87.9% vs 70.1%; *P*<0.0001). MRD-neg rates increased over time and were higher with D-VRd vs VRd at 12, 24, and 36 mo after Cycle 1 Day 1 (all *P*<0.0001; Table). Rates of sustained MRD neg for ≥12 mo were higher for D-VRd vs VRd (10^{-5}: 64.8% vs 29.7%; *P*<0.0001; 10^{-6}: 47.3% vs 18.6%; *P*<0.0001); results were consistent across prespecified clinically relevant subgroups. Among pts who were MRD positive (pos) at end of consol, significantly higher proportions of pts in the D-VRd group vs the VRd group achieved MRD neg during maintenance at 10^{-5} (68.8% vs 52.7%; *P*= 0.0330) and 10^{-6} (62.3% vs 31.0%; *P*<0.0001) and sustained MRD neg for ≥12 mo at 10^{-5} (44.2% vs 22.6%; *P*= 0.0028) and 10^{-6} (34.4% vs 12.7%; *P*<0.0001).End of consol and overall MRD neg at both 10^{-5} and 10^{-6} were associated with improved PFS. Additional data on response rates in different study phases and sustained MRD neg will be presented. **Conclusions:** During maintenance, a greater proportion of pts with MRD-pos status achieved MRD neg with D-R vs R. The higher rates of deep (10^{-6}) and sustained MRD neg achieved with D-VRd ind/consol and D-R maintenance vs VRd ind/consol and R maintenance translated to a clinically meaningful benefit of improved PFS. These data further support D-VRd and D-R maintenance as a new standard of care for TE pts with NDMM and highlight the benefit of DARA SC in maintenance. Clinical trial information: NCT03710603. Research Sponsor: European Myeloma Network in collaboration with Janssen Research & Development, LLC.

	10^{-5}			10^{-6}		
	D-VRd (n = 355)	VRd (n = 354)	*P*	D-VRd (n = 355)	VRd (n = 354)	*P*
Rates of MRD neg up to:						
12 mo	65.1%	38.7%	<0.0001	43.9%	20.9%	<0.0001
24 mo	72.1%	44.9%	<0.0001	57.7%	27.4%	<0.0001
36 mo	74.6%	46.9%	<0.0001	63.9%	30.8%	<0.0001

7503 Oral Abstract Session

DREAMM-7 update: Subgroup analyses from a phase 3 trial of belantamab mafodotin (belamaf) + bortezomib and dexamethasone (BVd) vs daratumumab, bortezomib, and dexamethasone (DVd) in relapsed/refractory multiple myeloma (RRMM).

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Background: Patients (pts) with RRMM and poor prognostic features, such as high-risk cytogenetics or disease refractory to major drug classes, have an unmet need. In DREAMM-7 (NCT04246047), BVd demonstrated a statistically significant and clinically meaningful progression-free survival (PFS) benefit vs standard-of-care (SOC) DVd in pts with RRMM and ≥1 prior line of treatment (LOT). We present further analyses from DREAMM-7 to better understand efficacy in key subgroups. **Methods:** Pts with ≥1 prior LOT were randomized (1:1) to BVd, B 2.5 mg/kg IV Q3W + V 1.3 mg/m^2 (D1, 4, 8, 11 of 21-day cycles [C]; up to 8 C) and d 20 mg (D1, 2, 4, 5, 8, 9, 11, 12; up to 8 C), or DVd, D 16 mg/kg (21-day C: C1-3, Q1W; C4-8, Q3W; Q4W from C9 on)—V and d schedules were the same. The primary endpoint was independent review committee–assessed PFS. Secondary endpoints include overall survival (OS), duration of response, and overall response rate (ORR). Pts with high-risk cytogenetics had ≥1 of t(4;14), t(14;16), or del(17p13). **Results:** The intent to treat (ITT) included 494 pts: BVd, n=243; DVd, n=251. Median PFS (mPFS) in the ITT was 36.6 mo with BVd vs 13.4 mo with DVd (HR, 0.41; 95% CI, 0.31-0.53; $P<.00001$). ORR in the ITT was 82.7% (95% CI, 77.4%-87.3%) with BVd and 71.3% (65.3%-76.8%) with DVd. BVd had a higher complete response rate vs DVd (34.6% vs 17.1%). At baseline, 79 pts (33%) in the BVd arm and 87 pts (35%) in the DVd arm were refractory to lenalidomide (LEN). In the LEN-refractory subgroup, mPFS favored BVd (25.0 mo; 95% CI, 18.1 mo to NR) vs DVd (8.6 mo; 6.4-13.5 mo) (HR, 0.31; 95% CI, 0.19-0.48). A higher ORR was reported with BVd (84%; 95% CI, 73.5%-90.9%) vs DVd (61%; 49.9%-71.2%) in LEN-refractory pts. In the BVd and DVd arms, 67 (28%) and 69 (27%) pts had ≥1 high-risk cytogenetic abnormality. In the high-risk cytogenetic subgroup, the mPFS was 33.2 mo (95% CI, 20.3 mo to NR) with BVd vs 10.5 mo (7.6-13.4 mo) with DVd (HR, 0.31; 95% CI, 0.18-0.52). ORR favored BVd (85%; 95% CI, 74.3%-92.6%) vs DVd (67%; 54.3%-77.6%) in this subgroup. Additional data including other subgroup analyses will be presented. More deaths occurred with DVd (35%) than BVd (22%) in the ITT; neither arm reached median OS (HR, 0.57; 95% CI, 0.40-0.80; nominal $P=.00049$). In the ITT, all pts in both arms had ≥1 AE, and 95% (exposure-adjusted rate [exp-adj], 69 per 100 person-years [PY]) of BVd pts and 76% (exp-adj, 62 per 100 PY) of DVd pts reported grade 3/4 AEs. Serious AEs were reported in 50% (exp-adj, 36 per 100 PY) of BVd pts vs 37% DVd (exp-adj, 30 per 100 PY) pts. Ocular AEs were more frequent with BVd vs DVd (79% vs 29%). **Conclusions:** In DREAMM-7 BVd demonstrated PFS benefit over DVd with an mPFS improvement of 23 mo in pts with RRMM and ≥1 prior LOT. These results, demonstrating efficacy benefit in key subgroups with a high unmet need, support BVd as a potential new SOC in this setting. Clinical trial information: NCT04246047. Research Sponsor: GSK plc; Drug linker technology licensed from Seagen Inc.; monoclonal antibody produced using POTELLIGENT Technology licensed from BioWa.

Ciltacabtagene autoleucel vs standard of care in patients with functional high-risk multiple myeloma: CARTITUDE-4 subgroup analysis.

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Background: Functional high-risk (FHR) multiple myeloma (MM) is associated with poor prognosis. In CARTITUDE-4, a single ciltacabtagene autoleucel (cilta-cel) infusion significantly improved progression-free survival (PFS) vs established standard of care (SC; hazard ratio [HR], 0.26 [95% CI, 0.18–0.38]; $P<.0001$) in patients (pts) with lenalidomide (len)-refractory MM after 1–3 prior lines of treatment (tx; LOT). This post hoc subgroup analysis of CARTITUDE-4 reports outcomes for pts who received cilta-cel vs SC as second-line tx, including pts with FHR MM. **Methods:** Pts randomized to cilta-cel underwent apheresis, received PVd or DPd bridging tx, and then cilta-cel infusion (target dose, 0.75×10^6 CAR+ viable T cells/kg) 5–7 d after the start of lymphodepletion. Pts randomized to SC received PVd or DPd until progressive disease (PD). FHR was defined as PD within 18 mo after receiving autologous SCT or the start of initial frontline tx. Efficacy was assessed in randomized pts (intent to treat) and safety in pts who received any part of study tx. **Results:** 136 pts received cilta-cel (n=68) or SC (n=68) as second-line tx. Of these, 79 had FHR MM (cilta-cel, n=40; SC, n=39). Median PFS was longer among pts who received cilta-cel vs SC as second-line tx including the subset who had FHR MM (Table). Overall survival was immature at the time of this analysis. A greater proportion of pts who received cilta-cel vs SC as second-line tx had an overall response, complete response (CR) or better, minimal residual disease (MRD) negativity, and longer median duration of response (DOR), with similar observations among the FHR subset. Proportion of pts with grade ≥3 TEAEs who received cilta-cel vs SC as second-line tx was comparable (96% vs 96%) including the subset with FHR MM (100% vs 97%). Among pts who received second-line tx, 22 died (cilta-cel, n=11; SC, n=11), 16 of whom had FHR MM (n=7; n=9). **Conclusions:** In pts with len-refractory FHR MM after 1 prior LOT, cilta-cel improved outcomes vs SC and had a safety profile consistent with the known mechanism of action of CAR-T tx, suggesting cilta-cel may overcome the poor prognosis associated with FHR MM. Clinical trial information: NCT04181827. Research Sponsor: Johnson & Johnson Innovative Medicine; Legend Biotech USA Inc.

	Cilta-cel as 2L tx – All pts (n=68)	SC as 2L tx – All pts (n=68)		Cilta-cel as 2L tx – FHR MM (n=40)	SC as 2L tx – FHR MM (n=39)	
Median PFS, mo (95% CI)	NR (NE–NE)	17 (11–NE)	HR=0.35 (95% CI 0.2–0.7) P=.0007	NR (18–NE)	12 (8–NE)	HR=0.27 (95% CI 0.1–0.6) P=.0006
12-mo PFS, % (95% CI)	78 (66–86)	59 (46–69)		77 (60–87)	49 (32–64)	
ORR, n (%)	61 (90)	54 (79)	OR=2.3 (95% CI 0.8–6.0) P=.0979	35 (88)	31 (80)	OR=1.8 (95% CI 0.5–6.1) P=.3400
≥CR, n (%)	48 (71)	24 (35)	OR=4.4 (95% CI 2.1–9.0) $P<.0001$	27 (68)	15 (39)	OR=3.3 (95% CI 1.3–8.4) P=.0102
MRD negativity (10^{-5}), n (%)	43 (63)	13 (19)	OR=7.3 (95% CI 3.3–15.9) $P<.0001$	26 (65)	4 (10)	OR=16.3 (95% CI 4.8–55.1) $P<.0001$
Median DOR, mo (95% CI)	NR (NE–NE)	20 (14–NE)		NR (16–NE)	16 (8–NE)	

NE, not estimable; NR, not reached; OR, odds ratio; ORR, overall response rate.

7505 Oral Abstract Session

Efficacy and safety of ciltacabtagene autoleucel ± lenalidomide maintenance in newly diagnosed multiple myeloma with suboptimal response to frontline autologous stem cell transplant: CARTITUDE-2 cohort D.

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Background: CARTITUDE-2 is a phase 2 multicohort study evaluating ciltacabtagene autoleucel (cilta-cel) across various clinical settings. Cohort D is evaluating cilta-cel ± lenalidomide (len) maintenance in patients (pts) with newly diagnosed multiple myeloma (NDMM) who achieved less than complete response (CR) after autologous stem cell transplant (ASCT) frontline therapy (tx). We report efficacy and safety for this cohort. **Methods:** Adults with NDMM per IMWG criteria, best response of <CR and ≥stable disease after 4–8 cycles of initial tx, including induction, high-dose chemotherapy and ASCT ± consolidation, and without exposure to CAR-T or anti-BCMA tx received a single cilta-cel infusion (target dose, 0.75×10^6 CAR+ viable T cells/kg) 5–7 d after the start of lymphodepletion. Per protocol, safety was assessed in the first 5 pts with cilta-cel only; subsequently, 12 pts initiated continuous len maintenance ≥21 d post cilta-cel for ≤2 yrs. Primary endpoint was minimal residual disease negativity (MRD neg) at 10^{-5} based on next-generation sequencing or flow. **Results:** As of Sept 5, 2023 (median follow-up, 22 mo [range, 5–39]), 17 pts received cilta-cel (with len, n=12; without len, n=5). Median age was 54 yrs; 6% had high-risk cytogenetics; and 100% were International Staging System stage I at baseline. Of 15 MRD-evaluable pts, 12 (80%) achieved MRD neg at 10^{-5}; median time to MRD neg was 1 mo (range, 1–6). Overall response rate was 94% (n=16/17; ≥CR, 94%). Median duration of response was not reached, and median time to first response was 1 mo. Progression-free survival (investigator-assessed) and overall survival rates at 18 mo were 94% each. CAR+ T cells peaked in blood at a median of 12 d post infusion (mean, 2187 cells/μL; SD, 2102 cells/μL) and remained detectable for a median of 43 d (range, 26–209). All pts had grade (gr) 3/4 TEAEs. Hematologic TEAEs included neutropenia (94%), lymphopenia (65%), thrombocytopenia (47%), and leukopenia (41%). Infections occurred in 12 (71%) pts (gr 3/4, 29%). CRS occurred in 14 (82%) pts, and median time to onset was 8 d. All CRS events were gr 1/2 and recovered in a median of 3 d. ICANS occurred in 1 pt (gr 1); median time to onset was 7 d and recovery was 1 d. Other neurotoxicities occurred in 6 pts (gr 1, n=1; gr 2, n=4; gr 3, n=1); median time to onset was 21 d and recovery was 70 d (n=4). No MNTs/parkinsonism occurred. 1 pt had a secondary malignancy of gr 3 MDS with an onset on d 353 that was not treatment related per investigator assessment. **Conclusions:** In pts with NDMM and <CR after frontline ASCT, a single cilta-cel infusion ± len maintenance demonstrated deep responses that were durable. TEAEs were consistent with the known safety profile of cilta-cel. These data show promising efficacy and safety with cilta-cel ± len maintenance in pts with NDMM who achieved <CR after ASCT frontline tx. Clinical trial information: NCT04133636. Research Sponsor: Johnson & Johnson Innovative Medicine; Legend Biotech USA Inc.

Safety results from the phase 3 MajesTEC-7 study in patients (pts) with transplant ineligible/not intended newly diagnosed multiple myeloma (NDMM).

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Background: Despite recent advances in the treatment (tx) of transplant ineligible/not intended NDMM, most pts still relapse and require alternative txs, highlighting a need for new frontline tx options with new mechanisms of action to improve pt outcomes. Teclistamab (tec) demonstrated rapid, deep, and durable responses in the MajesTEC-1 trial (NCT03145181/NCT04557098). Preliminary data from the MajesTEC-2 trial (NCT04722146) demonstrated that tec, daratumumab (dara), and lenalidomide (len) combination (tec + DR) is tolerable, with promising efficacy in pts with relapsed/refractory MM and NDMM. The phase 3 MajesTEC-7 (NCT05552222) study will compare tec + DR vs DR + dexamethasone (dex) in pts with NDMM who are ineligible/not intended for ASCT as initial tx. We report the results of the first safety run-in (SRI) from MajesTEC-7. **Methods:** Eligible patients were aged ≥18 yrs with NDMM and ineligible/not intended for ASCT as initial tx, with measurable disease and an ECOG performance status (PS) score 0–2. Pts in the SRI received tec (step-up dose [cycle 1], QW [cycle 2], Q2W [cycle 3–6], and Q4W [cycle 7+]) + DR (as SOC) until progression, unacceptable toxicity, or death. Response assessments were based on IMWG criteria. Adverse events (AEs) were graded per CTCAE v5.0; cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were graded per ASTCT criteria. Prophylactic immunoglobulin replacement was highly recommended. **Results:** As of Nov 27, 2023, 26 pts had received tec + DR (median, 11 cycles; range, 2–14) and 24 pts (92.3%) remained on tx. Median follow-up was 10.2 mo (range, 2–12). At baseline, median age was 72.5 yrs, 11.5% had an ECOG PS score of 2, and 15.4% had ≥1 soft-tissue plasmacytoma. 4 pts (15.4%) deferred transplant. Treatment-emergent AEs (TEAEs) occurred in 100% of pts (grade [gr] 3/4, 22 pts [84.6%]). Infections occurred in 25 pts (96.2%; gr 3/4, 8 pts [30.8%]). CRS occurred in 16 pts (61.5%; all gr 1). ICANS occurred in 1 pt (gr 1). Gr 3/4 TEAEs occurring in ≥3 pts were neutropenia (13 [50%]), febrile neutropenia (5 [19.2%]), thrombocytopenia (4 [15.4%]), COVID-19 (3 [11.5%]), maculopapular rash (3 [11.5%]), and hypertension (3 [11.5%]). 1 pt discontinued tec + DR due to withdrawal of consent. 2 discontinued len due to TEAEs (gr 3 maculopapular rash and gr 4 neutropenia). There was 1 death due to a TEAE in cycle 3 (pneumonia influenza). Overall response rate was 92.3% (complete response or better, 73.1%; very good partial response or better, 92.3%). **Conclusions:** These results from the first SRI of MajesTEC-7 demonstrate a manageable safety profile with early efficacy of tec + DR in NDMM. Two additional SRIs are ongoing investigating tec (less frequent dosing) + DR and talquetamab + DR. Clinical trial information: NCT05552222. Research Sponsor: Johnson & Johnson Innovative Medicine.

7507 Oral Abstract Session

All-oral triplet iberdomide, ixazomib, and dexamethasone in elderly patients with multiple myeloma at first relapse: Results of the IFM phase 2 study I2D.

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Background: The triplet combination daratumumab, lenalidomide and dexamethasone (DRd) and bortezomib, lenalidomide and dexamethasone (VRd) are to date the standard of care for patients with transplant ineligible (TI) newly diagnosed multiple myeloma (MM). Most TI patients therefore present with MM refractory to lenalidomide and daratumumab at first relapse and represent a difficult-to-treat population. Iberdomide is a novel oral cereblon E3 ligase modulator (CELMoD) that demonstrated promising activity in MM patients refractory to lenalidomide/pomalidomide. Here, we report efficacy and safety results of the oral triplet iberdomide, ixazomib and dexamethasone in elderly patients with MM at first relapse. **Methods:** The *Intergroupe Francophone du Myélome* (IFM) prospective, multicenter, phase 2 study I2D enrolled MM patients aged over 70 years at first relapse (NCT04998786).Patients received oral iberdomide (1.6 mg on day 1 to 21), ixazomib (3 mg on day 1,8,15) and dexamethasone (20 mg on day 1,8,15,22 on cycle 1-2 and 10 mg on day 1,8,15,22 on cycle 3-6) (28-day cycle) until disease progression or unacceptable toxicity. The primary endpoint was very good partial response (VGPR) rate. **Results:** Seventy patients were included from Dec 2021 to May 2023 in 19 IFM centers. Median age was 76. The International Myeloma Working Group (IMWG) frailty score was >2 in 35 (50%) patients. In evaluable patients (54/70), cytogenetic analysis revealed del(17p) in 10 patients (18.5%) and t(4;14) in 8 (15%) patients. Based on inclusion criteria, all patients received 1 prior line of treatment, including lenalidomide in 87% (refractory, 74%) and daratumumab in 40% (refractory, 37%) of patients. Median time from MM diagnosis to study enrolment was 28 months. At data cut-off, 36 (51%) patients discontinued the study due to disease progression (n=30), adverse event (n=4) or death (n=2). After a median follow-up of 12 months, the overall response rate was 64%, including 33% VGPR. The median progression-free survival (PFS) was 13 months and the 12-month overall survival (OS) was 85% (77-95% 95% CI). In patients with MM refractory to both lenalidomide and daratumumab (n=26), the median PFS was 10 months. Overall, the triplet I2D was well tolerated. Most common non-hematologic adverse events (AE) were infection (30% of patients), peripheral neuropathy (20%), diarrhea (19%), and were mostly grade 1 or 2. Most common grade 3-4 treatment related AEs (>5% of patients) were neutropenia (46%), thrombocytopenia (9%) and infection (8%). Four patients discontinued treatment due to a severe AE (cytopenia (n=3), skin rash (n=1). **Conclusions:** The oral tripletiberdomide, ixazomib and dexamethasone demonstrated a favorable efficacy / safety profile in elderly MM patients at first relapse, including in patients with lenalidomide and daratumumab refractory disease. Clinical trial information: NCT04998786. Research Sponsor: None.

Impact of extramedullary multiple myeloma on outcomes with idecabtagene vicleucel.

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Background: Idecabtagene vicleucel (Ide-cel) has demonstrated excellent efficacy in patients with relapsed/refractory multiple myeloma (RRMM). However, outcomes in patients with extramedullary disease (EMD) remain to be better characterized. **Methods:** We included patients from 11 US academic centers, who were evaluated for EMD and were infused with ide-cel between May 2021 and April 2023. Patients with soft tissue or visceral lesions non-contiguous from bony lesions were classified as having true EMD, with paraskeletal disease classified as non-EMD. Disease responses were evaluated using the IMWG criteria. Time-to-event analyses were performed from the date of ide-cel infusion. **Results:** Among 351 patients with RRMM treated with ide-cel, 84 (24%) had EMD prior to infusion. Median follow-up for the entire cohort was 18.2 months (95% CI: 17-19.3). Baseline characteristics at ide-cel infusion for EMD and non-EMD cohorts are depicted in the table. For the EMD and non-EMD cohorts, the Day 30 objective response rates (ORR) were 58% vs. 69% (p=0.1), Day 30 ≥complete response rates were 16% vs 24% (p=0.11), the Day 90 ORR were 52% vs 82% (p<0.001), and best ORR were 58% vs 82%, respectively. The median progression-free survival (PFS) was 5.3 months (95% CI: 4.1-6.9) for the EMD cohort vs. 11.1 months (95% CI: 9.2-12.6; p<0.0001) for the non-EMD cohort. The median duration of response for EMD among day 30 responders was 6.4 months (95% CI: 5.1-8.4). In a multivariable analysis, EMD was an independent predictor of inferior PFS [hazard ratio 1.8 (95% CI: 1.2-2.5), p<0.001] after adjusting for ECOG status, revised ISS stage, penta-drug refractoriness, elevated ferritin, prior BCMA-directed therapy and use of bridging therapy. Pattern of progression in the EMD cohort (n=68/84) included EMD site only (21%), hematologic only (22%), or both (57%), with comparable PFS for type of progression (p=0.19). The median overall survival (OS) was 14.8 months [95% CI: 9-Not reached (NR)] for EMD and 26.9 months [95% CI: 26.3 vs NR, p=0.006)] for the non-EMD group. Rates of Grade ≥2 cytokine release syndrome or neurotoxicity syndrome were comparable between the two cohorts. **Conclusions:** Patients with EMD demonstrate significantly inferior Day 90 ORR and presence of EMD is an independent risk factor for inferior PFS. Research Sponsor: None.

Patient Characteristics	Data Available in, n (%)	Extramedullary Disease (n=84)	No Extramedullary Disease (n=267)	P value
Age, median (interquartile range), years	351 (100)	62 (55-69)	66 (59-71)	**0.02**
ECOG 0-1, n (%)	333 (95)	62 (78)	225 (89)	**0.02**
Revised ISS Stage III, n (%)	256 (73)	11 (23)	42 (21)	0.65
High-Risk Cytogenetics [t(4;14), deletion 17p, t(14;16)], n (%)	308 (88)	20 (29)	79 (33)	0.47
Prior Lines of Therapy, median (interquartile range)	351 (100)	6 (5-8)	6 (5-8)	0.19
Triple Class Refractory, n (%)	351 (100)	74 (88)	215 (81)	0.11
Penta-refractory, n (%)	351 (100)	39 (46)	86 (32)	**0.02**
Bridging Therapy, n (%)	351 (100)	67 (80)	195 (73)	0.08

7509 Rapid Oral Abstract Session

Final results of a phase II study of lenalidomide-elotuzumab as maintenance therapy post-autologous stem cell transplant (AuSCT) in patients (Pts) with multiple myeloma (MM).

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Background: Randomized controlled trials oflenalidomide (LEN) maintenance after AuSCT have shown a progression free survival (PFS) benefit in pts with MM. We report final results of a phase 2 trial evaluating the efficacy and safety of adding elotuzumab (ELO) to LEN as maintenance therapy post- AuSCT. **Methods:** On 28-day cycles, patients received ELO 10mg/kg iv weekly for cycles 1-2.Between 4/15/2015-1/27/2016, 27 pts received ELO 10mg/kg q2 weeks for cycles 3-6 and 20mg/kg monthly for cycles 7+. From 1/28/2016 forward, 74 pts received ELO 20 mg/kg monthly from cycle 3+. LEN was dosed at 10 mg/day for cycles 1-3 and increased to 15 mg/day at physician discretion starting with cycle 4 in the absence of non-hematologic (HEME) toxicity $>$ grade 1, ANC $<$ 1000/mL and platelet count $<$ 100K/ml. For the 1st 8 weeks, pts $<$75 yrs received 28 mg of dexamethasone (DEX) 3-24 hours pre-infusion and pts $\geq$75yrs received 8 mg; pts received 4-10 mg iv DEX pre-infusion for all cycles. Zoster and thromboembolic prophylaxis were prescribed as per standard recommendations. The primary endpoint was PFS, defined as time from AuSCT to progressive disease (PD) or death (whichever occurred first), or censored at last contact date. Secondary objectives were best response, overall survival (OS), incidence of second primary malignancies (SPMs) and adverse event (AE) profile. Enrollment was completed on 6/5/2019. Eligible pts received $\leq$2 induction lines of therapy (LOT) and were 60-210 days post-AuSCT. **Results:** Pts (n=100) were treated for a median of 40 cycles (2-109). With a median follow up of 74.3 mos, 78% of pts (n=79) remain alive. Median PFS was 75.4 months. Median OS has not been reached; 5-year OS rate was 86.7%. At study entry, rate of $\geq$VGPR was 77.3% and $\geq$CR was 37.7%. On study, this improved to 91.1% $\geq$VGPR and 69.3% $\geq$CR. Of pts in $\geq$VGPR and tested for minimal residual disease (10^{-5} sensitivity by flow cytometry), 37/44 were negative. High-risk cytogenetics (n=44; p$<$0.0001), International Staging System (ISS) Stage III (n=10/95, p=0.049) and Revised-ISS Stage III (n = 3/89; p= 0.026) predicted shorter median PFS (39.2, 53.2 and 32.2 mos. respectively). Median PFS on next LOT was 21.8 mos. Grade 3-4 HEME AEs (n=102) were: neutropenia 35%, thrombocytopenia 7%, and anemia 10% . Grade 3-4 non-HEME AEs in $>$3 pts were: respiratory infections 23%, hypophosphatemia 19%, diarrhea 13% , fatigue 11% , peripheral neuropathy 7%, other infections 6%, myalgias 4%, and high ALT 4%. Incidence of HEME, non-invasive and solid tumor SPMs was 8%, 8% and 7%. Median time to HEME SPM diagnosis was 45.5 mos. **Conclusions:** ELO-LEN is a well-tolerated maintenance therapy on which 53% of patients had improved quality of response. Median PFS and 5-year OS compare favorably with results from CALGB 100104 and IFM 2005-02 trials of lenalidomide alone. SPM incidence is similar to rates reported in these trials. Clinical trial information: NCT02420860. Research Sponsor: Bristol Myers Squibb.

Efficacy of venetoclax-dexamethasone (VenDex) v pomalidomide-dexamethasone (PomDex) in patients (Pts) with t(11;14)-positive relapsed/refractory multiple myeloma [t(11;14)+ RRMM]: Phase 3 CANOVA study biomarker subgroup analysis.

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Background: The randomized Phase 3 CANOVA study's (NCT03539744) primary analysis showed multiple numerically improved efficacy endpoints with VenDex v PomDex, but the primary endpoint of mPFS by IRC was not statistically significant. Here, we report correlative biomarker analyses from CANOVA. **Methods:** CANOVA is a randomized, global, open-label Phase 3 study of VenDex v PomDex in pts with t(11;14)+ RRMM and ≥2 prior lines of therapy (LOTs). The primary endpoint was mPFS by IRC. Key secondary endpoints included ORR, ≥VGPR, mOS, and MRD negativity ($<10^{-5}$). In post hoc mPFS sensitivity analysis, disease progression, death, and start of next LOT were defined as events. *BCL2* gene expression by RNAseq (3.7 log2 FPKM prespecified median cutoff for $BCL2^{high}$ v $BCL2^{low}$) and chr1q abnormalities by whole-exome sequencing (normal, gain, or amp) were assessed centrally from pretreatment, CD138-enriched BM aspirates. **Results:** mPFS, post hoc mPFS, and mOS in the VenDex arm were similar by *BCL2* status, with numerically higher ORR, ≥VGPR, and MRD negativity rates in the $BCL2^{high}$subgroup. In contrast, mPFS and mOS within the PomDex arm were numerically longer in the $BCL2^{low}$subgroup, despite equal ORR in bothsubgroups (Table). Presence of 1q abnormalities was evenly distributed across $BCL2^{high}$ v $BCL2^{low}$ subgroups in the VenDex arm (51% v 45%) but not in the PomDex arm (59% v 31%). Normal 1q and gain(1q) subgroups had numerically improved mPFS, mOS, ORR, ≥VGPR, and MRD negativity with VenDex; pts with amp(1q) had poor outcomes regardless of treatment, albeit the sample size was small. **Conclusions:** Pts with $BCL2^{high}$ or gain(1q) had numerically improved clinical efficacy with VenDex v PomDex. Clinical benefit was consistent across *BCL2* subgroups ($BCL2^{high}$ or $BCL2^{low}$) with VenDex but not PomDex. Pts with amp(1q) fared poorly irrespective of treatment arm. Clinical trial information: NCT03539744. Research Sponsor: AbbVie and Genentech/Roche.

Efficacy Outcomes.

	All Pts (VenDex, n=133 v PomDex, n=130)	$BCL2^{high}$ (VenDex, n=54 v PomDex, n=45)	$BCL2^{low}$ (VenDex, n=45 v PomDex, n=53)	amp(1q) (VenDex, n=11 v PomDex, n=6)	gain(1q) (VenDex, n=35 v PomDex, n=29)	Normal 1q (VenDex, n=43 v PomDex, n=47)
mPFS, mo	9.9 v 5.8	9.4 v 3.8	10.4 v 7.4	2.1 v 2.8	9.4 v 3.8	12.3 v 7.4
HR (95% CI)	0.82 (0.60–1.14)	0.64 (0.38–1.06)	0.89 (0.52–1.55)	1.66 (0.30–9.10)	0.47 (0.24–0.91)	0.63 (0.36–1.11)
Post hoc mPFS, mo	9.4 v 4.0	7.4 v 3.2	8.5 v 5.6	1.9 v 1.1	7.4 v 2.8	10.4 v 5.6
HR (95% CI)	0.65 (0.49–0.87)	0.50 (0.31–0.80)	0.70 (0.44–1.13)	0.48 (0.14–1.69)	0.37 (0.21–0.68)	0.49 (0.30–0.82)
mOS, mo	32.4 v 24.5	32.4 v 19.0	28.7 v 30.0	9.2 v 14.8	39.2 v 16.0	32.4 v 27.9
HR (95% CI)	0.70 (0.47–1.03)	0.63 (0.35–1.12)	0.88 (0.46–1.68)	1.03 (0.27–3.94)	0.51 (0.24–1.07)	0.61 (0.31–1.23)
ORR (≥VGPR), %	62 (39) v 35 (14)	69 (48) v 36 (13)	58 (31) v 36 (13)	27 (18) v 17 (17)	63 (43) v 24 (7)	72 (40) v 43 (15)
MRD negativity (10^{-5}), %	8 v 0	15 v 0	2 v 0	0 v 0	11 v 0	12 v 0

7511 Rapid Oral Abstract Session

OriCAR-017, a novel GPRC5D-targeting CAR-T, in patients with relapsed/refractory multiple myeloma: Long term follow-up results of phase 1 study (POLARIS).

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Background: OriCAR-017 is a novel GPRC5D-targeting CAR T-cells. Previously we had presented early study results (Lancet Haematol 2023: 10: e107–16) following OriCAR-017 treatment, the results of good durable response and long-term safety profile support OriCAR-017 is highly probable to be developed as a promising therapy for patients with relapsed or refractory multiple myeloma. All patients had completed at least 2-year follow-up per protocol. **Methods:** Ten median age of 64 years (range 41–71) pretreated RRMM pts with a median of 5.5 prior lines therapies (range 3-17) received OriCAR-017. Seven (70.0%) pts were cytogenetics high risk, 4 (40.0%) pts had EMD, 3 (30.0%) pts had ISS stage(III), 2 (20.0%) pts had received prior anti-CD38 and 2 (20.0%) pts were treated with auto-HSCT and 5 (50.0%) pts were treated with BCMA CAR-T. Patients were administrated in a single dose of intravenous OriCAR-017 at 1×10^6CAR-T/kg (DL1,n=3), 3×10^6CAR-T/kg(DL2,n=4), or 6×10^6CAR-T/kg(DL3,n=3). **Results:** At data cut-off (Jan 16, 2024), all 10 enrolled pts had been evaluated for response with the last patient completed 24 months follow up. ORR was 100.0%, sCR was 80.0%, VGPR was 20.0%. All patients achieved MRD negativity at day 28. The mDOR was 10.43 months (95%CI, 5.00-17.00); mPFS was 11.37 months (95%CI, 5.93-18.00) while mOS has not reached (7 pts still undergo survival follow-up, 1 pt died from disease progress, 2 from COVID). The mDOR was 17.23 months (95%CI, 7.33-NR) and the mPFS was 19.10 months (95%CI, 8.30-NR) with 67% prior BCMA CAR-T pts at high dose level. Nine (90%) pts had grade 1 CRS, and 1 (10%) pt had grade 2 CRS. No ≥ G3 CRS was observed. Median time to CRS onset was 2 days (range 1–9) and median duration was 6 days (range 3–9). No ICANS, nor DLTs were observed. There were no SAE and no treatment-related deaths. No PK difference across dose levels with Cmax 7354.7 copies/μL and AUC_{0-28} 68587 copies·day/μg. At high doses, CAR-T cells were detectable at 9 months and one responder at 21 months above the LLOQ. The patients with T_{last} ≧ 9 months had a longer PFS than those with T_{last} <9 months. No correlation of antigen expression and efficacy was observed. All patients had the positive GPRC5D expression in bone marrow CD138+MMPC at baseline, compared with 50% of relapsed pts had a reduced expression measured by flow cytometry. **Conclusions:** The updated results showed OriCAR-017 continued to provide deep and durable responses, MRD negativity was achieved in all RRMM pts, including in pts refractory to anti-CD38, PIs and IMIDs and failure to BCMA-directed therapy with excellent safety profile. The results of long-term efficacy and safety follow up support that OriCAR-017 is highly probable to be developed as a promising therapy in RRMM. Further clinical development efforts are undertaking to confirm the clinical benefits of OriCAR-017. Clinical trial information: NCT05016778. Research Sponsor: None.

Exploring the role of the combination of FDG PET plus whole body MRI for staging newly diagnosed and relapsed/refractory multiple myeloma: A prospective trial.

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Background: The integration of FDG-PET/TC and WB-MRI in the diagnosis of MM may results in higher accuracy to detect bone lesion compared to them alone. This could be translated into better outcomes if early detection of myeloma defining events leads to earlier induction or re-induction treatments. **Methods:** In our Institution, from January 2021 to January 2023, we performed a prospective trial enrolling 73 consecutive newly diagnosed and relapsed/refractory MM (median age 63 years - range 85-35), according to IMWG, in which WB-MRI was performed according to MY-RADS criteria in combination with FDG PET/CT. 31/73 (42%) had a newly diagnosed MM, 25/73 (34%) were in follow-up after autologous stem cell transplantation and 17/73 (23%) patients were affected by relapsed/refractory MM. Subsequently, in 2 cases WB-MRI were aborted and not diagnostic so patients were excluded from the final analysis. **Results:** In these 71 patients: 52/71 (73%) cases of concordance of WB-MRI and 18F PET-CT, 18/71 (25%) cases of discordance. In this group 15/18 (83%) cases FDG-PET/CT was negative and WB-MRI showed positive findings according to MYRADS criteria (5 micronodular pattern, 9 diffuse pattern e 1 focal pattern) (Figure 1 Newly diagnosed MM – diffuse pattern in WB-MRI, PET negativity), in 3/18 (17%) FDG-PET/CT was positive for focal lesions and WB-MRI was negative. IMWG criteria showed concordance with WB-MRI data in 16/18 (89 %), in 2/18 (11%) case of follow-up after autologous stem cell transplantation PET-CT showed a relapsed focal lesion while WB-MRI was negative. Accuracy of WB-MRI was 69/71 (97%), whilst PET-CT was 55/71 (77%). These results are in agreement with the literature data about the ability of WB-MRI to depict diffuse and micronodular pattern of bone marrow infiltration. **Conclusions:** Our preliminary results support a potential complementary role of WB-MRI and FDG PET/CT findings, on the management of patients with MM at both diagnosis and relapse. To date, there is no wide availability of WB-MRI because in concerning about costs and technical issues, but data are consistent with its possible future leading role in MM diagnostic work-up. Research Sponsor: None.

Assessing the prognostic value of transcriptomic data in multiple myeloma through machine learning methodologies.

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Background: Multiple myeloma (MM) is a hematological malignancy characterized by the clonal proliferation of plasma cells in the bone marrow. Identifying the characteristics within transcriptomic data of MM patients could be imperative for elucidating long-term cancer prognosis. Prediction and bioinformatic evidence could be valuable for therapeutic intervention. **Methods:** To discover a precise collection of biomarkers, a large-scale disproportionality analysis of MM patients using the FDA Spontaneous Reporting System database is conducted. This analysis aims to provide pharmacovigilance evidence regarding severe adverse events (AEs) due to medications. Additionally, pharmacogenomic insights from OMIM and MM drug targets are integrated into the analysis to carefully select 84 essential biomarkers. Seven different machine learning (ML) algorithms, namely AdaBoost, K-Nearest Neighbors (KNN), Decision Tree (DT), Gaussian Naïve Bayes (GNB), Support Vector Machine (SVM), Random Forest (RF), and Multilayer Perceptron (MLP) were then employed to assess the classification of disease outcomes. Specifically, the focus was on distinguishing deceased patients (due to MM) from surviving patients in the MM Research Foundation (MMRF) dataset based on the identified essential biomarker. **Results:** The classification involved a total of 787 patients from MMRF (624 alive and 163 deceased). Four sampling strategies (original raw data, undersampling, oversampling, and simultaneous sampling) were included in the training and testing process on ML models to alleviate the influence of imbalanced data. SVM achieved the highest accuracy while RF achieved highest mean across four sampling methods (Table). We then performed the Kaplan-Meier survival analysis of the prognostic values of essential genes. The expression of two genes (BRAC1 and CTLA4) from MMRF data when comparing deceased to survival patients was associated with patient outcomes. Additionally, seven genes were potentially prognostic factors in MM (Positive prognostic: ATM, CYBA, NR3C1, PIK3CA, and PIK3CG; Negative prognostic: IFNG and NTRK2). **Conclusions:** This study successfully showcased a computational methodology that holds potential for optimizing future clinical trials in MM. The approach includes identifying the most suitable patient population for a particular MM regimen, thereby contributing to improved patient care. It also offers strategies for reducing AEs, lowering mortality rates, and ensuring the optimal allocation of healthcare resources. Research Sponsor: BioNexus KC; KC 20-7.

	Accuracy of Data Sampling Method (%)			
Classifier	**Imbalanced**	**Undersampling**	**Oversampling**	**Simultaneous**
RF	81.4	81.4	92.3	93.1
MLP	82.3	82.6	77.1	82.1
SVM	81.0	74.3	93.9	96.3
AdaBoost	38.9	40.0	93.8	93.0
KNN	81.0	75.7	79.5	83.2
DT	72.2	66.4	76.3	75.2
GNB	80.6	73.9	69.6	72.5

Expression of alternatively spliced BCMA RNA with skipping of transmembrane domain.

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Background: The TNFRSF17 gene, which encodes for the B cell maturation antigen (BCMA), is a small gene expressed mainly on the surface of plasma cells and some DLBCL cells. This gene is composed of three exons. Exon 1 is responsible for the extracellular domain, exon 2 for the transmembrane domain, and exon 3 for the TRAF binding domain. The BCMA is currently targeted by various types of immunotherapies as a major therapeutic approach for the treatment of multiple myeloma (MM). This includes CAR-T cells, bi-specific antibodies, and antibody-drug conjugates (ADC). However, emerging data indicates that alternative splicing in genes is an important mechanism for expression of different isoforms that may influence antibody-based therapies. We explored the potential of the presence of alternative splicing in BCMA transcripts via sequencing of BCMA RNA in patients with lymphoma or multiple myeloma. **Methods:** RNA was extracted from 587 fresh bone marrow samples with lymphoid/plasma cell neoplasms or from FFPE samples with lymphoma. In addition, cfRNA was extracted from 260 peripheral blood plasma samples from patients with lymphoma or multiple myeloma. RNA was sequenced using a hybrid capture-targeted RNA panel with analysis focused on TNFRSF17 (BCMA) gene transcript. Quantification of RNA transcript was done using Salmon algorithm. **Results:** Of the 587 lymphoma/plasma cell samples, 161 (27%) samples showed alternative splicing involving deletion of exon 2 (BCMAΔEx2). Of the 260 cfRNA samples, 14 (6%) showed BCMAΔEx2. The median percentage of BCMAΔEx2 transcripts was 0.7% of total BCMA transcripts in cellular samples as compared with 9% in cfRNA samples. In cellular samples, there was a correlation between levels of BCMA and BCMAΔEx2 (R=0.63). Cases with higher levels of BCMA had significantly higher levels of BCMAΔEx2 ($P<0.0001$, Kruskal-Wallis). In contrast, cfRNA showed no correlation between levels of BCMA and levels of BCMAΔEx2 (R=021, Spearman) and mildly higher level of BCMAΔEx2 in cases with higher levels of BCMA (P=0.002, Kruskal-Wallis). **Conclusions:** BCMA exon 2 skipping is detected in a significant number of patients with multiple myeloma and lymphoma. The percentage of skipping transcripts is low in cells and relatively higher in cfRNA. Since exon 2 skipping deletes the transmembrane domain, this BCMA protein may remain in the cytoplasm or perhaps is secreted as cell-free BCMA protein. The demonstration of relatively higher levels of BCMAΔEx2 in cfRNA is likely reflecting higher turnover of cells and raises the possibility that cells with this isoform of BCMA are more aggressive than cells without the expression of this isoform. Further studies are needed to explore the clinical relevance of the expression of such abnormal BCMA protein on treatment with the various forms of anti-body-based therapy or CAR-T. Research Sponsor: None.

7515 Rapid Oral Abstract Session

Class comparison of BCMA-directed therapies in relapsed multiple myeloma.

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Background: BCMA directed CAR T cells, antibody drug conjugates (ADCs), and T cell engagers (TCEs) each have distinct strengths and weaknesses. While these agents have shown unprecedented response rates and survival outcomes, no head-head comparisons exist. We assessed the relative efficacy of different BCMA-therapies in relapsed myeloma, with a focus on high-risk subgroups. **Methods:** Retrospective study of MM patients treated at Mayo Clinic with commercial or investigational BCMA targeted therapies between April 2018-June 2023. **Results:** 385 patients (ADC=59, TCE=134, CAR T=192) with a median follow up of 20-months. The median time from diagnosis was 6.1 years. The table shows disease, and treatment characteristics. Amongst ADCs and TCEs recipients, the median treatment duration was 1.9 and 3.5 months respectively, disease progression (64% and 79%) and intolerance (22% and 10%) were the most common reasons for discontinuation. The overall response rates were 27, 50, and 86% for ADCs, TCEs and CAR T, respectively. Compared to ADCs, CAR T was associated with improved PFS (adjusted HR_{PFS}=0.29, 95%CI=0.20-0.43) and OS (aHR_{OS}=0.28, 95% CI=0.18-0.44) when adjusting for age, R-ISS, double hit high risk cytogenetic abnormalities (HRCAs), extramedullary disease (EMD, excluding paraskeletal plasmacytomas), triple class refractoriness, and the number of lines of therapy (LOTs) received in the preceding 1 year. Likewise compared to ADCs, TCEs were associated with superior PFS (aHR_{PFS}=0.59, 95% CI=0.40-0.86) and OS (aHR_{OS}=0.60, 95%CI=0.39-0.93). Amongst patients with plasma cell leukemia (PCL) or EMD at the time of BCMA therapy (n=123), median PFS was poor irrespective of the therapeutic class at 1.3, 1.7 and 6.1 months for ADCs, TCEs and CAR T, respectively. Equally, for patients previously treated with BCMA therapy (n=58), median PFS was poor regardless of class at 1.9, 2.4 and 3 months for ADCs, TCEs and CAR T, respectively. Of 229 relapses the mode of relapse was known in 192 cases (84%), with 101 (52%) having EMD at relapse. **Conclusions:** While contingent on myriad other factors, patients able to receive BCMA-directed CAR T therapy experience superior survival compared to ADC and TCEs.EMD, PCL and BCMA-exposed populations are recalcitrant to BCMA-directed immunotherapy, and EMD is a common means of relapse. Research Sponsor: None.

	ADC, N = 59[1]	CAR T, N = 192[1]	TCE, N = 134[1]	p-value[2]
Age (years)	61 (56, 68)	58 (48, 64)	59 (53, 66)	**0.008**
R-ISS 3 at diagnosis	5 (8.5%)	20 (10%)	17 (13%)	0.7
Double hit HRCA prior to BCMA	4 (6.8%)	43 (22%)	25 (19%)	**0.027**
Triple class refractory	50 (85%)	149 (78%)	119 (89%)	**0.029**
Penta class refractory	37 (63%)	61 (32%)	65 (49%)	**<0.001**
≥4 LOTs in preceding 1-year	10 (17%)	14 (7.3%)	13 (9.7%)	0.089
No. of LOTs prior to BCMA	7.00 (5.00, 8.50)	5.00 (4.00, 7.00)	6.00 (4.00, 7.00)	**<0.001**
EMD/PCL prior to BCMA	19 (40%)	56 (30%)	48 (39%)	0.2
BCMA exposed	13 (22%)	15 (7.8%)	30 (22%)	**<0.001**

1 Median(IQR); n(%), 2 Kruskal-Wallis rank sum test; Pearson's Chi-squared test.

Outcomes of patients who received CAR T cell therapy and developed IEC-HS treated with cytokine directed therapy.

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Background: Immune effector cell hemophagocytic lymphohistiocytosis IEC-HS is a complication of CAR T cell therapy (CART). This study aims to look at the outcomes of CART patients who develop IEC-HS. **Methods:** Patients who developed IEC-HS after receiving CART and patients who developed IEC-HS without (nonCART) between December 2020 and March 2022 were included. **Results:** The 20 CART patients were older than the 25 nonCART patients. Peak ferritin, fibrinogen, CRP, serum creatinine and transaminases were similar between the 2 group. CART patients had lower white blood cell count and platelets and bilirubin than the nonCART patients. CART patients were more like to have markedly elevated IL-6 levels (> 315 mg/ml), higher IL-18, higher MCP-1, and suppressed IL-1β and GMCSF than nonCART patients (Table). Treatment of IEC-HS included tocilizumab (n = 19), anakinra (n = 18) siltuximab (n = 4) and basiliximab (n = 4), dexamethasone (n = 18) methylprednisolone (n = 6), etoposide (n = 1) and ruxolitinib (n = 1). A significant response defined by a 90% reduction or normalization of the cytokine was observed with IL-10 and IFN-ɣ in 92.3% and 84.6% of the CART patients respectively. An intermediate response was noted with TNF, IL-6, MCP-1 and MIP-1 in 38.4%, 30.8% and 61.6% and 38.5% of the patients respectively. No patient had a significant response in IL-2Rα or IL-1β and only 7.7% had a significant response in IL-18. Of the 5 patients who had a MIP-1 response, 4 were on basiliximab +/- high flow continuous venovenous hemofiltration and the only patient that had an IL-18 response was on both modalities. The 100-day mortality after IEC-HS in the CART patients was 40% and was associated with higher peak and lower best ferritin but not the percentage reduction (Table). Higher TNF (90.3 pg/ml vs 37.2 pg/ml, p = 0.05), markedly elevated levels of IL-6 (92% vs 50%, p = 0.03) and IL-10 (33% vs 0%) and an IL-6 response (44.4% vs 0%) were associated with survival at day 100. IL-6 responders had lower peak ferritin vs IL-6 nonresponders (14066 mcg/L vs 45051 mcg/L, p = 0.08). *Enterococcus faecium* bacteremia developed in 75% of the nonsurvivors vs 16.6% of the 100-day survivors (p = 0.009). Survivors cleared the enterococcus bacteremia within days while nonsurvivors had protracted bacteremia. **Conclusions:** IEC-HS is devastating complication of CART. Anti-cytokine therapy can reduce some cytokines and ferritin but overimmunosuppression may lead infectious complication, in particular with *E. faecium*. Better biomarkers are needed to finetune immunosuppressive therapy in order to avoid over-immunosuppression. Research Sponsor: None.

	Survivors (n = 12)	Non-Survivors (n = 10)	p - value
Age	63	66	0.71
Sex (female)	42%	38%	0.86
Peak ferritin (mcg/L)	17509	45035	0.003
Best ferritin (mcg/L)	1569	10945	0.002
TNF - pg/ml	90.3	37.2	0.05
IL-6 - (>315 pg/ml)	92%	50%	0.03
IL-10 - pg/ml (> 750 pg/ml)	0%	33%	
Ferritin reduction	86.8%	71.0%	0.07
IL-6 reduction	44.4%	0%	
Enterococcal bacteremia	75.0%	16.7%	0.009

7517 Rapid Oral Abstract Session

Longer-term follow-up of patients (pts) receiving prophylactic tocilizumab (toci) for the reduction of cytokine release syndrome (CRS) in the phase 1/2 MajesTEC-1 study of teclistamab in relapsed/refractory multiple myeloma (RRMM).

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Background: Emerging data suggest that administering toci prior to bispecific antibodies reduces the incidence of CRS, which may support outpatient therapy initiation. We previously showed that the incidence of CRS with teclistamab, the first approved BCMA×CD3 bispecific antibody with weight-based dosing for the treatment of pts with triple-class exposed RRMM, was reduced from 72% in the overall MajesTEC-1 study population to 26% in a cohort receiving a single dose of toci before the first teclistamab step-up dose. Here, we present an updated analysis with longer-term follow-up. **Methods:** Pts with triple-class exposed RRMM received subcutaneous teclistamab 1.5 mg/kg weekly in a prospective exploratory cohort or at a comparable fixed dose, following 2 step-up doses. Toci 8 mg/kg was given intravenously ≤4 hours before the first teclistamab step-up dose. CRS was graded per Lee et al (*Blood* 2014;124: 188-95) and managed per the study protocol. **Results:** This analysis included 24 pts with median follow-up 8.1 months (range, 0.9–13.2). Median age was 72 years (range, 50–82); 100% had ECOG PS score ≤1; 96% had International Staging System stage I/II; 74% had standard-risk cytogenetics; 21% had extramedullary plasmacytomas; 33% had ≥30% bone marrow plasma cells (biopsy or aspirate). Pts had a median of 4 prior lines of therapy (range, 2–9); 58% were triple-class refractory. CRS occurred in 6 pts (25%; 2 grade 1, 4 grade 2, no grade ≥3); 3 pts each had 1 recurrent CRS event. Median time to CRS onset was 2 days (range, 1–3); median duration was 2 days (range, 2–4). CRS was managed with additional toci in 5/6 pts and steroids in 1/6; all CRS events resolved and none led to teclistamab discontinuation. Most common adverse events (AEs; any grade/grade 3/4) were infections (79%/25%), neutropenia (63%/63%), and anemia (58%/25%); 5 pts had a neurotoxicity AE (grade 1 dizziness; grade 1 headache; grade 1 insomnia; grade 2 headache; grade 2 immune effector cell-associated neurotoxicity syndrome). Overall response rate (n=22) was 73% (59% very good partial response or better). Timing of interleukin (IL)-6 induction in the prophylactic toci cohort was consistent with the phase 1 MajesTEC-1 population, with higher IL-6 levels as observed in other studies of IL-6 receptor-blocking antibodies. **Conclusions:** Prophylactic toci reduced the incidence of CRS with teclistamab, with a 65% relative reduction vs the overall MajesTEC-1 population (grade 1, 8% vs 50%; grade 2, 17% vs 21%). No new safety signals or impact on response to teclistamab was observed with longer follow-up. Prophylactic toci may be a useful measure to consider when selecting pts for outpatient administration of teclistamab in the future. This approach is being evaluated in the phase 2, multicenter, prospective OPTec study (NCT05972135). Clinical trial information: NCT03145181 / NCT04557098. Research Sponsor: Johnson & Johnson Innovative Medicine.

BCMA-directed CART therapy in patients with multiple myeloma and CNS involvement.

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Background: CART therapy represents a breakthrough in therapy for patients (ptns) with relapsed or refractory (R/R) multiple myeloma (MM). Pts with MM who have CNS involvement are commonly excluded from clinical trials and have limited therapeutic options. We evaluated the safety and efficacy of BCMA-directed CART therapies in ptns with MM and CNS involvement. **Methods:** 5 US academic medical centers contributed data to this retrospective analysis. 11 ptns with MM with CNS involvement received BCMA-directed CART (7 and 4 pts received ide-cel and cilta-cel, respectively). **Results:** Eight (72%) ptns were male, 3 (27%) had high-risk (HR) cytogenetics, and 10 (91%) had extramedullary disease (dz). Four (36%) ptns had brain/cranial nerve dz, 1 (9%) had spine dz, and 6 (55%) had both. CNS dz was evident on MRI in 100% of ptns and on CSF in 4 ptns (36%). Five ptns (45%) had ≤60 days between CNS diagnosis and CART therapy, 3 (27%) had >300 days from CNS dz with 2 requiring CNS-directed therapy (CNS-Tx) close to CART during bridging, and 3 (27%) were diagnosed soon after CART infusion. Six (55%) ptns received CNS-Tx as part of bridging; radiotherapy (RT, 2 ptns), RT + intrathecal (IT) chemotherapy (chemo) (2 ptns), IT chemo (1 ptn), and surgery + RT (1 ptn). Five (45%) ptns didn't receive CNS-Tx as part of bridging for the following reasons; 3 were diagnosed soon post CART and received RT post-infusion, 1 had recent chemo, and 1 was treated for CNS dz 587 days prior to CART and didn't require CNS-Tx during bridging. Seven ptns (64%) had treated CNS dz at the time of lymphodepleting chemo. Nine (82%) ptns had grade (G) 1/2 CRS and none had G ≥3CRS. Two ptns (18%) had G1 ICANS, 1 (9%) had G3 ICANS, and none had G4 ICANS. Two ptns experienced delayed neurotoxicity post ide-cel, 1 with delayed lethargy that was treated with steroids, and the other with progressive multifocal leukoencephalopathy that was treated with steroids plus pembrolizumab. None had delayed parkinsonian side effects. With a median follow-up of 104 days post-infusion, the best responses achieved were 45% CR/sCR, 18% VGPR, 9% PR, with an overall response (ORR) of 73%. Seven ptns were evaluable for CNS responses by day 90 with a 100% CNS response rate defined by improved imaging findings or clearance of CSF involvement. CNS recurrence occurred in 1 ptn (9%) by day 172 while 5 (45%) had continued systemic response at last assessment. **Conclusions:** This study suggests that BCMA directed CART therapy in ptns with MM and CNS involvement is safe and feasible. Of the evaluable ptns for CNS response, 100% showed CNS response by day 90. Larger studies with longer follow up are needed to confirm these findings. Research Sponsor: None.

Key characteristics and outcome.

	N=11 (%)
Age, median (range)	58 (36-71)
HR Cytogenetics	3 (27%)
Extramedullary Dz	10 (91%)
CRS G ≥3	0
ICANS G≥3	1 (9%)
Delayed Neurotoxicity	2 (18%)
Parkinsonian side effects	0
ORR	73%
CNS Response	100%

Real world outcome of patients with multiple myeloma who received bispecific antibodies after CAR-T therapy.

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Background: There are 2 CAR-T products and 3 bispecific antibodies (BsAbs) that are FDA-approved for patients (pts) with relapsed, refractory multiple myeloma (MM). Clinical trials experience to date suggests that clinical response of BsAb is less impacted after CAR-T therapy. We examined the outcome of pts who received BsAb in standard-of-care (SOC) practice at Mayo Clinic Rochester. **Methods:** Retrospective analysis of MM patients who received FDA-approved BsAb at Mayo Clinic, Rochester between 12/2022- 1/2024. IMWG criteria was used for clinical response. **Results:** Sixty-two patients received BsAbs: 77% (48/62) received teclistamab, and 23% (14/62) received talquetamab. Median age was 62 years (range: 33-81), 60% (37/62) were males, and 45% (28/62) received prior CAR-T. Patients who had prior CAR-T therapy had more prior lines of therapy compared to those who did not. Overall, ORR to teclistamab was 61%, which is comparable to previous studies and other real-world reports. ORR and ≥CR rates were comparable between patients with and without prior CAR-T (Table). Of the 28 pts who received CAR-T before BsAbs, 61% (17/28) received idecabtagene vicleucel, 10% (3/28) were ciltacabtagene autoleucel, and 29% (8/28) on clinical trial. We then compared outcome of BsAb between pts who had relapsed from CAR-T within 1 year (n=21, median PFS: 8.84 months (range, 1.12, 10.84)) or after 1 year (n=7, median PFS: 16.62 months (range, 13.30, 36.20)). At the time of BsAb infusion, pts with who relapsed < 1 year vs ≥1 year post CAR-T had comparable blood counts, ALC, M-protein and involved FLC levels, CRP, ferritin and LDH. BsAb CR/sCR rate was significantly higher in pts with disease relapse ≥1 year compared to <1 year post CAR-T (57% vs 14%, p=0.02). **Conclusions:** Irrespective of prior CAR-T exposure, BsAb have clinical activity in SOC practice in pts with MM. Our preliminary data suggest that responses to BsAbs are better in pts with late compared to early relapse post CAR-T. Longer follow-up is needed to understand the duration of response. Larger, multi-center studies with longer follow-up will help identify factors that impact BsAb response post CAR-T. Research Sponsor: None.

Baseline demographics and clinical outcomes.

Variables at BsAb Infusion	CART Exposed (N=28)	No Prior CAR-T (N=34)	Total (N=62)	p value
Prior lines of therapy, median (Range)	7.0 (4.0, 17.0)	5.0 (2.0, 14.0)	6.0 (2.0, 17.0)	**< 0.01**
ORR, n (%)	14.0 (50.0)	18.0 (52.9)	32.0 (51.6)	0.54
CR/sCR, n (%)	7.0 (25.0)	5.0 (14.7)	12.0 (19.4)	0.31
PFS (months), median (95%CI)	3.1 (2.3, NR)	NR (1.2, NR)	5.1 (2.6, NR)	0.75
Timing of relapse post CAR-T	**Relapse <1 year (N=21)**	**Relapse≥1 year (N=7)**	**Total (N=28)**	**P value**
ALC at BsAb infusion, x10(9)/L, median (range)	0.63 (0.2, 5.6)	0.79 (0.5, 1.4)	0.65 (0.2, 5.6)	0.14
ORR, n (%)	11.0 (52.4)	6.0 (85.7)	17.0 (60.7)	0.12
CR/sCR, n (%)	3.0 (14.3)	4.0 (57.1)	7.0 (25.0)	**0.02**
PFS, months, median (95%CI)	3.1 (1.8, NR)	NR (2.3, NR)	3.1 (2.3, NR)	0.13

Evaluation of cytokine release syndrome (CRS) in patients with relapsed or refractory multiple myeloma (RRMM) receiving step-up priming doses and longer dosing intervals of elranatamab: MagnetisMM-9.

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Background: Elranatamab (ELRA) is a humanized BCMA-CD3 bispecific antibody. In the phase 2 registrational MagnetisMM-3 (MM-3) trial, SC ELRA was given as 2 step-up priming doses (12 mg on C1D1 and 32 mg on C1D4) followed by 76 mg QW in patients (pts) with RRMM. Overall, 56.3% of pts had CRS (grade 2, 14.3%; no grade ≥3). Most events occurred after doses 1 (44.5%), 2 (20.2%), and 3 (5.9%); 0.8% (1 pt) had CRS with doses 4+. Recurrent CRS (>1 event) occurred in 15.1% of pts (Lesokhin *Nat Med* 2023). **Methods:** MagnetisMM-9 (MM-9; NCT05014412) is a phase 1/2, open-label, nonrandomized study of ELRA examining an alternative 2-dose step-up priming regimen (4 and 20 mg on C1D1 and C1D4, respectively). Eligible pts had RRMM and were refractory to ≥1 IMiD, ≥1 PI, and ≥1 anti-CD38 antibody. After the priming doses, ELRA 76 mg was given QW for 6 cycles (Part 1) or for 1 cycle followed by 116 or 152 mg Q2W for 5 cycles (Part 2A). The RP2D from Part 2A (152 mg) was evaluated in Part 2B (dose expansion). The rate of grade ≥2 CRS per ASTCT criteria during C1 is the primary endpoint for both parts. Secondary endpoints include evaluation of AEs and PK. Here, we report the overall safety and CRS profile associated with the 4/20 mg priming regimen. **Results:** For 85 treated pts, median age was 64.0 y; 49.4% were male; 23.5% had EMD; 31.8% had high-risk cytogenetics. Pts had a median of 5.0 (range, 1-12) prior LOTs; 85.9% had triple-class refractory disease. After a median follow-up of 7.4 mo, the most common (>50%) AEs were CRS (63.5%; grade ≥2, 15.3%) and neutropenia (54.1%; all grade ≥2). ICANS occurred in 4.7% of pts (all grade ≤2). The grade ≥2 CRS rate in C1 was 14.1% (90% CI, 8.4-21.9). CRS rates after the first 3 doses are in the the table. For doses 4+, any grade (grade ≥2) CRS was observed in 10.6% (3.5%) of pts overall, 12.1% (3.0%) of pts continuing to receive 76 mg (n=33), 25.0% (0%) of pts receiving 116 mg (n=12), and 5.0% (5.0%) of pts receiving 152 mg (RP2D; n=40). Overall, recurrent CRS was observed in 20.0% of pts. The geometric means (CV%) of free ELRA concentrations 24 h ($C_{max-24h}$) after step-up doses 1 and 2 were 85.64 (48%) and 242.8 (55%). **Conclusions:** The 4/20 mg step-up priming regimen and alternative dosing schedules resulted in similar safety and incidence of overall and grade ≥2 CRS events vs the regimen used in MM-3 (12/32 mg), with no new safety signals identified. However, the CRS profile in this study differed, with more CRS after doses 2, 3, and 4+ and a higher prevalence of recurrent CRS. The $C_{max-24h}$ of free ELRA (CV%) after the priming doses were lower than those in MM-3 (107.4 [47%] and 405.1 [72%], respectively). Thus, the priming regimen used in MM-3 remains the optimal regimen for mitigating CRS. Future analyses of ongoing studies will be used to confirm these results. Clinical trial information: NCT05014412. Research Sponsor: Pfizer Inc.

	Any Grade CRS, %	Grade ≥2 CRS, %
4 mg step-up dose	29.4	5.9
20 mg step-up dose	27.1	2.4
First full 76 mg dose	21.2	4.7

Effect of talquetamab on responses in patients with relapsed and refractory multiple myeloma with prior exposure to T-cell directed therapies.

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Background: Talquetamab (Talq) is a GPRC5D and CD3 bispecific antibody approved for use in RRMM in pts previously treated with at least 4 lines of therapy, including a PI, IMiD, and CD38 monoclonal antibody. Data from the MonumenTAL-1 study showed an ORR of 63% at 11.8 median months of follow-up in pts previously receiving T-cell directed therapies (TCDT). CRS was noted in 77% of pts, and ICANS in 3% of patients receiving TCDT. Here, we present data further supporting the safety and efficacy of Talq in RRMM pts previously treated with TCDT. **Methods:** We performed a retrospective chart review with IRB approval to identify pts with RRMM previously receiving TCDT now receiving Talq. CRS and ICANS were graded per ASTCT consensus criteria, while responses were graded based on the IMWG response criteria. **Results:** 21 pts were evaluable for response, safety, and survival analyses. Median age was 64 years (range 39-89), 52.4% (n = 11) were male, and 23.8% (n = 5) had an ECOG PS $\geq$2. 61.9% (n = 13) had high risk cytogenetics (defined as del17, t(4;14), t(14;16)). Pts were heavily pretreated with a median of 7 (4-11) prior lines of therapy. 85.7% (n = 18) were triple-class refractory, and 57.1% (12) were penta-class refractory. 76.2% (n = 16) received prior CAR-T; 38.1% (n = 8) received prior Antibody Drug Conjugate (ADC);19.0% (n = 4) received both prior CAR-T and ADC. 9.5% (n = 2) of pts received prior tri-specific NK cell engagement therapies. 85.7% (n = 18) of patients in our study did not meet inclusion criteria for the MonumenTAL-1 study, including 38.1% (n = 8) for Hgb $<$ 8.0, 28.6% (n = 6) for Plt $<$ 50, 33.3% (n = 7) for EGFR $<$ 40, 23.8% (n = 5) because of ECOG $\geq$2, and 42.9% (n = 9) for gene modified adoptive cell therapy within 3 months prior to Talq. With a median follow up of 2(1-5) months, OR and CR response rates were 71.4% (n = 15) and 28.6% (n = 6), respectively. Toxicity was comparable to the MonumenTAL-1 trial. CRS occurred in 57% (n = 12) of patients, (7 pts with grade 1, 5 pts with grade 2), with 23.8% requiring Tociluzumab. Median time to onset of CRS was 4 (1-7) days after the first dose, and median duration was 3.5 (1-10) days. 19.0%(n = 4) patients had ICANS, (1 pt with grade 1, 2 pts with grade 2, and 1 pt with grade 3). Infections were seen in 3 (14%) pts. 8 (38%) pts had treatment delays, mainly due to CRS, ICANS, and infections. 61.9% (n = 13), 28.6% (n = 6), and 76.2% (n = 16) of patients experienced skin AEs, nail AEs, or dysgeusia, respectively. 1 (4.8%) patient discontinued treatment after initial step-up dose due to ICANS and infection. There were no Talq related deaths. **Conclusions:** This single center study in pts with heavily pretreated and prior TCDTs demonstrated favorable ORR (71.4%) and CR (28.6%) rates, comparable to patients in the MonumenTAL-1 trial with and without exposure to prior T cell directed therapies. Results on PFS, OS, and AEs will be reported with continued follow up and will be presented in the meeting. Research Sponsor: None.

Rapid reduction of free light chains and improvement in renal outcomes in patients with newly diagnosed multiple myeloma admitted with acute kidney injury with daratumumab-based therapy and without plasmapheresis.

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Background: Cast nephropathy is the most common cause of acute kidney injury (AKI) in patients with multiple myeloma (MM), where light chain accumulation in the distal nephron leads to obstruction and injury of the distal and collecting tubules. A prompt reversal of renal injury is paramount to improve outcomes. Daratumumab (dara), an anti-CD38 monoclonal antibody, has significant clinical efficacy in MM. We report the effects of early initiation of dara-based therapy on sFLC reduction and renal recovery in pts admitted with a new diagnosis of MM and AKI. **Methods:** Between April 2016 and Dec 2023, pts admitted with newly diagnosed MM (NDMM) with AKI (sCr ≥2 mg/dL and/or eGFR <30 mL/min/1.73 m^2 by CKD-EPI) and involved sFLC ≥500 mg/L who started dara-based therapy were identified and retrospectively reviewed. We studied pts who started treatment ≤14 days of presentation. Outcomes included sFLC kinetics and renal outcomes per IMWG criteria at 3 months. **Results:** We identified 20 NDMM pts. Median age was 65 (range 44-87). Median peak sCr at admission was 6.5 mg/dL (range 3.1-17.8) with median eGFR of 8 mL/min/1.73 m^2 (range 2-16). Nine pts started hemodialysis (HD). The median peak sFLC at diagnosis was 6603 mg/L (range 1839-26,023). Initial dara regimens included cyclophosphamide, bortezomib, and dexamethasone in 11 pts (55%) and with bortezomib and dexamethasone in 9 pts (45%). Median time between presentation and dara start was 3 days (range 0-10). No pts underwent plasmapheresis. Within 1 cycle of therapy, all 20 pts achieved sFLC reduction ≥50% at a median of 3 days (95% CI, 3-7 days). Median time to sFLC ≤500 mg/L was 13 days (95% CI, 9-33 days), and this was in 15 out of 16 pts (94%) assessable for response after 1 cycle of treatment. At 3 m, the overall renal response (≥minor response) was 85% (N=17), with complete, partial, and minor responses in 50% (N=10), 10% (N=2), and 25% (N=5), respectively. Twelve pts (60%) recovered renal function with eGFR ≥40 mL/min. Of 9 pts who required HD, 4 and 6 pts were free of HD at 3 m and 12 m, respectively. Two pts on HD died within 3 m (age 86, from aspiration pneumonia; age 87, from progressive disease); and 1 continued on HD at 12 months. Fourteen pts (70%) later added lenalidomide, and 3 pts (15%) underwent autologous stem cell transplant. The IMWG ORR was 100% with VGPR 90%. With a median follow up of 25 m, median PFS was 47 m (95% CI 12-not reached) and 2-year OS was 84% (95% CI 68-100%). **Conclusions:** This is the largest reported cohort of NDMM pts hospitalized with AKI treated with dara-based induction therapy. Treatment with dara combinations shows rapid and deep reductions in sFLC, improving renal recovery outcomes. These findings highlight the efficacy of early use of dara in pts with MM-induced AKI and provide an approach without plasmapheresis. Research Sponsor: None.

Supplement use habits and perceptions in patients with plasma cell disorders.

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Background: Dietary supplement usage is prevalent among cancer patients in the United States (US), estimated at 70% (Du *et al.*, 2020). For patients with plasma cell disorders (PCDs), there is a strong interest in supplement use. Our 23-question survey aims to understand the perceptions, habits, and knowledge surrounding specific supplements — Vitamin D, omega-3 fatty acids, turmeric/curcumin, and probiotics. **Methods:** From September 2023 to January 2024, 480 survey responses were collected via HealthTree Cure Hub. Deidentified demographic and survey data were retrieved, and summary statistics were used to evaluate responses. **Results:** Survey participants were predominantly female (58%), white (78%), aged ≥65 (61%), with a college degree or above (67%), and from the US (90%). While most patients (71%) used supplements pre-diagnosis, there was a 46% increase in supplement use post-diagnosis, where95% used supplements. Most patients obtained supplement information online — including medical media (45%) and myeloma education websites (28%)— and from physicians, such as oncologists (46%) or primary care providers (34%). Patient's goals for supplement use included immune support (70%), prevention of nutritional deficiencies (54%), or halting cancer progression (38%). Of patients, 63% discussed their supplement use with their physician, with 74% preferring their oncologist's recommendations. Overall, 91% of patients expressed interest in research on the risks and benefits of supplement use. **Conclusions:** This survey underscores the unmet need for research on supplements. Despite limited evidence, most survey participants reported an increase in supplement use after being diagnosed with a PCD, primarily interested in their oncologist's recommendations. Research Sponsor: None.

Question	N (%)
Supplement use	Pre-diagnosis **342 (71%)** Post-diagnosis **458 (95%**
Source of Information on supplements*	Online Medical Media **216 (45%)** Hematologist/oncologist **221 (46%)** Primary care provider **161 (34%)** Myeloma Education Website **136 (28%)** Online Patient Forums **97 (20%)** Dietitian **11 (2%)** Naturopathic Doctor **2 (0.4%)**
Motivation for Supplement Use*	Immune Support **337 (70 %)** Prevent nutritional deficiencies **258 (54%)** Stop cancer progression **184 (38%)**
Monthly Supplement Spending	$0 **8 (2%)** $1-20 **164 (34%)** $21-50 **162 (34%)** $51-100 **64 (13%)** $101-200 **44 (9%)** >$200 **28 (6%)**
Since being diagnosed, has your spending on supplements	Increased **282 (59%)** Decreased **25 (5 %)** No change **160 (33%)** Not applicable **13 (3%)**
Received financial support to pay for supplements	Yes - **24 (5%)** No- **442 (92%)** Don't use supplements - **14 (3%)**
Would you like your hematologist/oncologist to give you recommendations about supplement use and your diagnosis?	Yes **355 (74 %)** No **44 (9%)** Not Sure **75 (16%)** Blank **6 (1%)**
Interested in more research on the risks and benefits of supplements for a plasma cell disorder diagnosis?	Yes **435(91%)** No **19 (4%)** Not sure **26 (5%)**

*Question with select all that apply.

Association of patient (pt) factors and pharmacodynamic biomarkers with progression-free survival (PFS) after idecabtagene vicleucel (ide-cel) in pts from KarMMa-3.

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Background: Ide-cel, a B-cell maturation antigen (BCMA) CAR T cell therapy (tx), significantly improved PFS vs standard regimens in pts with triple-class–exposed relapsed or refractory MM (13.8 vs 4.4 mo, $P<0.001$) in KarMMa-3. Median PFS in the ide-cel treated population (pop; n=225) was 15.7 (95% CI, 12.5–18.9) mo (Rodríguez-Otero ASH 2023). PFS benefit of ide-cel was consistent across high-risk pt subgroups. Previous analyses indicated that lower levels of baseline soluble BCMA (sBCMA; measure of tumor burden) and lower basal inflammatory markers were positively associated with response to ide-cel. This analysis identified pre- and post-tx pt factors and pharmacodynamic biomarkers associated with longer PFS with ide-cel in the treated pop. **Methods:** Median PFS (15.7 mo) of the treated KarMMa-3 pop was used to divide pts into 2 groups: longer PFS (>15.7 mo; n=106) or shorter PFS (≤15.7 mo; n=110). Censored pts (n=9) who had a PFS <15.7 mo were excluded. Pre- and post-tx values for laboratory parameters, MM assessments, sBCMA, inflammatory cytokines, ide-cel transgene persistence, and minimal residual disease (MRD; 10^{-5} sensitivity) were evaluated. Serum free light chains (sFLCs) were evaluated as biomarkers of plasma cell clearance; clearance was defined as level below limit of detection of both involved and heterotypic sFLC. Analyses were post hoc and exploratory; statistical tests were used to identify relationships of interest. **Results:** In total,94% of pts with longer PFS achieved a best overall response of ≥very good partial response and had lower levels of β-2 microglobulin ($P<0.01$), lactate dehydrogenase ($P<0.01$), and sBCMA ($P<0.01$) at baseline. Inflammatory markers (eg, tumor necrosis factor, ferritin, C-reactive protein) were significantly higher ($P<0.05$) in pts with shorter vs longer PFS at baseline. All pts with longer PFS (100%) achieved sFLC clearance after ide-cel infusion. Among pts who achieved initial clearance, pts with longer PFS had a longer duration of sFLC clearance than shorter PFS ($P<0.001$), suggesting more durable engraftment of ide-cel and tumor control. Within MRD-evaluable pts, those with longer PFS achieved higher MRD negativity vs shorter PFS (87% vs 41%) at 6 mo post infusion with sustained MRD negativity (53% vs 4%) lasting 8–12+ mo. No apparent relationship was observed between PFS and ide-cel persistence at 6-, 9- and 12-mo post-infusion. **Conclusions:** Pts with longer PFS after ide-cel infusion had relatively lower tumor burden and lower levels of peripheral inflammatory markers before tx, highlighting the importance of managing baseline tumor burden before CAR T cell infusion to achieve optimal response. Complete and sustained clearance of sFLCs within the first few mo post infusion was associated with longer PFS. MRD negativity at 6 mo and sustained MRD negativity were enriched in pts with longer PFS. Clinical trial information: NCT03651128. Research Sponsor: 2seventy bio and Celgene, a Bristol-Myers Squibb company.

OPTec: A phase 2 study to evaluate outpatient (OP) step-up administration of teclistamab (Tec), a BCMA-targeting bispecific antibody, in patients (pts) with relapsed/refractory multiple myeloma (RRMM).

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Background: Tec is the only approved BCMA×CD3 bispecific antibody with personalized, weight-based dosing for triple-class exposed RRMM. In the MajesTEC-1 study, Tec showed deep, durable responses and a manageable safety profile. Cytokine release syndrome (CRS) occurred in 72% of pts during Cycles 1-2, and 33% of pts had recurrent CRS grade (gr) ≤3 (gr 3, 0.6%). Tocilizumab (Toci) is used to manage CRS. In a separate MajesTEC-1 cohort, pts who received prophylactic Toci (proToci) experienced less CRS, compared with pts who did not (26% vs 72%). Administering the Tec step-up dosing (SUD) regimen in the OP setting may make Tec more accessible, especially at community centers. Therefore, we are investigating whether proToci can reduce the incidence and severity of CRS associated with Tec and facilitate safe OP administration. **Methods:** This single-arm, non-randomized, multicenter, prospective study (NCT05972135) will evaluate proToci in pts treated with Tec using an OP SUD regimen. The primary endpoint is the overall incidence of CRS. Secondary endpoints include recurrent CRS gr ≥3, and any gr infections, neurotoxicity (NT) including ICANS, neutropenia, and efficacy. Eligible pts are ≥18 years with RRMM and ≥4 prior lines of therapy. Pts with rapidly progressing MM, CNS involvement, active infection, or contraindication to Toci are excluded. Toci 8 mg/kg IV is administered 2 to 4 hours prior to SUD 1 of Tec in an OP setting. The Tec SUD regimen consists of 0.06 mg/kg subcutaneously (SC), 0.3 mg/kg SC 2 to 4 days later, and 1.5 mg/kg SC 1 week after SUD 1. Tec 1.5 mg/kg SC is then given weekly for 12 cycles (28-day) or until MM progression or unacceptable toxicity. Pts with ≥PR after 6 mo can receive 1.5 mg/kg SC biweekly. IVIG is allowed in pts with serum IgG <400 mg/dL. **Results:** Ten pts will be enrolled at 4 Sarah Cannon / US Oncology community sites in a safety and PK/PD cohort, followed by 40 pts at 12 sites. After the first 6 pts, a Data Review Committee (DRC) meeting was held. Median age was 74 (56 to 83) yrs; half of pts were male. Pts had received a median of 4.5 (4 to 6) prior therapies. One pt with diffuse bony lesions had an SAE of bilateral leg weakness and pain unrelated to Toci or Tec, did not complete the SUD regimen, and died on C1D40 of unknown causes. The other 5 pts completed the SUD regimen per protocol. AEs in >1 pt were fatigue, headache and neutropenia (2 each). Gr 2 hypotension (1 pt) and gr 1 confusion and dizziness (1 pt each) were not felt due to CRS or ICANS. Stopping criteria (gr >3 CRS or NT/ICANS) were not met. The DRC recommended proceeding with enrollment. **Conclusions:** Initial results indicate that proToci prior to SUD 1 of Tec may mitigate the risk of CRS. Enrollment is ongoing to determine if proToci may make Tec safe to give in an OP setting and increase accessibility in community centers. The full safety cohort will be presented at ASCO. Clinical trial information: NCT05972135. Research Sponsor: Johnson & Johnson Innovative Medicine; Sarah Cannon Research Institute.

Validation of prototype biomarkers to identify risk factors of inflammatory adverse events (iAEs) following idecabtagene vicleucel (ide-cel) infusion in patients with relapsed and refractory multiple myeloma (RRMM) in KarMMa-3.

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Background: iAEs, such as cytokine release syndrome (CRS) and macrophage activation syndrome (MAS), can occur after infusion of chimeric antigen receptor T cell therapies such as ide-cel, but are typically low-grade and manageable with tocilizumab and corticosteroids. Although high-grade iAEs are rare with ide-cel, identification of patients at increased risk may improve management and remains an unmet need. Three composite biomarkers (multivariate models) of iAE risk were previously developed in a discovery cohort from the KarMMa and KarMMa-2 studies of ide-cel in RRMM (Mashadi-Hossein A, et al. *J Clin Oncol* 2023; 41(16_suppl):e20005). Here, we validate these 3 prototype models for risk of developing high-grade iAEs after ide-cel infusion. **Methods:** Two models used pretreatment patient and routine clinical laboratory parameters; the third model also included change in 6 exploratory cytokines from baseline to 1 day following ide-cel infusion. To validate, each model was retrospectively applied to KarMMa-3 (NCT03651128) data in a blinded fashion, and sensitivity and specificity to identify grade ≥3 CRS and any-grade MAS were determined. Model performance thresholds used for sensitivity and specificity were 90% and 50%, respectively. Performance for identifying grade 2 CRS was also analyzed post hoc. **Results:** The first and simplest model comprised a manual algorithm with 7 features; it identified patients with grade ≥3 CRS or MAS with 85% sensitivity and 60% specificity. The second model comprised 19 routinely measured pretreatment features; it identified grade ≥3 CRS with 91% sensitivity and 59% specificity, and any-grade MAS with 60% sensitivity and 88% specificity. The third and most complex model comprised 7 pretreatment clinical features and 6 exploratory cytokines; it identified grade ≥3 CRS with 100% sensitivity and 51% specificity, and any-grade MAS with 100% sensitivity and 81% specificity. None of the models identified grade ≥2 CRS with passable sensitivity or specificity. Clustering analyses across all features showed that only a subset of grade 2 CRS cases was within the previously identified high-risk iAE cluster while the remaining grade 2 CRS cases were spread across other clusters. **Conclusions:** Two of the 3 composite biomarkers met validation criteria for grade ≥3 CRS risk. Criteria were not met for grade 2 CRS, suggesting these models are specific to higher-grade events and that grade 2 CRS represents a more heterogeneous group of patients. While high-grade iAEs are rare with ide-cel, these models may further optimize the robust benefit–risk profile that ide-cel has demonstrated by helping identify, prior to or shortly after infusion, patients most at risk for severe events. Clinical trial information: NCT03651128. Research Sponsor: 2seventy bio and Celgene, a Bristol-Myers Squibb company.

Evaluation of a novel method to guide belantamab mafodotin dosing in multiple myeloma based on a patient-reported questionnaire.

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Background: Ocular adverse events (OAEs, best corrected visual acuity [BCVA] change from baseline and keratopathy) are common with belantamab mafodotin (belamaf; GSK2857916) and often necessitate an ophthalmic exam to guide dosing. Herein, we evaluate a novel approach for belamaf dose modifications in transplant ineligible patients (pts) with newly diagnosed MM, treated with an extended schedule of belamaf with lenalidomide and dexamethasone (Rd) in the BelaRd study. **Methods:** BelaRd (NCT04808037) is an ongoing, phase 1/2 study of 2 Parts. Part 1 established the recommended phase 2 dose (RP2D) of 1.9 mg/kg q8w, extended to q12w to account for OAEs. Part 2 assesses the safety/efficacy of RP2D in Groups A and B, of 15 pts each, and evaluates two sets of guidelines for OAE management. In Group A, dosing is determined by an ophthalmic exam performed by a certified ophthalmologist; in Group B it is determined by the pts' responses in the Vision Related Anamnestic (VRA) tool and the presence of ≥Grade (Gr) 3 OAEs. VRA is a patient-reported questionnaire capturing ocular symptoms and their impact on activities of daily living (ADL). Herein, we present the OAEs and preliminary efficacy results after 205 ophthalmic and VRA assessments for all Part 2 pts (cut-off date 05/10/2023). **Results:** By the cut-off date, the median belamaf administrations and number of cycles reached were 3.0/3.0 and 8.0/7.0 for Groups A and B, respectively. The respective rates of Gr2 and ≥Gr3 BCVA change from baseline were 34.6%/24.2% and 6.4%/0.0%, while a meaningful BCVA decline (Snellen score <20/50) and ≥3 lines drop in the better-seeing eye was recorded in 11.0%/7.2% ophthalmological assessments; no ≥Gr3 keratopathy was observed. Among 110/94 VRA assessments, ocular symptoms and ADL impairment, manifesting for ≥50% of the time in the last 24 hours prior to belamaf administration (substantial time), were noted in 6.4%/10.6% and 3.6%/7.4%. Of note, VRA captured a "substantial time" response in 86% of assessments with ≥Gr3 OAEs. Finally, for the response-evaluable pts, at a median follow-up of 7.7 months, ORR was 93.3%/85.7% in Groups A and B (PR/VGPR/CR: 26.7%/53.3%/13.3%; 21.4%/64.3%/0.0%) and the median time to first response was ~ 1 month. **Conclusions:** The VRA tool was safe and effective in informing belamaf dose modifications. Future analyses will determine if VRA may effectively eliminate the need for an ophthalmic exam prior to belamaf dosing. Clinical trial information: NCT04808037. Research Sponsor: None.

Belamaf dose skips and OAEs.

	Group A, N=15	Group B, N=15
Belamaf doses skipped /Planned doses (%)	17/69 (24.6)	7/61 (11.5)
BCVA Decline, na/Na (%)		
Grade 2	38/110 (34.6)	23/95 (24.2)
Grade ≥3	7/110 (6.4)	0/95 (0.0)
Keratopathy, na/Na (%)		
Grade 2	5/110 (4.6)	16/94 (17.0)
Grade ≥3	0/110 (0.0)	0/94 (0.0)
BCVA decline < 20/50 with ≥3 lines drop in the better seeing eye, na/Na (%)	11/100 (11.0)	6/83 (7.2)

N, number of patients; na, number of assessments; Na, total number of assessments

Efficacy, safety, and determination of RP2D of ABBV-383, a BCMA bispecific antibody, in patients with relapsed/refractory multiple myeloma (RRMM).

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Background: MM eventually becomes refractory to current treatments, and new therapeutic options with convenient dosing and improved safety are needed to enhance patient (pt) adherence, access, and outcomes. ABBV-383 is a distinctive next-generation BCMA x CD3 bispecific antibody composed of 2 high-affinity BCMA-binding domains, a low-affinity CD3-binding domain designed to reduce cytokine release syndrome (CRS) risk, and a silenced Fc tail for an extended half-life allowing convenient dosing. ABBV-383 monotherapy has shown promising activity in the ongoing first-in-human phase 1 trial in RRMM (Vij et al. *Blood* 2023;142[suppl 1]:3378). Here, safety and efficacy results are reported that support the RP2D of 60mg Q4W as the optimal therapeutic ABBV-383 monotherapy dose. **Methods:** This phase 1 open-label, dose-escalation/expansion trial (NCT03933735) enrolled pts with RRMM who received ≥3 prior lines of therapy with exposure to PI, IMiD, and anti-CD38 mAb. ABBV-383 regimens explored in the expansion phase included 60mg Q4W and 40 or 60mg Q3W. A modified dexamethasone premedication schedule and shortened CRS monitoring period were implemented in the 60mg Q4W cohort for cycle 1. IV ABBV-383 was administered as a flat dose with no step-up schedule. Treatment was continued until disease progression/unacceptable toxicity. Primary objectives were to assess safety, tolerability, PK, PD, and determine the RP2D. Efficacy evaluation was a secondary objective. TEAEs were assessed per CTCAE v5.0 and tumor response per IMWG 2016 criteria. **Results:** As of May 2023, 220 pts received ABBV-383 (median age: 68 yr [35–92]; median prior therapy lines: 5 [3–23]). Median FU was 4.1 mo (0.8–5.2) at 60mg Q4W (n=21), 12.2 mo (1.3–34.4) at 40mg Q3W (n=55), and 24.2 mo (0.6–33.4) at 60mg Q3W (n=61). At 60mg Q4W, with the modified premedication regimen, CRS was reported in 43% of pts (38% G1, 5% G2), and ICANS in 5% of pts (G2). In Q3W cohorts, CRS was reported in 71% (40mg; 45% G1, 25% G2) and 70% (60mg; 51% G1, 18% G2, 2% G3) of pts. The incidence of G3/4 neutropenia, anemia, and thrombocytopenia was 14/24/10% at 60mg Q4W, 31/31/16% at 40mg Q3W, and 34/13/13% at 60mg Q3W. G3/4 infections occurred in 10/24/34% of pts at 60mg Q4W, 40mg and 60mg Q3W, respectively. ORR and ≥VGPR were 65/50% at 60mg Q4W, 64/53% at 40mg Q3W, and 60/52% at 60mg Q3W. Corresponding exposure-response (ER) analyses and correlative analyses further supported RP2D determination (separate abstract submissions). **Conclusions:** The optimal therapeutic dose of 60mg Q4W ABBV-383 monotherapy was selected on the basis of safety, efficacy, and ER analyses. The extended interval of Q4W, with a shortened CRS monitoring period in cycle 1 and no step-up dosing, will improve convenience and reduce the treatment burden for pts. ABBV-383 at 60mg Q4W will be investigated in the registrational phase 3 trial (NCT06158841) in RRMM. Clinical trial information: NCT03933735. Research Sponsor: AbbVie.

Correlative biomarker analyses for optimal therapeutic dose determination of ABBV-383, a B-cell maturation antigen (BCMA) x CD3 bispecific antibody, in patients with relapsed/refractory multiple myeloma (RRMM).

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Background: ABBV-383 is a BCMA x CD3 bispecific antibody with 2 high-affinity BCMA-binding domains and a low-affinity CD3 engaging arm that has been shown to decrease the negative impact of soluble BCMA (sBCMA) and drive sustained T-cell activation with reduced cytokine release in preclinical models of MM. Here, we describe correlative biomarker results of baseline and longitudinal sBCMA levels and immune profiles in the ongoing first-in-human trial that supports 60 mg Q4W as the optimal therapeutic dose of ABBV-383 monotherapy. **Methods:** Peripheral blood and serum samples from patients with RRMM enrolled in the phase 1 open-label, dose-expansion study (NCT03933735) who received ABBV-383 at 20, 40, or 60 mg Q3W or 60 mg Q4W were collected at baseline (post-dexamethasone, pre–ABBV-383), on treatment, and at disease progression. Samples were analyzed by flow cytometry for immune cell populations, Luminex for cytokines, and electrochemiluminescence ligand binding for sBCMA. **Results:** Median sBCMA levels at baseline were highly variable among patients, but did not associate with clinical response (≥ partial response [PR]) to ABBV-383 at the selected optimal dose level of 60 mg Q4W (<PR: 244.7 ng/mL; ≥PR: 52.2 ng/mL; P=0.13). Reduction in sBCMA levels over time associated with clinical response (C_{min} at cycle 5: <PR, 244.7 ng/mL; ≥PR, 4.7 ng/mL; P=0.04). ABBV-383 treatment led to a rapid and transient increase of proinflammatory cytokines, including IL-6, IL-8, IL-10, TNF-α (C_{max} within cycle 1: 29, 349.5, 1375, 456.5 pg/mL, respectively), and promoted T-cell redistribution (89% reduction of CD8+ T cells from periphery), activation (1.9-fold increase in CD69+CD8+ T cells), and proliferation (2-fold increase in Ki67+CD8+ T cells) within cycle 1 in 60-mg Q4W-treated patients. The frequency of baseline CD8+ T-cell exhaustion (PD-1/TIM3) did not impact clinical response at the optimal dose level of 60 mg Q4W ABBV-383 (<PR: 3.5%; ≥PR: 3.9%; P=0.9). Peak induction levels of proinflammatory cytokines during cycle 1 correlated with occurrence of cytokine release syndrome (≥G1) as well as clinical response across dose levels. **Conclusions:** High-avidity BCMA binding coupled to low-affinity T-cell engagement distinguishes the resulting mechanism of action for ABBV-383. Responses to 60 mg Q4W ABBV-383 were independent of baseline sBCMA levels and resulted in rapid and transient proinflammatory cytokine production that promoted robust T-cell redistribution, activation, and proliferation, indicating that the optimal dose of ABBV-383 maximizes its clinical potential as a convenient, safe, and effective therapy for MM. Clinical trial information: NCT03933735. Research Sponsor: AbbVie.

Second primary B-ALL after exposure to lenalidomide for multiple myeloma: A US multicenter study.

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Background: Maintenance treatment (rx) with lenalidomide (R) improves overall survival (OS) in multiple myeloma (MM). We report a retrospective cohort of patients (pts) with second primary B-cell acute lymphoblastic leukemia (ALL) diagnosed after R-rx for MM. **Methods:** We included pts who were exposed to at least 1 yr of R for MM rx prior to ALL dx. After approval by institutional review board, data were collected by chart review at participating centers using Redcap. OS was the primary endpoint. We used BlueSky statistics v10.3.1 for analysis. **Results:** Analysis included 33 ALL pts diagnosed from 2014-2022 at 7 sites. 52% pts were female. Median follow up was 9.6 yrs (95%CI,7.6-11.8) from MM dx and 3.2 yrs (CI, 2.1-4.7) from ALL dx. Pt characteristics at MM dx are given in Table. Induction rx included: proteasome inhibitor (PI) +immunomodulatory drug (IMiD) (43%), PI+alkylator (24%), IMiD (18%) & others (15%). 50% pts received autologous stem cell transplantation (ASCT). Median OS from MM dx was 11.2 yrs (CI, 8.9-NR). Time from MM dx and initial R rx to ALL dx were 5.0 yrs (range, 2.4-18.5) and 4.4 yrs (2.2-10.6) respectively. Median duration of R exposure before ALL dx was 3.8 yrs (1.6-10.4). Table shows characteristics of pts at B-ALL dx and genetic classification based on karyotyping (n=30), ALL FISH (n=28), chromosomal microarray (n=5) and next-generation sequencing (n=5). 31 pts received ALL-directed rx while 1 pt was initially managed with close observation as the pt attained CR on stopping R (Lakshman et al; ASH 2019). Rx was unknown in 1 pt. Initial rx included: hyper-CVAD+/- rituximab- 49%, pediatric inspired protocols-18%, reduced intensity rx for frail pts- 21% and others- 12%. Response to first line rx were: CR- 56%, CRi-28%, induction failure- 16%. 32% pts attained measurable residual disease (MRD) negativity. 48% pts underwent SCT for ALL. 14 pts died during follow up. 3-yr OS from ALL-dx was 50% (CI, 33%-76%). 3 pts required rx for MM after ALL diagnosis (2 had allo-SCT for ALL before MM relapse). **Conclusions:** Most pts had standard risk MM and were exposed to R for several years prior to dx of B-ALL, characterized by high incidence of hypodiploid karyotype; *IKZF1* loss and *TP53* deletions/mutations were detected in a subset of pts.MRD-adapted timely discontinuation of R in standard risk MM may decrease risk of second primary ALL. Research Sponsor: American Society of Hematology; Mayo Clinic.

MM		B-ALL	
Age at dx, median (range)	58 (38-78)	Age at dx, median (range)	64 (43-81)
Isotype: IgG/ IgA/ others (n=29)	76%/14%/ 10%	Median WBC count (x10^9/μL) (range)	2.2 (0.63-76.3)
Hb<10 g/dL; Cr≥2 mg/dL; Ca>11 mg/dL; bone lesions	18%; 11%; 19%; 83%	Blast %- peripheral blood/bone marrow, median (range)	2% (0-89)/ 83 (31-98)
ISS I/II/III (n=24)	46%/37%/ 17%	Hypodiploid	40%
Elevated LDH (n=18)	17%	Hyperdiploid; Tetraploid	15%; 3%
High risk FISH abnormalities (n=24)		Ph-like	3%
None	83%	Unclear primary subtype	39%
1	13%	*IKZF1* loss/del17p (cytogenetics, FISH and array), n	5 & 3
≥2	4%	mut*TP53* on NGS (n=5), n	3

Post-ASCT consolidation with EPD or ERD in patients with high-risk multiple myeloma.

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Background: Patients (pts) with high-risk (HR) Multiple Myeloma (MM), characterized by at least two cytogenetic abnormalities often experience rapid disease progression and early relapse post-autologous stem cell transplant (ASCT) with median Progression-Free Survival (PFS) of 24 or 12 months with or without lenalidomide maintenance (Panopoulou et al, Blood 2023). This study assesses the efficacy and safety of EPD (Elotuzumab, Pomalidomide, Dexamethasone) or ERD (Elotuzumab, lenalidomide , Dexamethasone) as consolidation therapy post-ASCT in HR MM pts. **Methods:** In this single-center retrospective study, we reviewed records of MM pts treated with consolidative ERD or EPD from September 2016 to March 2023. We collected baseline MM characteristics, treatment history, adverse events (AEs), and survival outcomes. HR MM pts were defined by 2 or more cytogenetic abnormalities (del 17p, 1q21 gain or amplification, t(14;16), t(14;20), complex karyotype) and/or high-risk gene expression profiling scores (GEP, SKY92). All patients, aged ≥21, underwent ≥1 full cycle of EPD or ERD post-ASCT, administered for a total of four 28-day cycles, following the standard dosing regimen with a rapid dexamethasone taper over the last two cycles. **Results:** A total of 78 HR MM pts, median age 64 years with 51.2% males and 71.7% caucasians were included. Of them, 62 pts received ERD and 16 received EPD. FISH revealed 62.7% of pts had 2 or more high risk cytogenetic abnormalities. Other pts expressed a combination of cytogenetic abnormalities and/or high-risk GEP or SKY92 scores. The table shows improvement in MRD negativity rates from 21.7% to 26.9% pre and post consolidation, and in VGPR or better from 78.2% to 85.8%. Median PFS for all pts, defined from the time of ASCT to disease progression, was 26.9 months. Most common adverse effects were anemia (71.7%), fatigue (55.1%) and thrombocytopenia (51.2%). Five patients experienced grade 3 adverse events, including 3 with infectious etiology (3.8%) and 2 with immune-mediated toxicity (2.5%). No treatment-related serious adverse events were reported. **Conclusions:** Four cycles of EPD or ERD consolidation therapy post-ASCT, demonstrated promising efficacy in HR MM pts. The observed median PFS of 26.9 months was comparable to that seen with chronic lenalidomide maintenance and superior to patients who do not receive lenalidomide maintenance. The improvement in PFS was achieved with a fixed duration rather than continuous therapy and without lenalidomide-associated toxicities such as secondary malignancies, chronic diarrhea, and financial toxicity. Further prospective confirmatory studies are needed. Research Sponsor: None.

Best response rates.

Response Category	Best Response Post-induction	Best Response Post-ASCT	Best Response Post-EPD/ERD
MRD Negative	2	17	21
VGPR or better	35	61	67
PR	40	15	9
MR or worse	3	2	2

7535 Poster Session

Ciltacabtagene autoleucel in patients with lenalidomide-refractory multiple myeloma: CARTITUDE-2 cohort A expansion subgroup.

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Background: The phase 2 multicohort CARTITUDE-2 study is evaluating ciltacabtagene autoleucel (cilta-cel) in patients (pts) with MM across multiple settings. Cohort A is examining cilta-cel in earlier lines of treatment (tx; LOT) in pts with lenalidomide (len)-refractory multiple myeloma (MM). Initial results for cohort A (N=20; median follow-up, 30 mo) showed cilta-cel led to minimal residual disease negativity (MRD neg) at 10^{-5} in 100% of pts with evaluable samples (n=17). ORR was 95% (19/20), median DOR was not reached (NR), and the 24-mo PFS rate was 75%. We report protocol-specified results for the expansion subgroup. **Methods:** Pts with len-refractory MM after 1–3 LOT, including a PI and IMiD, and no anti-BCMA tx were enrolled. A single cilta-cel infusion (target dose, 0.75×10^6 [range, $0.5–1.0\times10^6$] CAR+ viable T cells/kg) was given 5–7 d after the start of lymphodepletion. Cohort A initially evaluated cilta-cel manufactured by clinical trial processes and later expanded to evaluate cilta-cel manufactured by commercial processes. Primary endpoint was MRD neg at 10^{-5}. Efficacy is reported for pts who received cilta-cel at target dose; demographics, baseline disease characteristics, and safety are reported for all treated pts in the expansion subgroup. **Results:** As of Sept 5, 2023, median follow-up was 16 mo. Of 24 pts enrolled, 23 received cilta-cel infusion (22 at target dose). Median age was 63 y, 52% were male, and 61% were triple-class exposed. Of 16 MRD-evaluable pts, 100% achieved MRD neg at 10^{-5}; median time to MRD neg was 2 mo (range, 1–12). ORR was 91% (20/22). Median DOR was NR; 79% of responders remained in response at 12 mo. Median (range) time to first and best responses were 1 mo (1–10) and 6 mo (1–19), respectively. 12-mo PFS and OS rates were 77% and 91%, respectively. All pts had TEAEs (grade [gr] 3/4, n=22; gr 5, n=1). Hematologic TEAEs included neutropenia (96%), leukopenia (65%), lymphopenia (65%), anemia (57%), and thrombocytopenia (57%). Infections occurred in 8 (35%) pts (gr 3/4, n=1; gr 5, n=1 due to sepsis). CRS occurred in 23 (100%) pts (gr 1/2, n=23); median time to onset was 8 d and recovery was 4 d. ICANS occurred in 4 (17%) pts (gr 1, n=3; gr 4, n=1); median time to onset was 10 d and recovery was 2 d. No other neurotoxicities or MNTs/parkinsonism occurred. 2 pts had secondary malignancies (SM); 1 pt had separate SM of gr 2 basal cell carcinoma and gr 2 squamous cell carcinoma and 1 pt had MDS diagnosed on d 846 that later transformed to AML. Per investigator assessment, SM were not tx-related. **Conclusions:** In the expansion subgroup of cohort A, cilta-cel led to deep and durable responses in pts with len-refractory MM as early as after first relapse; safety was consistent with the known mechanism of action of CAR-T tx. Results in the expansion and initial subgroups are comparable. Data for CARTITUDE-2 cohort A underscore observations in CARTITUDE-4 which enrolled a similar pt population. Clinical trial information: NCT04133636. Research Sponsor: Johnson & Johnson Innovative Medicine; Legend Biotech USA Inc.

Real-world schedule de-escalation of teclistamab in patients with relapsed/refractory multiple myeloma.

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Background: Teclistamab (Tec) is the first BCMAxCD3 bispecific antibody approved for triple-class-exposed relapsed/refractory multiple myeloma (RRMM). The MajesTEC-1 study demonstrated an overall response rate (ORR) of 63% and a median progression-free survival (mPFS) of 11.3 months (mos). Herein, we examined real-world pt characteristics and outcomes associated with Tec in (1) pts treated within the first 4 mos of Tec approval (early initiators who were expected to have high disease burden) as compared to recent initiators, and (2) any pts who switched to de-escalated dosing schedules. **Methods:** This is a retrospective study of pts with RRMM treated with Tec at Memorial Sloan Kettering Cancer Center from 11/29/22 to 11/30/23 (analysis cut-off: 12/31/23). Responses were evaluated per IMWG Response Criteria. Pt characteristics were summarized by frequency (%) or median (interquartile range [IQR]). PFS was evaluated using the Kaplan-Meier method. **Results:** In 77 pts who received ≥1 Tec dose, the median age was 70 (IQR 63-77); 55% male; 14% Black; and 42% had high-risk cytogenetic abnormalities (HRCA). The ORR was 62% for 69 response-evaluable pts, including 42% with ≥very good partial response (VGPR). The median time to first response was 1.9 mos (IQR 1.0-2.4). After a median follow-up (mFU) of 7.6 mos, 6-mo PFS rate was 52.3% (95%CI 41.5-66%). The median duration of response has not been reached. In the cohort of early initiators (n=34), pts had more prior lines of therapy (LOT; median 8 vs 5, P=0.002) and higher proportion of prior BCMA therapy use (62% vs 23%; P=0.002) as compared to recent initiators treated after 3/31/23 (n=43). ORR was 67% and 59%, respectively (P=0.80; Table). Among all pts at data cut-off, 25 (32%) switched from weekly to every-other-week or monthly Tec after a median time of 3.1 mos from Tec initiation (95%CI 1.8-4.6) and based on achieving ≥PR and/or toxicity. At mFU of 5.3 mos since switching, 6-mo PFS rate was 94.1% (95%CI 83.6-100%). **Conclusions:** In this real-world study, Tec demonstrated comparable ORR to MajesTEC-1. Both early and recent Tec initiators had high baseline risk features. A higher proportion of early initiators had prior BCMA therapy and more LOTs, but both cohorts yielded consistently high treatment response rates. In pts who responded, schedule de-escalation was feasible with a high subsequent 6-mo PFS. Updated multicenter findings will be presented at the meeting. Research Sponsor: Johnson & Johnson Innovative Medicine, Horsham, PA, USA.

Characteristics	Early Initiators (N=34)	Recent Initiators (N=43)	P-value
Median follow-up, mo (95%CI)	10.9 (9.8-11.7)	5.1 (3.9-6.6)	
Median age, yr (IQR)	69 (63-77)	71 (65-77)	0.41
Male %	50	58	0.50
HRCA[†], n/N (%)	12/32 (38)	19/41 (46)	0.87
Extramedullary disease, n/N (%)	12/31 (39)	16/40 (40)	1
Median # prior LOT, n (IQR)	8 (5-9)	5 (4-7)	0.002
Prior BCMA therapy, n(%)	21 (62)	10 (23)	0.002
ORR, n/N (%)	20/30 (67)	23/39 (59)	0.80

[†]High-risk includes 1q+, t(4;14), t(14;16), t(14;20), and del(17p) or monosomy 17.

Impact of renal impairment (RI) on pharmacokinetics (PK) and clinical outcomes with mezigdomide plus dexamethasone (DEX) in relapsed/refractory multiple myeloma (RRMM).

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Background: RI is a common complication in MM and may alter drug elimination, leading to increased systemic exposures, risk of adverse events (AEs), and dosing adjustments. The novel CELMoD agent mezigdomide (MEZI) is being investigated alone or with DEX in the CC-92480-MM-001 (NCT03374085) phase 1/2 trial. MEZI has shown dose-dependent linear PK with rapid absorption and is mainly eliminated through hepatic metabolism, with renal elimination playing a smaller role. Here we investigate the impact of RI on the efficacy, safety, and PK of MEZI + DEX in RRMM. **Methods:** Eligible patients (pts) had RRMM, ≥ 3 prior lines of therapy, triple-class refractoriness, and disease progression ≤ 60 days of last therapy. Pts were stratified by creatinine clearance (CrCl), excluding those with CrCl < 45 mL/min or needing dialysis. Oral MEZI (1 mg) was given on days 1–21 per 28-day cycle + weekly DEX. MEZI doses were not adjusted based on RI. Responses, AEs, and PK were assessed descriptively over the full population and in pts with no RI (CrCl ≥ 90 mL/min), mild RI (CrCl 60–$<$ 90 mL/min), and moderate RI (CrCl 30–$<$ 60 mL/min) at baseline. MEZI clearance and PK exposure were estimated from an integrated population PK model. PK exposure parameters were stratified by chronic kidney disease (CKD) staging. **Results:** 101 pts received MEZI + DEX in the dose-expansion cohort; 37 had no RI, 41 had mild RI, and 23 had moderate RI. Grade (Gr) 3/4 treatment-emergent AEs (TEAEs) were similar, occurring in 91.1% (overall), 89.2% (no RI), 90.2% (mild RI), and 95.7% (moderate RI) of pts. TEAEs were mostly hematologic, with neutropenia the most common Gr 3/4 TEAE; its occurrence did not differ in no RI (75.7%), mild RI (75.6%), and moderate RI (73.9%) cohorts. Non-hematologic Gr 3/4 TEAEs were low. Eighty-nine (88.1%) and 32 (31.7%) pts had MEZI dose interruptions and reductions, respectively. Overall response rate (ORR) was 40.6% in all pts, 56.8% in no-RI pts, 29.3% in mild-RI pts, and 34.8% in moderate-RI pts (Table). Evaluated as a continuous variable, CrCl showed no apparent relationship with MEZI oral clearance or systemic exposures. This was supported by subgroup evaluation of MEZI exposures by CKD stage. Results showed MEZI exposures in mild or moderate RI are consistent with no RI. **Conclusions:** Based on renal function, there was no adverse trend between efficacy, safety, and PK of MEZI + DEX. MEZI dose modifications are likely not required for pts with mild to moderate RI. Clinical trial information: NCT03374085. Research Sponsor: Bristol Myers Squibb.

Response rate by renal function.

	MEZI + DEX (N = 101)	No RI (N = 37)	Mild RI (N = 41)	Moderate RI (N = 23)
ORR, % (95% CI)	40.6 (30.9–50.8)	56.8 (39.5–72.9)	29.3 (16.1–45.5)	34.8 (16.4–57.3)
sCR, n (%)	2 (2.0)	1 (2.7)	0	1 (4.3)
CR, n (%)	3 (3.0)	1 (2.7)	2 (4.9)	0
VGPR, n (%)	20 (19.8)	13 (35.1)	5 (12.2)	2 (8.7)
PR, n (%)	16 (15.8)	6 (16.2)	5 (12.2)	5 (21.7)
Duration of response, median (95% CI), mo	7.6 (5.4–9.5)	8.3 (5.1–10.0)	6.9 (4.0–NA)	6.2 (0.6–NA)

Long-term follow-up from the phase 1/2 MajesTEC-1 trial of teclistamab in patients with relapsed/refractory multiple myeloma.

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Background: Teclistamab, the first approved B-cell maturation antigen × CD3 bispecific antibody (BsAb) with weight-based dosing for the treatment of patients (pts) with triple-class exposed relapsed/refractory multiple myeloma (RRMM), demonstrated rapid, deep, and durable responses in the pivotal MajesTEC-1 study. Here, we report updated results from MajesTEC-1. **Methods:** Eligible pts received teclistamab at the recommended phase 2 dose (RP2D; 1.5 mg/kg subcutaneous QW preceded by step-up dosing) with the option to switch to Q2W dosing if a partial response or better after ≥4 cycles of therapy (phase 1) or complete response or better (≥CR) for ≥6 mo (phase 2) was achieved; pts not in ≥CR could switch due to adverse events (AEs). Pts could subsequently switch to less frequent dosing if they continued to demonstrate a response. The primary endpoint was overall response rate (ORR) assessed by independent review committee per International Myeloma Working Group 2016 criteria. AEs were graded per Common Terminology Criteria for Adverse Events v4.03. Cytokine release syndrome (CRS) was graded per American Society for Transplantation and Cellular Therapy guidelines. **Results:** At median follow-up of 30.4 mo, 165 pts had received teclistamab at the RP2D. ORR was 63.0%, and responses continued to deepen, with 46.1% achieving ≥CR. 85.7% (48/56) of MRD-evaluable pts were MRD negative (10^{-5} threshold). Median duration of response (mDOR) increased to 24.0 mo; median progression-free survival (mPFS) and overall survival (mOS) improved to 11.4 and 22.2 mo, respectively. For pts with ≥CR, mDOR, mPFS, and mOS were not yet reached, and estimated 30-mo DOR, PFS, and OS rates were 60.8%, 61.0%, and 74.2%, respectively. Of the 38 pts who remain on treatment, 37 have switched to a less frequent dosing schedule (eg, Q2W), all of whom maintained responses. Hematologic AEs (any grade/grade 3/4) included neutropenia (72%/65%), anemia (55%/38%), thrombocytopenia (42%/23%), and lymphopenia (36%/35%). Infections occurred in 79% of pts (55% grade 3/4). Of grade 5 infections, 18/22 were due to COVID-19, reflecting study conduct during the COVID-19 pandemic. Onset of new grade ≥3 infections generally decreased over time, which aligned approximately with the median time of switch to Q2W dosing; other factors, such as increasing use of IVIG, may also contribute to this trend. AEs leading to dose reduction (n=1) or discontinuation (n=8; 5 due to infection) were infrequent. No new safety signals were reported. **Conclusions:** With the longest follow-up of any BsAb in MM, teclistamab continues to demonstrate deep and durable responses, including in pts who switch to less frequent dosing. The safety profile of teclistamab remains consistent with that of BCMA-targeted bispecific therapies, with a notable decrease in new onset of severe infections with time. Clinical trial information: NCT03145181 / NCT04557098. Research Sponsor: Johnson & Johnson Innovative Medicine.

Exposure-response analyses for optimal therapeutic dose selection of ABBV-383 in patients with relapsed/refractory multiple myeloma (RRMM).

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Background: ABBV-383 is a fully human, B-cell maturation antigen (BCMA) × CD3 T-cell–engaging IgG4 bispecific with an effector-silenced Fc region, 2 high-affinity BCMA- and a low-affinity CD3-binding domains. ABBV-383 monotherapy has shown promising activity in patients (pts) with RRMM (Blood 2023;142[suppl 1]:3378). Here, exposure-response (ER) analyses of efficacy and safety endpoints supporting the optimal therapeutic ABBV-383 dose selection are reported in alignment with US FDA's Project Optimus. **Methods:** Efficacy (n=218) and safety (n=220) data from the phase 1 study (NCT03933735) escalation cohorts of 0.025 - 120 mg Q3W and expansion cohorts of 20, 40, 60 mg Q3W and 60 mg Q4W including objective response rate (ORR), very good partial response or better (≥VGPR), stringent complete response (sCR)/CR, adverse events (≥G3 and serious), infections (≥G3, overall and serious), cytokine release syndrome (CRS; any-grade, G1, G2, and ≥G2) were modeled. *Total*(unbound + bound to soluble BCMA) and *free* (unbound + partially bound to soluble BCMA) Cycle 1 AUC_{inf}, C_{max}, and C_{trough} and population pharmacokinetic model-derived up to the time of event C_{avg} and $avgC_{trough}$ metrics were utilized in the ER analyses (logistic regression; R Version 4.2.2). Relevant pt-specific covariates were tested. Dexamethasone premedication (36 *vs* 10 mg) was included in CRS models. The ER relationships were utilized to predict the probabilities of efficacy and safety endpoints for relevant doses and thereby, support justification of the optimal therapeutic dose selection. **Results:** Based on overall assessment, ORR, ≥VGPR, sCR/CR and ≥G3 neutropenia strongly correlated with *free* Cavg; CRS endpoints (any-grade CRS and G1 only CRS) strongly correlated with Cycle 1 *total* C_{max} ($p < 0.05$). No other endpoints had ER relationships ($p > 0.05$). Only MM type (IgG *vs* Others) was selected in ≥VGPR and sCR/CR models. ER relationships suggested high response rates of >63% ORR, >53% ≥VGPR, and ≥30% sCR/CR for 40, 60 mg Q3W and 60 mg Q4W. Predictions demonstrated that 20 mg Q3W (<39% ORR and ≥VGPR; <13% sCR/CR) and untested 40 mg Q4W (<60% ORR, <45% ≥VGPR and <23% sCR/CR) provide suboptimal efficacy. The 60 mg Q4W with 36 mg dexamethasone in Cycle1 (limited follow-up and data) was predicted to have ~30% sCR/CR and 31% ≥G3 neutropenia (≈ 40 mg Q3W) and substantially lower any-grade CRS events compared with 40 and 60 mg doses with 10 mg dexamethasone in Cycle 1. **Conclusions:** While ER analyses indicated promising efficacy and acceptable safety profiles for 40, 60 mg Q3W, and 60 mg Q4W, they support 60 mg Q4W as the optimal ABBV-383 therapeutic dose due to its predicted better therapeutic benefit/risk profile (high response rates, improved/equivalent ≥G3 neutropenia, and lower CRS events) and extended dosing interval. ABBV-383 at 60 mg Q4W will be investigated in the registrational phase 3 trial (NCT06158841) in RRMM. Research Sponsor: AbbVie.

Incidence of acute kidney injury in patients with relapsed and refractory multiple myeloma treated with teclistamab vs chimeric antigen receptor T-cell therapy.

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Background: Teclistamab, a novel bispecific monoclonal antibody targeting CD3 and BCMA, exhibits promising effects for patients with relapsed and refractory multiple myeloma (MM). However, rates of acute kidney injury (AKI) associated with this therapy remains inadequately characterized. **Methods:** This was a retrospective observational cohort study of patients with relapsed refractory MM who received teclistamab or Chimeric Antigen Receptor T-cell Therapy (CAR-T) therapy at Mayo Clinic between 12/1/2022-5/15/2023 and who were not in kidney failure at the time of treatment. The primary endpoint was incidence of AKI during follow-up; secondary endpoints included treatment and recovery from AKI. AKI was defined based on Kidney Disease Improving Global Outcomes criteria as an increase of serum creatinine levels $>$ 1.5 times their baseline value after starting therapy. Cumulative incidences and Cox proportional hazard regression models were used to evaluate time to event data. **Results:** A total of 64 patients met inclusion criteria for the study (30 received CAR-T and 34 received teclistamab therapy). There were 14 AKI events occurring during follow-up (10 teclistamab [n = 6 stage 1, n = 3 stage 2 and n = 1 stage 3] and 4 CAR-T [n = 3 stage 1 and n = 1 stage 2]). Cumulative incidence estimates of AKI at 120 days after treatment were 32% (95% CI: 14%-47%) for teclistamab patients and 10% (95% CI: 0%-21%) for CAR-T patients. While patients receiving teclistamab were found to be at increased risk of an incident AKI event compared to patients receiving CAR-T therapy, results were not statistically significant (HR (95% CI): 3.38 (0.93-12.31), p = 0.065). Median time to development of AKI was 30 days (IQR 16, 73) in teclistamab and 59 days (IQR 9, 146) in CAR-T patients. Among the 10 patients in the teclistamab group with an AKI event, 4 (40%) had complete renal recovery and 4 (40%) had partial recovery, while among the 4 patients with CAR-T with an AKI event, 2 (50%) experienced complete renal recovery and 2 (50%) experienced partial recovery. **Conclusions:** Our study showed that almost one third of patients receiving teclistamab therapy for relapsed and refractory multiple myeloma experienced an incident AKI event during follow-up. This finding underscores the importance of monitoring for kidney function in these patients. Research Sponsor: None.

7543 Poster Session

Patient-reported outcomes (PROs) from the DREAMM-7 randomized phase 3 study comparing belantamab mafodotin, bortezomib, and dexamethasone (BVd) vs daratumumab, bortezomib, and dexamethasone (DVd) in patients with relapsed/refractory multiple myeloma (RRMM).

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Background: Belantamab mafodotin(belamaf), a first-in-class antibody-drug conjugate targeting B-cell maturation antigen, acts through a multimodal mechanism including direct cell killing and immune-mediated mechanisms. The global, phase 3, open-label, randomized, DREAMM-7 trial (NCT04246047) met its primary endpoint of demonstrating statistically significant progression-free survival benefit favoring BVd vs DVd in patients with RRMM who had received ≥1 prior line of therapy; here, we report PRO findings for BVd vs DVd. **Methods:** Patients were randomized (1:1) to receive BVd or DVd and completed electronic PRO measures at baseline and every 3 weeks (Q3W) during treatment. PRO measures included EORTC-QLQ-C30, EORTC-QLQ-MY20 disease symptoms (pain), PRO-CTCAE patient-reported tolerability, and OSDI vision-related functioning (Q3W up to the sixth dose of belamaf, then Q6W). Each domain was summarized using descriptive statistics. **Results:** Among 494 patients (BVd, n=243; DVd, n=251), adherence to PRO assessments was >90% for most study visits. There was no difference in EORTC QLQ-C30 global health status/quality-of-life assessments between the study arms over time. Similarly, role functioning, physical functioning, fatigue, and pain were stable (change from baseline in EORTC score was within 10 points) over time and consistent between arms. Most symptomatic adverse events evaluated by PRO-CTCAE were reported at no to low severity, frequency, and interference (PRO-CTCAE ratings ≤2) in both arms throughout the study. The severity and interference of blurred vision and frequency of watery eyes were reported at higher levels (PRO-CTCAE ratings ≥3) in the BVd arm. Among patients in the BVd arm with a clinically meaningful deterioration in vision-related functioning (a change from baseline of ≥12.5 points), EORTC-QLQ-C30 global health status, role functioning, and physical functioning were comparable to the DVd arm over time. **Conclusions:** Overallquality of life, role functioning, physical functioning, fatigue, and pain were comparable in patients treated with BVd vs DVd. In patients treated with BVd who reported a clinically meaningful deterioration in vision-related functioning, overall quality of life was consistent with the DVd arm. Research Sponsor: GSK plc.

Long-term follow-up of ARI0002h (cesnicabtagene autoleucel), an academic point-of-care B-cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR) T-cell strategy: Activity and safety after fractionated initial therapy and booster dose in 60 patients with relapsed/refractory multiple myeloma (RRMM).

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Background: The activity and safety ofARI0002h, an academic autologous CAR T-cell product with a humanized single chain variable fragment targeting BCMA has been reported in a pilot multicenter clinical trial (CARTBCMA-HCB-01) treating 30 patients (pts) with RRMM (NCT04309981) (Oliver-Caldés, Lancet Onc 2023). Here, we describe results of the final cohort of 60 pts with longer follow-up. **Methods:** Patients aged 18-75 years old with RRMM were eligible if they had measurable disease, were refractory to the last line of treatment and received ≥2 prior regimens, including a proteasome inhibitor, an immunomodulatory drug and an anti-CD38 antibody. The target dose ($3x10^6$/kg CAR+cells) was administered in a fractionated manner (10%/30%/60%). A second dose of up to $3x10^6$ CAR+ cells/kg was planned at least 3 months after the first dose in pts with any kind of response and no limiting side effects. Primary endpoints were overall response rate (ORR) within the first 3 months and rate of cytokine release syndrome (CRS) and/or neurotoxicity in the first 30 days. Bone marrow minimal residual disease (MRD) was analyzed by next-generation flow at a sensitivity of 10-6. **Results:** As of December 18th 2023, 72 pts with RRMM were screened, 69 underwent apheresis and 61 received LD, with 60 pts finally receiving ARI0002h. The ORR in the first 3 months was 95% (≥ very good partial response (VGPR) in 77%). Median time to first response was one month. Responses deepened over time, achieving 58% complete response (CR) (55% stringent CR). MRD-negative rates on evaluable samples on days 28 and 100 were 98% and 96%, respectively. With a median follow-up of 24 months (95%CI 9.8-39.9), estimated median progression-free survival (PFS) was 20 months (95% CI 13.2-26.8). Median overall survival (OS) was not reached with OS rate at 24 months of 63%. CRS was observed in 90% with 5% grades ≥ 3. Median time to CRS was 7 days (1-14) with a median duration of 4.5 days. Mild acute neurotoxicity was reported in only 2 pts (3%) with no late neurologic events. 6 pts (10%) developed a macrophage activation syndrome (4 grades 1-2, 1 grade 3, 1 grade 5). Seven patients (11.7%) developed second primary malignancies after ARI0002h infusion, including 3 skin cancers (one in situ melanoma), 3 solid tumors and one acute myeloid leukemia. 80% (44 out of 5) eligible pts had already received the booster dose, with no relevant toxicities. Median time after first infusion was 4.4 months. Response was evaluable in 42 pts; 45% (n=19) were already in sCR, 29% (n=12) maintained the response and 26% (n=11) improved the response. **Conclusions:** Results from 60 pts and a longer follow-up confirm the safety profile and the deep and durable responses obtained after ARI0002h infusion. Clinical trial information: NCT04309981. Research Sponsor: Instituto de Salud Carlos III; “La Caixa” Foundation.

Characterization of the BCMA epitope bound by BCMA-CD3 T cell engager elranatamab.

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Background: Elranatamab is a BCMA-CD3 bispecific antibody with an accelerated approval in the US and EU for relapsed/refractory multiple myeloma (RRMM). Elranatamab binds to CD3 on T cells and BCMA on MM tumor cells; this dual binding results in T cell activation, cytokine release, and tumor cell killing. Engagement of the BCMA surface receptor by its ligands, APRIL and BAFF, mediates plasma cell proliferation and survival. Elevated BCMA, as well as BAFF and APRIL are present in MM patients, yet in vitro functional assays have shown physiologically relevant soluble APRIL or BAFF concentrations did not significantly impact elranatamab activity. Moreover, emerging clinical data from relapsed patients has identified novel, yet relatively rare BCMA protein mutations that may impact BCMA ligand or targeted modality binding. Here we characterized the BCMA binding affinity, evaluated the impact on BCMA binding to BAFF and APRIL interactions, and identified the BCMA binding epitope. We also generated a model from crystal structure data to map reported BCMA mutations identified in patients. **Methods:** Elranatamab binding affinity to recombinant human BCMA and characterization of BAFF and APRIL interactions with elranatamab-bound BCMA were calculated via SPR at 37˚C with a classical sandwich format. The elranatamab BCMA binding epitope was identified by a co-crystal structure with a parental anti-BCMA Fab that has identical CDR sequences to elranatamab. Alpha-fold modeling was used to map identified BCMA mutations on the antibody/BCMA interface. **Results:** Elranatamab binds to BCMA with higher affinity (~38 pM) compared to reported binding affinities of BAFF (μM range) and APRIL (nM range) ligands. The identified elranatamab epitope largely overlaps with known ligand epitopes, supporting that elranatamab higher affinity BCMA binding blocks ligand binding. Alpha fold modeling of four recently reported rare BCMA mutations shows that they lie along the binding interface. **Conclusions:** Due to its high affinity for BCMA, elranatamab potency is unlikely to be impacted by elevated levels of soluble BAFF or APRIL in RRMM patients. Future studies are needed to characterize the impact of emerging MM patient BCMA mutations on the binding and function of anti-BCMA targeting modalities, particularly given the small extracellular domain of BCMA available for therapeutic targeting and the highly overlapping binding epitopes reported for approved BCMA agents. Research Sponsor: None.

Patterns and predictors of electronically measured oral anticancer medication (OAM) adherence among patients with multiple myeloma (MM).

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Background: Adherence to costly, long-term OAM is a mainstay of life-extending therapy for patients with MM and can dramatically affect cancer outcomes, but little is known about adherence in patients with MM. The purpose was to describe temporal patterns and predictors of OAM adherence among patients with MM via electronic event monitoring (EEM) adherence data. **Methods:** This was a six-month prospective study of OAM adherence, symptoms, and quality of life among n=70 patients prescribed OAM maintenance therapy for MM who used EEM. Patient reported measures of symptoms (Edmonton Symptom Assessment Scale; Patient Health Questionnaire-9; PROMIS Fatigue; Brief Pain Inventory; Comprehensive Score for financial Toxicity), sociodemographic data, and medical record clinical data were collected at enrollment and 3 and 6 months. Group-based trajectory modeling (GBTM) was applied to EEM data based on AARDEX MEMS smart pill bottles, aggregated monthly (i.e., 30-day intervals) over 6 months of monitoring. Adherence indices were % of prescribed *dose*taken and % of *days* with correct intake. Predictors of adherence trajectory group membership were explored and summarized as bivariate correlations as effect sizes. **Results:** Participants were on average 63.9 y/o (SD=10.6) and predominantly male (55.9%) and non-Hispanic white (86.8%) or Black (10.3%). At enrollment, participants had been prescribed lenalidomide (68.6%) or pomalidomide (31.4%) for a median 11.5 (IQR: 22, range: 0-100) months. For mean dose adherence, GBTM revealed 3 distinct trajectories: 62.9% were in the high (~97% adherence) and slightly linear decreasing adherence group (π_3=.627); 27.1% were in the high/moderate and curvilinear decreasing group (π_2=.272), representing 85% adherence at start, dropping to <70% by 6 months; and 10% had a low and curvilinear (π_1=.100) pattern, representing only ~40% adherence over time. For mean days adherence, 2 distinct trajectories were identified: high and linear decreasing (81.4%, π_2=.801), representing adherence starting at 90%, dropping to 85%; and low and stable (18.6%, π_1=.199), representing ~40% adherence over time. Effect sizes for baseline predictors of the low trajectory group ranged from .02 to .37 (median r = .20, small), In particular, participants who self-identified as non-Hispanic Black or Hispanic "other" race being more likely to be in the low trajectory groups for both dose (p=.009) and days (p=.010) adherence. **Conclusions:** OAM adherence measured with EEM data was dynamic and suggests potential mechanisms of health inequities by race and ethnicity and a need for interventions to monitor for and address disparate adherence. Larger studies with longer observation and more frequent assessments with in-depth social determinants of health are needed to better understand OAM adherence patterns and correlates over time. Research Sponsor: National Institute of Nursing Research; K23NR019296, Belcher; The Doris Duke Foundation, in partnership with the University of Pittsburgh and the American Heart Association; 202182-OF, Davis, Rubio, & Weisz; awardee: Belcher.

Apixaban versus warfarin for primary thromboprophylaxis in patients with multiple myeloma undergoing immunomodulatory treatment.

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Background: Immunomodulatory drugs (IMiDs) have been demonstrated to improve clinical outcomes in patients with multiple myeloma (MM), but are associated with an elevated risk of thromboembolism. Existing guidelines recommend low-dose direct oral anticoagulants as an alternative to warfarin for primary thromboprophylaxis in MM. However, the data comparing these two therapies are limited. We aim to compare the efficacy and safety of apixaban versus warfarin in patients with MM undergoing IMiD treatment. **Methods:** We conducted a retrospective propensity score-matched cohort study using the TriNetX Analytics Network database, which contains de-identified data from over 120 participating healthcare institutions. We included adult patients with MM who underwent IMiD treatment. Patients treated with apixaban were matched in a 1:1 ratio to those treated with warfarin using clinical variables a priori. The primary safety outcomes included all-cause mortality, intracranial hemorrhage, and gastrointestinal bleeding, while the primary efficacy outcomes included thromboembolic events including pulmonary embolism, deep venous thrombosis, and ischemic stroke within a 3-year period following IMiDs initiation. **Results:** We identified 448 patients on apixaban who were matched to patients on warfarin. In a Cox proportional hazard analysis, apixaban was associated with a 30% lower risk of all-cause mortality compared to warfarin (Hazard ratio (HR), 0.70 [95% CI: 0.56-0.88]).There was a tendency toward a reduced risk of gastrointestinal bleeding in patients treated with apixaban compared to warfarin (HR, 0.58 [95% CI: 0.31-1.08], log-rank p = 0.083). The risk of intracranial hemorrhage was similar between the two groups.The risks of thromboembolic events including pulmonary embolism, deep venous thrombosis, and ischemic stroke were comparable between the apixaban and warfarin cohorts. **Conclusions:** Apixaban was associated with a lower risk of all-cause mortality and a comparable risk of bleeding and thromboembolism compared with warfarin among MM patients undergoing immunomodulatory treatment. Research Sponsor: None.

	Apixaban		Warfarin			
Outcomes	Patients at Risk	Cases	Patients at Risk	Cases	Hazard ratio[a] (95% CI)	P-value (Log-Rank)
All-cause mortality	448	115	448	193	0.70 (0.56-0.88)	0.002
Intracranial hemorrhage	439	10	440	10	0.64 (0.19-2.19)	0.47
Gastrointestinal bleeding	409	15	415	29	0.58 (0.31-1.08)	0.083
Pulmonary embolism	406	10	402	10	1.07 (0.41-2.78)	0.89
Deep venous thrombosis	355	15	357	24	0.70 (0.36-1.33)	0.27
Ischemic stroke	408	10	400	11	0.90 (0.37-2.18)	0.82

[a]After propensity score matching by incorporating variables: age, sex, metastatic disease, proteasome and immunomodulatory therapy, underlying comorbidities, use of cardiovascular medications.

Associations of T-cell fitness prior to B-cell maturation antigen (BCMA)–targeted chimeric antigen receptor T-cell (CART) and bispecific T-cell engager (BiTE) therapies and efficacy/toxicity in relapsed/refractory multiple myeloma (RRMM).

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Background: While CART and BiTE have led to unprecedented responses in RRMM, some patients (pts) do not respond or have short-lived responses. Currently no predictive markers exist to identify these pts. This study explored pretreatment T-cell fitness and efficacy/toxicity in RRMM using a novel single-cell secretome analysis. We hypothesized that pretreatment Polyfunctional Strength Index (PSI) may predict efficacy to BCMA-directed T-cell therapies. **Methods:** We included 14 RRMM pts treated with idecabtagene vicleucel or teclistamab at Yale Cancer Center with ≥6 mos post-treatment follow-up. Peripheral blood prior to treatment was frozen and then PBMC's thawed for analysis. PSI, a metric for T-cell fitness combining polyfunctional T-cells % with the intensity of secreted cytokines, was obtained using the IsoPlexis' Single-Cell Secretome Platform. The overall PSI was an average of CD4+ and CD8+ PSIs. Response was assessed by the International Myeloma Working Group criteria and response duration was defined as time from response to disease progression. Responder (R) was defined as ≥very good partial response for ≥6 mos. Non-responder (NR) was defined as stable or progressive disease ≤3 mos. Cytokine release syndrome (CRS) and immune-effector cell associated neurotoxicity syndrome (ICANS) were graded using the American Society for Transplantation & Cellular Therapy system. Statistics were performed with Mann-Whitney U test using GraphPad PRISM v.9. **Results:** There were 7 pts in R group (2 BiTE & 5 CART) and 7 pts in NR group (3 BiTE & 4 CART). Median follow-up time was 13.5 mos(range, 7-27). Median age at treatment was 64 yrs in R and 63 yrs in NR. Extramedullary disease (EM) was present in 14.3%(n=1) in R and 71.4%(n=5) in NR. High-risk cytogenetics, defined as del17p, t(4;14), t(14;16), t(14;20), 1q gain/amplification and del1p, were seen in 42.9%(n=3) in R and 85.7%(n=6) in NR. Median prior lines of therapy was 6(range, 4-9) in R and 8(range, 4-10) in NR. CRS/ICANS occurred 85.7%(n=6) in R and 28.6%(n=2) in NR. Overall PSI was 184 in R and 91 in NR(p=0.1649). CD4+ PSI was 160 in R and 75 in NR(p=0.1649). CD8+ PSI was 207 in R and 108 in NR(p=0.1981). Overall PSI was 143 in CRS/ICANS and 130 in no CRS/ICANS(p=0.7546). **Conclusions:** Overall PSI, CD4+ PSI and CD8+ PSI were 1.9-2.1 times higher in R compared to NR and overall PSI was slightly higher in CRS/ICANS compared to no CRS/ICANS though the difference was not statistically significant. One limitation was a small sample size and thus testing PSI in a larger cohort might yield statistically significant results. The NR group had more high-risk cytogenetics and higher EM. One confounder could be that measuring peripheral T-cell fitness may not be sufficient to predict response in EM where spatial determinants of T-cell influx play a role. Research Sponsor: The Frederick A. DeLuca Foundation.

Real world outcomes of high dose melphalan conditioning prior to autologous stem cell transplant in extramedullary multiple myeloma vs. multiple myeloma without extramedullary involvement: A single center experience.

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Background: Extramedullary multiple myeloma (EMM) is defined as the presence of multiple myeloma plasma cells, which develop outside of the bone marrow. It is an aggressive form of multiple myeloma that is associated with a poor prognosis. The current standard of care for multiple myeloma consists of induction, high dose melphalan autologous stem cell transplant (ASCT), followed by maintenance. However, there is limited data on the outcome of patients with extramedullary multiple myeloma who undergo ASCT. Therefore, we examined the outcomes of high dose melphalan conditioning prior to ASCT in EMM patients compared to multiple myeloma patients without extramedullary involvement (non-EMM) at an academic institution in Los Angeles. **Methods:** We retrospectively reviewed 246 multiple myeloma patients who underwent ASCT after receiving high dose melphalan conditioning at USC Norris Comprehensive Cancer Center from Jan 2017 to Dec 2022. The cohort was subdivided into 70 EMM patients and 176 non-EMM patients. Outcomes were measured as the status of disease response, which was evaluated at 100 days (D+100) and 365 days (D+365) after the date of transplant. **Results:** In the EMM group, 1.43% (n=1) was found to have progression at D+100 and 12.86% (n=9) at D+365. In the non-EMM group, 0.57% (n=1) was found to have progression at D+100 and 11.93% (n=21) at D+365. There was no statistical significance between the EMM and non-EMM groups for progression free survival at D+100 (p-0.50) and D+365 (p-0.75). Regarding overall survival, there were 0 deaths observed at D+100 in both the EMM and non-EMM groups. For D+365, the overall survival was 98.57% (n=69) for the EMM group and 99.43% (n=175) for the non-EMM group. There was no statistical significance between the overall survival at D+365 (p-0.14). **Conclusions:** The EMM cohort exhibited similar rates of progression free survival (87.14% vs. 88.07%) and overall survival (98.57% vs. 99.43%) compared to the non-EMM cohort at one year post ASCT after receiving high dose melphalan conditioning. We observed that there was no significant statistical difference between the EMM and non-EMM cohorts regarding progression-free survival (p-0.75) and overall survival (p-0.14) on day 365. According to our data, high dose melphalan conditioning prior to autologous stem cell transplant is equally as effective for patients with multiple myeloma with or without extramedullary involvement. Future studies with long-term follow-up are recommended to further explore these findings. Research Sponsor: None.

	EMM (n=70)	Non-EMM (n=176)
D+100 Progression Free Survival	98.57%	99.43%
D+100 Overall Survival	100.00%	100.00%
D+365 Progression Free Survival	87.14%	88.07%
D+365 Overall Survival	98.57%	99.43%

7551 Poster Session

Uncontrolled diabetes mellitus and the progression of monoclonal gammopathy of undetermined significance to multiple myeloma in US veterans.

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Background: Studies have shown that, independent of obesity, the metabolic effects of diabetes mellitus (DM) promote the progression of monoclonal gammopathy of undetermined significance (MGUS) to multiple myeloma (MM). However, it is unclear whether glycemic control is associated with MGUS progression in DM patients. We aimed to evaluate the association between poor glycemic control, measured by HbA1c >6.5%, and progression. **Methods:** Patients diagnosed with MGUS from 1999-2021 in the Veterans Health Administration (VHA) were identified using a published natural language processing (NLP)-based algorithm. We focused on patients whose MGUS subtype was IgG, IgA, or light chain. We excluded patients lacking body weight measurements from the time of MGUS diagnosis to the end of follow-up to ensure receiving care in the VHA. We further excluded patients with extended gaps >1 year between HbA1c measurements. Time-varying HbA1c measurements during the follow-up, evaluated at 1-day intervals and categorized into uncontrolled (HbA1c >6.5%) or controlled (≤6.5%) DM was the exposure variable. Progression of MGUS to MM was also confirmed by a published NLP algorithm. The association between the time-varying controlled/uncontrolled DM and progression was estimated by multivariable-adjusted hazard ratio (aHR) with death as a competing event. The covariates included sex, race, MGUS subtype as well as age, body mass index, monoclonal protein level, Charlson Comorbidity Index, DM medication, and DM type (type 1, type 2 with insulin-dependency status, type 2 without insulin-dependency status), all at MGUS diagnosis. Same analysis was conducted in a subgroup of patients with non-insulin dependent DM type 2 (NIDDMT2) without insulin use between MGUS diagnosis and the end of follow-up. **Results:** After applying inclusion and exclusion criteria, we identified 9,682 patients with both DM and MGUS. The multivariable analysis revealed a positive association between poor glycemic control and MM progression (see Table): (aHR 1.27, 95% CI 1.13-1.42). In NIDDMT2 without insulin use (n=3,498), poor glycemic control was associated with MM progression (aHR 1.81; 95% CI 1.57-2.10). **Conclusions:** For patients with DM and MGUS, the risk of MGUS progression to MM was 27% higher in uncontrolled DM and 81% higher in patients with NIDDMT2. This finding highlights a modifiable risk factor for MM progression in MGUS patients. Future studies should examine if interventions to enhance glycemic control could potentially reduce MGUS progression. Research Sponsor: U.S. National Institutes of Health; CA253475; U.S. National Institutes of Health; CA265735.

Population attributable fractions for risk factors for the progression of monoclonal gammopathy of undetermined significance to multiple myeloma in the Veteran population.

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Background: Multiple myeloma (MM) is the most common type of plasma cell cancer in the U.S. MM is consistently proceeded by monoclonal gammopathy of undetermined significance (MGUS). Studies have identified several risk factors for the progression of MGUS to MM. However, the contribution of each of these risk factors has not been quantified. We computed the population attributable fractions (PAFs) for selected risk factors in the U.S. Veterans Health Administration (VHA) health system. **Methods:** Veterans diagnosed with MGUS from 1999-2021 were identified and confirmed via a published natural language processing (NLP) model. We included Black and White patients whose immunoglobulin (Ig) subtype was IgA, IgG, or light chain. Patients who progressed to MM ≤6 months after MGUS diagnosis were excluded. We fit a multivariable time-to-event model controlling for sex, race (Black, White), Ig subtype (IgA, IgG, light chain), agent orange (AO) exposure, as well as M-protein level (≤, >1.5 g/dL), Charlson Comorbidity Index (CCI), obesity status (underweight, normal weight, overweight, obese), and age, all at MGUS diagnosis. The outcome was progression of MGUS to MM, which was also confirmed by a published NLP model. PAF for a risk factor is the fraction of all MM cases in the veteran population that is attributable to this specific risk factor. It accounts for both the prevalence and relative risk of this factor in the population. We calculated PAF for black race, IgA, AO exposure, and overweight/obesity. **Results:** The analysis included 24,917 patients with MGUS. Among them, 7.8% (n=1,944) progressed to MM (follow-up median 5.6, IQR 3.3-8.8 years). In the veteran population with MGUS, 17.9% of all MM cases was attributable to overweight or obesity (PAF 17.9%, 95% confidence interval [CI] 11.0-24.3%); 7.6% was attributable to black race (PAF 7.6%, 95% CI 4.3-10.9%), 5.7% was attributable to IgA (PAF 5.7%, 95% CI 4.0-7.4%), and 2.4% was attributable to AO exposure (PAF 2.4%, 95% CI 1.0-3.9%). **Conclusions:** In the veteran population with MGUS, overweight/obesity, the only modifiable factor, is the top contributor to progression to MM cases. In veterans with MGUS, had the overweight or obese MGUS patients to be reversed to normal weight, an estimated 17.9% of the progression cases could have been avoided.Our findings highlight the importance of maintaining a normal weight for reducing the risk of progression of MGUS to MM. Research Sponsor: Foundation for Barnes-Jewish Hospital; Siteman Cancer Center; U.S. National Institutes of Health; U01CA265735.

PAF for selected risk factors for progression of MGUS to MM in the veteran population.

Risk Factor*	PAF (%)	95% Lower CI	95% Upper CI
Overweight/obese (vs normal weight)	17.9	11.0	24.3
Black (vs White) race	7.6	4.3	10.9
IgA (vs IgG) MGUS	5.7	4.0	7.4
AO (vs no AO) exposure	2.4	1.0	3.9

*Multivariable time-to-event model adjusted for sex, race, Ig subtype, AO exposure, as well as M-protein level, CCI, obesity status, and age, all at MGUS diagnosis.

Mortality trends (1999-2022) in patients with multiple myeloma with pneumonia, influenza, and COVID-19.

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Background: Patients (pts) with multiple myeloma (MM) are immunosuppressed either due to the hypogammaglobulinemia and impaired plasma cell function or due to pharmacological management and stem cell transplantations. Consequently, they are at a higher risk of infections. This study aims to evaluate the changes in mortality from COVID-19 (CVD), influenza virus (FLU), and pneumonia (PNA) in MM pts in the era of CVD pandemic. **Methods:** Using the Wide-ranging Online Data for Epidemiologic Research (WONDER) database from the CDC, we collected mortality data for pts with CVD (U07.1 code), FLU and PNA (J09-J18 codes), and MM (C90.0 code). Using sex and ethnicity-specific stratification, the gathered data made it easier to calculate age-adjusted mortality rates (AAMRs) per 100,000 people. Using the collected data we were able to analyze mortality patterns over the years 1999-2022. **Results:** Overall, 25,271 MM pts died from CVD, FLU and PNA between 1999 to 2022. The mortality rate remained stable from 1999 to 2019 ranging between 0.4 AAMR per 100,000 to 0.3 AAMR, representing an annual percentage change (APC) of -0.5%. However, the mortality rate increased in 2019, rising from 0.3 AAMR per 100,000 to 0.5 in 2022, with APC of 7%. When evaluating the trends by gender, there was an increase in mortality among male pts, rising from 0.4 AAMR per 100,000 to 0.7 between 2019 and 2020, while the increase among females was minimal, from 0.3 AAMR per 100,000 to 0.4. While Hispanic, White, and African American ethnicities mortality increased in 2020-2022, Asian pts maintained a rate of 0.2 AAMR in 2019, 2020, and 2022 (Table). **Conclusions:** We showed an increase in mortality among pts with MM combined with CVD, FLU, or PNA between 2020 and 2021. It might be attributable to the CVD pandemic, announced by WHO in March 2020. Despite the FDA's approval of the first CVD vaccine in December 2020, the emergence of new CVD variants and limited vaccine availability could have contributed to a continued increase in mortality in 2021.In 2022, we noticed a drop in mortality. It might be explained by the wider accessibility to CVD vaccination or to diminished virulence. Additionally, increased awareness of the importance of CVD vaccinations in immunocompromised pts could also lead to increased FLU vaccination rates. It might explain the downtrending mortality of pts with MM, FLU and PNA only in 2021. This is the first study presenting the mortality trend of MM pts with FLU, PNA and CVD, and comes to highlight the importance of vaccination in immunocompromised MM pts. Research Sponsor: None.

AAMR per 100,000 for FLU, CVD and PNA related Mortality in MM pts.

Year	Overall	Male	Female	Asian	African American	White	Hispanic or Latino
1999	*0.4*	*0.5*	*0.4*	*0.3*	*0.5*	*0.4*	*0.2*
2003	*0.4*	*0.5*	*0.3*	*0.2*	*0.4*	*0.4*	*0.1*
2007	*0.3*	*0.4*	*0.3*	*0.3*	*0.4*	*0.3*	*0.1*
2011	*0.3*	*0.4*	*0.2*	*0.1*	*0.3*	*0.3*	*0.1*
2015	*0.3*	*0.4*	*0.2*	*0.2*	*0.4*	*0.3*	*0.1*
2019	**0.3**	**0.4**	**0.3**	**0.2**	**0.4**	**0.3**	**0.2**
2020	**0.5**	**0.7**	**0.4**	**0.2**	**0.9**	**0.5**	**0.4**
2021	**0.6**	**0.7**	**0.4**	**0.3**	**0.8**	**0.6**	**0.3**
2022	**0.5**	**0.7**	**0.4**	**0.2**	**0.8**	**0.5**	**0.3**

Effect of daratumumab on light chain reduction in newly diagnosed multiple myeloma with light chain cast nephropathy.

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Background: Light chain cast nephropathy (LCCN) is present in 16-31% of patients (pts) in newly diagnosed multiple myeloma (NDMM). In pts with an involved serum free light chain (iFLC) >150mg/dL and predominant LC proteinuria, the probability of LCCN is high enough for a clinical diagnosis without the need for kidney biopsy. Early mortality is higher in pts with renal impairment (RI) who did not achieve a renal response (RR), and a rapid reduction in iFLC may predict RR. While the use of bortezomib and dexamethasone (Vd) in upfront therapy has led to marked improvements in outcomes, the optimal regimen is unclear. **Methods:** We included pts with NDMM and RI (creatinine >2 mg/dL or eGFR <40 ml/min/1.73m^2) and a diagnosis of LCCN (iFLC >150mg/dL and light chain proteinuria) at a single center from 2005-2023. Pts with >10% albuminuria or a diagnosis of MGRS or amyloidosis were excluded. Primary outcome was FLC response (iFLC <50mg/dL and >90% reduction, FLC-R) at day 30 (d30). Other outcomes included hematologic response (partial response or better) at d30 and RR (minimal response or better) at d90, based on International Myeloma Working Group criteria. **Results:** We included 51 pts with characteristics depicted in the table. All pts received therapy with Vd, adding cyclophosphamide (VCd) in 26 (51%), daratumumab (dara, DVd) in 13 (25%), both (DVCd) in 6 (12%) and alone in 6 (12%). At d30, 11 pts (58%) in dara-containing regimens (DVd, DVCd) and 10 pts (31%) in non-dara-containing regimens (Vd, VCd) achieved a FLC-R (p=0.08); dara was associated with higher odds of achieving a FLC-R at d30 (OR 2.9, p=0.03) after adjusting for age, stage and eGFR at diagnosis. At d90, pts receiving dara had a higher rate of RR than those who did not (69% vs 58%, p=0.5); dara was associated with higher odds of a RR at d90 (OR 1.6, p=0.5). After adjusting for age, stage and eGFR at diagnosis, achieving a FLC-R at d30 was associated with higher odds of a RR at d90 (OR 8.9, p=0.02). **Conclusions:** Prompt reduction of iFLC is an important objective during the early treatment of LCCN in order to achieve a RR, and dara increases the odds of achieving a FLC-R. The use of dara led to higher odds of a RR at d90, but not statistically significant. We confirmed that achieving a FLC-R at d30 was associated with achieving a RR at d90. Our results suggest that the role of a dara should be explored in prospective studies for the upfront treatment of LCCN in NDMM. Research Sponsor: None.

	Dara (n = 19)	Non-Dara (n = 32)	Total (n = 51)
Age, median (IQR)	70 (60-80)	68 (54-75)	68 (56-77)
Female, n (%)	7 (37%)	14 (44%)	21 (41%)
ISS 3, n (%)	19 (100%)	25 (78%)	44 (86%)
eGFR at diagnosis, median (IQR)	16.3 (10.6-22.8)	18.6 (6.4-25.1)	17.3 (8.3-24.7)
iFLC, median (IQR)	869 (356-1258)	1200 (743-1456)	1155 (490-1435)
Cyclophosphamide-containing regimens, n (%)	6 (32%)	26 (81%)	32 (63%)
Hematologic response at d30, n (%)	17 (89%)	23 (72%)	40 (78%)
FLC-R at d30, n (%)	11 (58%)	10 (31%)	21 (41%)
RR at d90*, n (%)	11 (69%)	15 (58%)	26 (62%)

Outcomes of myeloma cast nephropathy in the era of anti-CD38 monoclonal antibody-based frontline therapy: A retrospective cohort study.

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Background: Myeloma cast nephropathy (MCN) has been a well-known negative predictive marker in newly diagnosed multiple myeloma (NDMM). Anti-CD38$^+$ monoclonal antibodies (mAb) have improved outcomes, but little is known about their impact in patients with MCN. We performed a retrospective cohort study to investigate the outcomes of patients with MCN in the era of anti-CD38$^+$ mAb-based frontline therapy. **Methods:** 115 NDDM patients received frontline anti-CD38$^+$ mAb from 11/15/18 to 1/24/23. MCN was defined as evidence of light chain casts on biopsy, serum creatinine of >2mg/dL, or 2021 CKD-EPI eGFR of <40mL/min/1.73m^2; ≥1g/d proteinuria; and involved FLC ≥50mg/dL. 23 had MCN; 92 were contemporary controls. We obtained data regarding clinical course. **Results:** 6 MCN patients needed hemodialysis (HD) at diagnosis. MCN patients had similar R2-ISS to controls. Median proteinuria in MCN patients was 5.7g/d more than in controls; serum creatinine (Cr) was 3.2mg/dL higher; and median hemoglobin was 1.5g/dL less. More MCN patients received quadruplet regimens (86.9% vs 62.0%, p = 0.010); similar proportions were transplanted. At 1, 3, and 6 months, serum Cr was higher in MCN patients ($p < 0.001$, p = 0.002, p = 0.002). Urine protein:creatinine ratios trended toward difference at 1 month (2.04 vs 0.15g/g MCN vs controls, p = 0.061) but were similar at 3 and 6 months. Response rates at 6 months did not differ. 4 MCN patients still required HD after 6 months. Median follow-up was 23.0-23.5 months. 4 MCN patients died, 1 due to progressive disease. No significant difference in disease-free survival (DFS; HR = 0.58, 95% CI 0.20-1.64, p = 0.295), time to next treatment (TTNT; HR = 0.53, 95% CI 0.20-1.39, p = 0.191), or overall survival (OS; HR 0.610, 95% CI 0.19-1.98, p = 0.406) was seen at any point between MCN and control cohorts. 1 year DFS, TTNT, and OS were: 87.0% MCN, 94.5% control; 77.2% MCN, 91.7% control; 87.9% MCN, 96.1% control. By statistical equivalence testing, MCN DFS and TTNT were within 6 months of control DFS and TTNT (p = 0.038, p = 0.032); MCN OS was within 5 months of control OS (p = 0.034). **Conclusions:** Patients with NDMM and MCN who receive upfront anti-CD38$^+$ mAb therapy experience prolonged survival compared to prior findings. Anti-CD38$^+$ mAb may substantially reduce, though not fully eliminate, the negative survival impact of MCN. Multiple mechanisms, including time to proteinuria resolution, may be involved. Further study is warranted. Research Sponsor: T32 CA203703.

Selected characteristics.

	MCN	Controls	p-value
Age	65 (40-82)	69 (38-93)	0.194
Sex, F/M	11/12	46/46	0.852
Baseline creatinine (mg/dL)	5.18 +/- 3.06	1.17 +/- 0.75	**<0.001***
Baseline urine protein (g/d)	5.54 +/- 3.97	1.56 +/- 3.36	**<0.001***
ASCT			
Mel-140	6/23 (26.1%)	7/92 (7.6%)	
Mel-200	3/23 (13.0%)	22/92 (23.9%)	**0.040***
6 month response			
CR	9/22 (40.9%)	26/72 (36.1%)	
VGPR	2/22 (9.1%)	19/72 (26.4%)	
PR	8/22 (36.4%)	21/72 (29.2%)	0.335
MR or worse	3/22 (13.6%)	6/72 (8.3%)	

From criteria to clinic: How updated SLiM CRAB criteria influence multiple myeloma diagnostic activity.

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Background: Multiple myeloma (MM) is a plasma cell malignancy, which is preceded by asymptomatic, precursor state of monoclonal gammopathy of undetermined significance (MGUS). Once diagnosed with MGUS, monitoring for progression to MM is recommended. The diagnostic criteria for active MM include presence of ≥1 CRAB features (hypercalcemia, renal failure, anemia, or one or more osteolytic bone lesions on skeletal radiology, CT or PET/CT imaging) in addition to clonal plasma cells on bone marrow. In 2014, the International Myeloma Working Group (IMWG) added SLiM to the criteria: clonal bone marrow plasma cells ≥60%, serum free light chain (FLC) ratio ≥100, and >1 focal lesion on magnetic resonance imaging (MRI). This study investigated the longitudinal influence of the updated diagnostic criteria on the utilization of imaging examination and the number of MM diagnoses overtime among patients with MGUS. **Methods:** We used data from the U.S. Veterans Health Administration (VHA) 2010-18. Patients with MGUS were identified by a published natural language processing (NLP) model. MM cases diagnosed under the old criteria were identified using International Classification of Diseases (ICD)-9/10 codes for CRAB symptoms, while cases diagnosed under the new criteria were identified using a published NLP-assisted model developed based on the SLiM-CRAB criteria. We then performed a counterfactual comparison to contrast the number of MM cases that would have been diagnosed under the old criteria with those under the new criteria. To monitor changes in the use of advanced imaging technology, we calculated the frequency of imaging examinations orders <1 year following MGUS diagnosis, including whole-body/spine computed tomography (CT), MRI and positron emission tomography-CT. **Results:** A total of 29,336 MGUS patients were identified. MGUS patients undergoing whole-body or spine MRI/CT scans <1 year following-MGUS diagnosis increased from 15.72% during 2010-13 to 21.06% during 2015-18 (P = 0.002). In 2010-13, 346 MM cases were diagnosed per year on average with the old criteria. This number increased to 666 cases in 2015-18 with the updated criteria. Had the new criteria been applied retrospectively to 2010-13, the number of diagnoses would have increased 28% (to 441 cases per year). Conversely, had the old criteria been applied to 2015-18, the number of diagnoses would have decreased by 29% (to 473 cases per year). **Conclusions:** Our study revealed a significant increase in MM diagnoses after adding the SLiM biomarkers into the updated diagnostic criteria. In parallel, there has been an increase in the use of CT/MRI imaging for MGUS patients, suggesting a shift towards more aggressive diagnostic strategies. Further analysis is warranted to evaluate the positive detection rate of active MM through imaging and to understand the implications of early detection on MM patient outcomes. Research Sponsor: U.S. National Institutes of Health; R01 CA253475; U.S. National Institutes of Health; Foundation for Barnes-Jewish Hospital.

Effect of dose-adjusted melphalan on MRD-negativity to full dose melphalan in patients with multiple myeloma post-autologous stem cell transplant.

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Background: Despite significant therapeutic advancements, Multiple Myeloma (MM) remains an incurable disease. Autologous stem cell transplantation (ASCT) is a standard treatment for eligible patients, with high-dose melphalan (MEL200) as the preferred conditioning regimen. Reduced-dose melphalan (MEL140) is used for older or less fit patients. However, this was not prospectively studied and there has been ongoing debate about the efficacy of reduced dosing. This study aimed to investigate the impact of melphalan dose on minimal residual disease (MRD) negativity rates in MM patients undergoing upfront ASCT. **Methods:** We conducted a retrospective, single-center study involving 74 MM patients who underwent ASCT between 2018 and 2022 at UHCMC, Cleveland, OH and had MRD testing done after transplant. MRD testing was performed using the ClonoSEQ next generation sequencing platform. **Results:** Median age was higher in the MEL140 group compared to MEL200 (70.3 vs 59.8 years), both groups were similar in terms of sex and race distribution, BMI and KPS scores. Both groups have comparable ISS staging and high-risk cytogenetics. Similar numbers of lines of treatment prior to transplant were seen, with approximately 64% having only one line. First-line induction therapy included triplet therapy (Lenalidomide, Bortezomib, and Dexamethasone) in 73% of patients. Depth of remission at transplant was comparable between groups. MRD negativity rates at 10^{-5} and 10^{-6} were comparable between MEL140 and MEL200 groups (64% and 39% in MEL140; 61% and 41% in MEL200; p=0.8 and 0.7 respectively). Sustained MRD negativity at 10^{-5} over at least 12 months was also comparable (43% in MEL140; 50% in MEL200, p=0.8). After a median follow-up of 37 months, PFS was not reached for either group (p=0.69). Patients achieving MRD negativity at levels of 10^{-5} had a not reached median PFS, while those not achieving MRD negativity had a median PFS of 41 months (95%CI 23-NR; p=0.024). There was no significant difference in hospital stay duration, time to neutrophil engraftment, readmission rate, or infections within 100 days post-transplant between the MEL140 and MEL200 groups. **Conclusions:** Our real-world analysis demonstrates that MEL140 yields similar deep post-transplant remissions as MEL200, translating to improved PFS for patients achieving MRD negativity, regardless of the dose used. This is the first report to our knowledge of MRD negativity rate in patients receiving MEL140. Research Sponsor: None.

	MEL 140 N = 28	MEL200 N = 46	P-value
Hospital Stay (d)	15.07 (2.14)	15.61 (5.51)	0.3
Readmissions	4(14%)	10(22%)	0.4
Infections	4(14%)	9(20%)	0.8
MRD negativity 10^{-5}	18(64%)	28(61%)	0.8
MRD negativity 10^{-6}	11(39%)	20(43%)	0.7
Sustained MRD negativity 10^{-5}	12(43%)	23(50%)	0.8

First relapse in patients with multiple myeloma: Outcomes and predictors.

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Background: Survival in patients with multiple myeloma (MM) continues to improve with the newer therapies, but there is no clear evidence of a cure and patients continue to relapse. However, most patients have the most extended period without progression with their first-line therapy, and subsequent therapies often provide a shorter duration of response due to the use of drugs with overlapping mechanisms of action and, more importantly, a shorter first remission, pointing toward more aggressive disease biology. With newer immunotherapies being used at 1st relapse, this may change. We designed this study to explore the natural history of MM after the 1st relapse and define the predictors of outcome after the initial relapse. **Methods:** We identified all patients in the Mayo Clinic database diagnosed between Jan 2004-June 2019 who had had initial disease progression. The study cohort included 2005 patients. We explored the overall survival (OS) from the time of documented disease progression or the start of second-line treatment in patients who had not met IMWG criteria before second-line therapy. Front-line therapy was grouped into those with either an IMiD or PI, both IMiD and PI, daratumumab with IMiD and PI, and none of these agents. The IMiD and PI were always used with dexamethasone with or without an alkylator. **Results:** The median age was 63 (range 24-95) years and 60% were male. The median estimated follow-up from diagnosis for all patients was 86 mos. (95% CI; 82, 88) and the median time to progression from the start of therapy was 25 mos. (95% CI; 24, 26). The median OS from the first progression was 45 mos. (95% CI; 42, 50), 36 mos. for those diagnosed before 2009, and 52-53 mos. for those diagnosed later. On univariate analysis, age <70 at 1st relapse, RISS I, novel agents in initial therapy, CR in the first line, diagnosis after 2009, initial remission >18 mos, and initiation of therapy before IMWG progression were all associated with improved OS after 1st relapse (Table). On multivariate analysis, age <70, RISS I, initial remission >18 mos, and initiation of therapy before IMWG progression were all associated with improved OS after 1st relapse. **Conclusions:** The study provides an estimate of the outcomes and significant predictors of outcomes after 1st relapse in patients with MM. These factors should be taken into consideration when designing clinical trials in this patient population. In particular, these factors identify a high-risk group of patients not always identified by baseline characteristics and should be the focus of future trials.
Research Sponsor: None.

Factors affecting overall survival from progression.

Variable	HR (Univariate)	(HR) Multivariate
Age ≥70 vs <70	1.7	***1.6***
RISS III/II vs I	3.6/1.9	***2.8/1.8***
Dara-Len-PI/ Len-PI/Len or PI vs none	0.35/0.55/0.7	NS
CR with 1st line Rx vs No CR	0.65	NS
Duration of response <18 mos/18-36 mos vs >36 mos with 1st line Rx	3.5/2	***3/1.8***
Rx start before IMWG progression vs. not	0.5	***0.3***
Diagnosis in/after 2009 vs. before	0.75/0.68	NS

7559 Poster Session

Open-label, single-arm phase Ib/II study of immune combination therapy with elotuzumab and belantamab mafodotin in patients with relapsed refractory multiple myeloma.

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Background: The B cell maturation antigen (BCMA)-targeted antibody drug conjugate belantamab mafodotin enhances cell-mediated antibody-dependent cellular cytotoxicity and antibody-dependent cellular phagocytosis. Elotuzumab, a signaling lymphocytic activation molecule family member 7 (SLAMF7) checkpoint inhibitor, activates NK cells and induces antibody-dependent cellular cytotoxicity. Bela-Elo (NCT05002816) is an ongoing phase Ib/II trial evaluating the safety, tolerability and preliminary efficacy of the unique combination of these two agents in patients with relapsed/refractory myeloma (RRMM). We report data from phase I part of this trial. **Methods:** This single-arm phase Ib/II study is enrolling patients with triple-class refractory RRMM. Patients with progression after prior BCMA-targeted therapy are eligible. Elotuzumab is administered via intravenous (IV) infusion at an established dose of 10 mg/kg on days 1, 8, 15, 22 every 28 days for cycles 1 and 2; followed by 20mg/kg on day 1 of each 28-day cycle. Belantamab mafodotin is administered via IV infusion with the starting dose of 1.9 mg/kg IV at every 4-week interval, with subsequent dose-reduction based on toxicity. Descriptive statistics were used to summarize patient demographics and safety and efficacy outcomes. **Results:** As of data cut-off (January 20, 2024) 12 subjects have been enrolled; and 10 subjects received treatment on study. Median age of patients was 66.5 years (range 59-79). The patient population was heavily pretreated with 5 prior median lines of therapy (range 2-8); 40% (4/10) of patients were refractory to prior BCMA-targeted therapy (2 post-BCMA bispecific antibody, 2 post-BCMA chimeric antigen receptor T-cell therapy [CART]). Phase I part of the study has completed. Median duration of treatment was 4 months (range 2-19). No dose-limiting toxicities were observed. Four severe adverse events were observed possibly related to the study treatment in 3 patients, including grade 3 pulmonary infection (n=1) and lymphopenia (n=3). Ocular keratopathy developed in 40% of patients, all were grades 1-2 and resolved after discontinuation or dose-reduction of belantamab. Preliminary activity is noted with partial responses (PR) in 4/10 (40%) and stable disease (SD) in additional 3/10 (30%) of patients. Among the four patients who were refractory to prior BCMA therapy, 2 (50%) achieved PR, with duration of response (DOR) of 19 months and 9 months, respectively. **Conclusions:** This novel combination immune therapy with belantamab mafodotin and elotuzumab appears to have an encouraging safety profile and a promising preliminary efficacy in patients with heavily pretreated RRMM, including in those with prior failure of BCMA-targeted therapy. Clinical trial information: NCT05002816. Research Sponsor: GSK.

Indirect comparison of linvoseltamab versus teclistamab for triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM).

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Background: No head-to-head clinical trials have compared effectiveness of anti-BCMA×CD3 bispecific antibodies for TCE RRMM. This analysis compared efficacy of linvoseltamab vs teclistamab via an unanchored matching-adjusted indirect comparison (MAIC). **Methods:** A MAIC was deemed feasible after excluding 10 patients (pts) with prior BCMA antibody–drug conjugate exposure from LINKER-MM1 (linvoseltamab) to match MajesTEC-1 (teclistamab) criteria. Pt-level data from LINKER-MM1 (107 pts receiving 200 mg in Phase 1/2, data cut-off [DCO] 9/2023, median follow-up 11.1 months [mos]) and published data from MajesTEC-1's efficacy population (150 pts, DCO 11/2021, median follow-up 9.8 mos) were analyzed. LINKER-MM1 pts were weighted to match key baseline characteristics in MajesTEC-1 (cytogenetic risk, age, refractory status, ISS stage, ECOG score, extramedullary disease/plasmacytoma status) selected via a prespecified algorithm (Kumar et al., 2023). Objective response rate (ORR), very good partial response or better (≥VGPR), complete response or better (≥CR), and minimal residual disease (MRD) negativity (- [at 10-5 threshold]) rates, duration of response (DOR), progression-free survival (PFS), and overall survival (OS) were compared. Odds ratios (ORs) and hazard ratios (HRs) with 95% confidence intervals (CIs) were reported before and after matching; a sensitivity analysis included all LINKER-MM1 200 mg pts (n=117). **Results:** Effective sample size for linvoseltamab was 82 after matching and baseline characteristics were balanced with MajesTEC-1. Before and after matching, linvoseltamab exhibited higher ORR, ≥VGPR, ≥CR, and MRD(-) rates, with significant differences in ≥CR. Linvoseltamab had significantly longer PFS and a trend toward longer OS and DOR (Table). Sensitivity analysis results were similar. **Conclusions:** The results suggest potentially greater efficacy for linvoseltamab vs teclistamab for all outcomes, highlighting its potential as a highly effective treatment option for TCE RRMM. Research Sponsor: Regeneron Pharmaceuticals, Inc.

	Teclistamab	Linvoseltamab before matching	Linvoseltamab after matching	Linvoseltamab vs teclistamab before matching	Linvoseltamab vs teclistamab after matching
	%	%	%	*OR (CI)*	*OR (CI)*
ORR	63	71	70	1.46 (0.98, 2.18)	1.42 (0.91, 2.22)
≥VGPR	59	63	61	1.18 (0.82, 1.70)	1.10 (0.74, 1.65)
≥CR	32	47	45	1.86 (1.28, 2.71)*	1.75 (1.17, 2.62)*
MRD(-)	13	20	19	1.59 (0.90, 2.82)	1.55 (0.84, 2.84)
	Median, mos (CI)	*Median, mos (CI)*	*Median, mos (CI)*	*HR (CI)*	*HR (CI)*
DOR	Not reached (NR) (not estimable [NE], NE)	NR (NE, NE)	NR (NE, NE)	0.94 (0.46, 1.90)	0.82 (0.38, 1.73)
PFS	10.10 (8.00, NE)	NR (14.72, NE)	NR (15.47, NE)	0.56 (0.37, 0.86)*	0.53 (0.33, 0.86)*
OS	18.27 (18.27, NE)	NR (21.62, NE)	NR (21.62, NE)	0.75 (0.46, 1.22)	0.77 (0.45, 1.31)

*Statistically significant at $p<0.05$ OR >1 or HR <1 indicate better efficacy for linvoseltamab.

Comparative effectiveness of linvoseltamab versus standard-of-care (SOC) treatment (tx) in real-world patients (pts) in the United States (US) with triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM).

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Background: Pts with TCE RRMM have poor outcomes and a high unmet need, with no established SOC tx. LINKER-MM1 (NCT03761108) is a single-arm, Phase 1/2 study investigating linvoseltamab, a B-cell maturation antigen × CD3 bispecific antibody, in pts with RRMM who were previously treated with a proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody, or were triple-class refractory (TCR) to these tx. The aim of this study was to contextualize LINKER-MM1 by comparing outcomes with linvoseltamab vs a real-world (RW) external control arm (ECA). **Methods:** A RW ECA was derived from 2 US electronic health record databases (COTA, Guardian Research Network) of pts who started a new line of therapy (LOT) after classification as TCE or TCR and met key eligibility criteria for LINKER-MM1. Eligibility was assessed at the initiation of each new LOT, and all eligible LOTs were included in the ECA. Data in Phase 2 pts who received linvoseltamab 200 mg in LINKER-MM1 were included (data cutoff: Sep 8, 2023). Inverse probability of tx weighting (IPTW) was used to reduce imbalances between the RW and LINKER-MM1 cohorts. Key prognostic factors were identified using a systematic review and rank ordered by an international committee of MM experts (Kumar et al., 2023). Outcomes included overall response rate (ORR), progression-free survival (PFS), time to next treatment (TTNT), and overall survival (OS). An independent committee of epidemiology and oncology experts reviewed the comparability of the cohorts and endpoint assessments prior to conducting comparative analyses. **Results:** Comparative analyses were performed in 105 pts in the linvoseltamab cohort and 101 RW pts (137 LOTs). Following IPTW, the distribution of cytogenetic risk, age, TCR status, Eastern Cooperative Oncology Group Performance Status, and platelet count were balanced between the 2 cohorts (absolute standardized mean difference <0.10). After adjustment, pts receiving linvoseltamab had significantly improved ORR, PFS, TTNT, and OS vs the RW ECA (see table). **Conclusions:** Linvoseltamab significantly improved outcomes vs RW SOC in the US, highlighting its potential as a highly effective tx in pts with TCE RRMM. Research Sponsor: Regeneron Pharmaceuticals, Inc.

Outcome	Linvoseltamab (N=105)	RW ECA (N=101; 137 LOTs)‡
Proportion achieving response	69.5%	32.4%
OR (95% CI)*	5.34 (2.73–10.65)	-
Median PFS, months (95% CI)†	NE (13.57–NE)	3.39 (2.53–4.08)
HR (95% CI)*	0.23 (0.18–0.32)	-
Median TTNT, months (95% CI)†	15.41 (14.06–NE)	5.75 (3.72–7.13)
HR (95% CI)*	0.23 (0.17–0.35)	-
Median OS, months (95% CI)†	NE (NE–NE)	12.20 (7.89–17.69)
HR (95% CI)*	0.41 (0.28–0.62)	-

CI, confidence interval; HR, hazard ratio; NE, not estimable; OR, odds ratio.
* Comparative effectiveness estimate after IPTW.
† Kaplan–Meier estimates after IPTW.
‡ Effective sample size = 93 LOTs.

Effect of maintenance therapy (MT) on real-world outcomes (RWO) of patients (pts) with newly diagnosed multiple myeloma (NDMM) post stem cell transplant (SCT).

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Background: SCT followed by MT is the standard of care for pts with transplant-eligible (TE) NDMM. Five randomized clinical trials (RCTs) comparing lenalidomide MT versus no MT showed improved progression free survival (PFS), but no overall survival (OS) benefit except for one by McCarthy et al. that allowed pt crossover between treatment arms. Use of MT has also been associated with an increased risk of second primary malignancies and an inferior quality of life. We report RWO post SCT with and without MT in TE NDMM. **Methods:** We performed a multi-center, retrospective, observational study using the de-identified COTA real-world database derived from the EMRs of US centers. Pts with NDMM from 1/1/2012 to 1/1/23 were included in the study. Kaplan-Meier method was used to evaluate time to next treatment (TTNT), OS, follow-up time (reverse OS endpoint), and report log-rank test p-values. TTNT was defined in two ways: time from SCT to the earliest of initiation of next line of therapy (LOT) or death (TTNT1) and the time from 2nd LOT post-SCT to the earliest of initiation of next LOT or death (TTNT2). A propensity score (PS) matched analysis was used to compare study cohorts and report hazard ratios (HRs) using the Cox proportional hazards method. High risk cytogenetic abnormalities (HRCA) were defined as pts with 17p(-), t(4;14), t(14;16), t(14;20) and 1q+. **Results:** 1928 ptsmet the study criteria: 957 pts received SCT with MT (M) and 971 pts received no MT (NM). Median age at Dx was 61 y, 57% were male, 70% were White, and 31.2% had HRCA with a median follow-up of 64 months (mos) (95% CI: 61.6, 66.7). In the M vs NM arms, 29.6% and 32.7% pts had HRCA, respectively. Median TTNT1 for M vs NM was 51 vs 36 months (mos), ($p<0.001$), respectively. Median TTNT2 for M vs NM was 11.7 vs 21.6 mos, ($p<0.001$), respectively. Median OS for M vs NM was 108.8 mos vs 126.3 mos, ($p=0.08$), respectively. In the PS model, the NM group had significantly lower hazard of TTNT2 and OS events (HRs 0.65 and 0.85, $p<0.001$ and $p=0.08$, respectively). **Conclusions:** Our study demonstrates improved TTNT2 outcomes with the NM approach. M therapy did not have an impact on OS in this cohort. Both results indicate an absence of long-term benefit with the use of M therapy. OS is a difficult primary outcome to achieve in MM RCTs where survival may have to be collected for decades. Thus, our large study of RWO with long-term follow-up is valuable.
Research Sponsor: None.

Unadjusted and Adjusted Analysis - SCT M (ref) vs. SCT NM	SCT M Median (95% CI)	SCT NM Median (95% CI)	Unadjusted HR (95% CI), p-value	Adjusted HR (95% CI), p-value
OS	108.82 (96.95, 122.17)	126.25 (119.05, NR)	0.85 (0.71, 1.02), p=0.09	0.85 (0.71, 1.0), p=0.08
TTNT1	50.99 (47.38, 55.86)	35.93 (32.75, 38.6)	1.40 (1.24, 1.57), p<0.001	1.39 (1.24, 1.57), p<0.001
TTNT2	11.67 (9.96, 13.51)	21.63 (18.15, 26.47)	0.64 (0.55, 0.75), p<0.001	0.65 (0.56, 0.75), p<0.001

Access to palliative care in patients with multiple myeloma in the USA: A National Cancer Database (NCDB) analysis of years 2004-2020.

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Background: Palliative care (PC) can improve the quality of life for patients with multiple myeloma (MM). Despite its recognized importance, research gaps persist in understanding factors influencing PC accessibility and utilization, particularly in the diverse MM patient landscape in the real-world setting. This study explores potential associations between race, ethnicity, socioeconomic factors, and PC access for MM patients in the USA. **Methods:** Utilizing the NCDB, we identified 202,949 MM patients diagnosed from 2004 to 2020. Multivariate logistic regression analysis was conducted with SAS version 9.4, to determine independent factors predicting PC access. **Results:** Analysis of 202,949 MM patients revealed notable disparities for access to PC. Female patients exhibited lower PC odds (OR: 0.94, $p < 0.0001$) compared to male patients, as did Black patients (OR: 0.80, $p < 0.0001$) and other racial groups (OR: 0.84, $p < 0.0001$) compared to White patients. Hispanic ethnicity was associated with lower PC utilization odds (OR: 0.84, $p < 0.0001$) compared to non-Hispanics. Earlier years (2004-2007) showed higher PC odds (OR: 1.12, $p < 0.0001$), while subsequent years (2008-2011, 2012-2015) exhibited lower odds (OR: 0.93, $p = 0.0009$; OR: 0.87, $p < 0.0001$, respectively) compared to the most recent years (2016-2020). Academic settings had lower PC odds than non-academic facilities (OR: 0.78, $p < 0.0001$). Insurance status varied, with no insurance (OR: 1.40, $p < 0.0001$), Medicaid (OR: 1.17, $p < 0.0001$), and other government insurance (OR: 1.38, $p < 0.0001$) linked to higher PC odds compared to private insurance. Lower annual household incomes (<$38,000, $38,000-$47,999, $48,000-$62,999) had increased PC odds compared to higher incomes (>$63,000) (all $p < 0.0001$). Areas with a higher percentage of individuals without a high school degree exhibited lower PC odds, notably 21% (OR: 0.83, $p < 0.0001$) and 13.0%-20.9% (OR: 0.94, $p = 0.0222$) compared to <7.0% without a high school degree. Greater distance (>30 miles) reduced PC odds compared to shorter distance (<10 miles) to treatment facility (OR: 0.83, $p < 0.0001$). A Charlson-Deyo score of 1 increased PC odds compared to a score of 0 (OR: 1.12, $p < 0.0001$). **Conclusions:** Our real-world analysis reveals substantial disparities in MM patients' PC access and utilization. Female patients and minority groups (Blacks and Hispanics) face significant challenges. The dynamic trends over time and socioeconomic impacts underscore the need for integrating PC and targeted interventions for overall MM patient well-being. Our findings pave grounds for future prospective studies. Research Sponsor: Maroone Cancer Center Hematological Malignancies Research Fund.

Real-world outcomes (RWO) with tandem transplantation in patients (pts) with newly diagnosed multiple myeloma (NDMM).

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Background: Stem cell transplant (SCT) followed by maintenance therapy (MT) is the standard of care for transplant eligible NDMM pts. Tandem transplantation has been found to have progression free (PFS) and overall survival (OS) benefit particularly for patients with high-risk cytogenetic abnormalities (HRCA). However, this modality remains under-utilized in clinical practice. We report RWO with tandem transplant (TT) in comparison with single SCT followed by MT (STM). **Methods:** We performed a multi-center, retrospective, observational study using the de-identified COTA real-world database derived from the EMRs of US centers. Pts with NDMM from 1/1/2012 to 1/1/23 were included in the study. Kaplan-Meier method was used to evaluate time to next treatment (TTNT), OS, follow-up time (reverse OS endpoint), and report log-rank test p-values. TTNT was defined in two ways: time from 1st SCT (2nd if TT) to the earliest of initiation of next line of therapy (LOT) or death (TTNT1) and the time from 2nd LOT post-SCT to the earliest of initiation of next LOT or death (TTNT2). A propensity score (PS) model was used to compare study cohorts, and hazard ratios (HRs) were estimated using the Cox proportional hazards method. HRCA were defined as pts with 17p(-), t(4;14), t(14;16), t(14;20) and 1q+. **Results:** 1117 pts met the study criteria. Median age at diagnosis was 60 yrs. 56.9% were male, 68.9% were White, and 32% had HRCA. 937 pts received STM and 180 pts received TT with median follow-up time of 68 months (mos) (95% CI: 65.4, 71.9) and 39 mos (95% CI: 31.9, 50.1), respectively. Median TTNT1 for TT vs STM was 52.7 vs 51 mos, (p=0.85), respectively. Median TTNT2 for TT vs STM was 33.9 vs 11.8 mos, (p<0.001). respectively. Median OS for TT vs STM was not reached (NR) vs 108.1 mos, (p<0.001), respectively. In the PS model, the TT group had significantly lower hazard of TTNT2 and OS events (HRs 0.49 and 0.47, p<0.001 and p=0.01, respectively) as compared to STM. **Conclusions:** Our study demonstrates significant improvement in unadjusted TTNT2 and OS RWO for TT pts, despite higher incidence of HRCA compared to STM pts. PS analysis demonstrated a similar effect with decreased HRs for TT. OS is an extremely difficult primary outcome to achieve in MM RCTs where survival may have to be collected for decades. Thus, our large study of RWO with long-term follow-up is valuable. Research Sponsor: None.

Unadjusted and Adjusted Analysis - STM (ref) vs. TT	Single SCT M Median (95% CI)	TT NM Median (95% CI)	Unadjusted HR (95% CI), p-value	Adjusted HR (95% CI), p-value
OS	108.13 (96.95, 122.17)	NR (NR, NR)	0.37, (0.21, 0.63), p<0.001	0.47, (0.26, 0.85), p=0.01
TTNT1	50.99 (47.38, 55.86)	52.67 (37.51, 71.38)	1.02, (0.80, 1.31), p=0.85	1.04, (0.76, 1.40), p=0.82
TTNT2	11.77 (9.96, 13.58)	33.9 (29.72, 53.26)	0.44, (0.31, 0.63), p<0.001	0.49, (0.33, 0.73), p<0.001

7565 Poster Session

Automated myeloma cell selection using machine learning and artificial intelligence.

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Background: Precision of sampling is critical to achieve accurate results relevant to diagnostics and prognostics. Sampling errors may compromise the sensitivity and specificity of otherwise credible diagnostics technologies. Our 3- dimensional (3D) telomeres profiling methodology is conducted on individual target cells selected from the patient sample processed using 3D immuno-FISH. In our traditional workflow target cells are manually selected by highly trained personnel based on morphological characteristics and/ or immunophenotypic characteristics, namely cells positive for CD138 and CD56. However, the variability among trained operators required rounds of verification by a second and third operator and an approval by a Hematopathologist or the Lab Director to confirm the selected cells in some cases. Therefore, automated detection of myeloma cells is of paramount importance. **Methods:** In this study we employed machine learning and artificial intelligence (AI) tools to develop an automated algorithm capable of streamlining target cell (i.e. myeloma) selection and minimize or eliminate operator introduced variability. Training libraries were built using positive and negative cells. Over 5000 cells were used in the algorithm training process. We employed iterative rounds of validation and refinement to achieve a high precision automated tool. AI then identified myeloma cells in an automated fashion and the results of AI identification were confirmed by a Hematopathologist. **Results:** We report the results of a comparative analysis done on 20 myeloma patients at different stages of the disease including MGUS, smouldering myeloma and active myeloma. Also, the sample type included bone marrow smears, purified mononucleated plasma cells and bone marrow biopsies. 50 verified manually selected target cells and 50 target cells selected by the automated cell selection tool, approved by a skilled operator, from the same sample of each patient were analyzed using the TeloView platform. The TeloView platform quantifies 6 telomeric molecular and structural parameters. We conducted statistical analysis to calculate Coefficient of Variation (CV) between the results of each patient. We set the acceptable variability to $< 15\%$. We achieved CVs of less than 10% among all patients included in the analysis. **Conclusions:** The automated cell selection tool streamlined this critical sampling process in our workflow minimizing operator-introduced variability, reducing the processing time to a fraction of the time required for manual cell selection and verification which enables high throughput for the 3D telomeres profiling while maintaining precision. Research Sponsor: Telo Genomics Corp.

Genome-wide 5-hydroxymethylation mapping and epigenetic pathways in multiple myeloma.

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Background: Multiple myeloma (MM), a B-cell neoplasm characterized by bone marrow infiltration of malignant plasma cells, is the second most common blood malignancy, with an estimated number of ~35,000 new patients annually in the United States. The molecular pathogenesis of MM is complex and involves various genetic and epigenetic alterations. Key molecular mechanisms, including chromosomal abnormalities such as translocations involving the immunoglobulin heavy chain locus and various oncogenes (e.g., MMSET, FGFR3, CCND1, MAF), alterations in epigenetic regulators (e.g., EZH2, DNMT3A), dysregulation of cell cycle control, and aberrant activation of signaling pathways (e.g., NF-kB, PI3K/AKT, and JAK/STAT), play critical roles in MM pathogenesis. However, epigenetic pathways implicated in MM has not been comprehensively investigated, partly due to technical limitations that cannot distinguish major cytosine modification types. **Methods:** Using the 5hmC-Seal, a highly sensitive chemical labeling technique, we profiled genome-wide 5-hydroxymethylcytosines (5hmC) in circulating cell-free DNA (cfDNA) from a population-based case-control study of MM (cases, n = 313; controls, n = 317) conducted in Canada. **Results:** The 5hmC modification levels were summarized for various genomic features, showing an enrichment in gene bodies and enhancer markers, consistent with the putative role of gene regulation for 5hmC modification. A genome-wide scan of gene bodies identified 771 differential features between cases and controls, adjusting for age, sex, smoking status, education, and first two principal components, at a permutation-based empirical p-value cutoff of 10^{-4}. For instance, IL1RAP, a component of the interleukin-1 signaling cascade, may impact tumor progression and immune system evasion. Furthermore, functional analysis indicated canonical pathways associated with MM pathology and treatment, such as calcium signaling, and synthesis and secretion of cortisol/aldosterone, were enriched in the differential 5hmC features between cases and controls. Notably, the calcium signaling pathway, integral to Ca^{2+} transport and involved in various physiological and pathological processes, plays a critical role in MM pathogenesis. Within this pathway, the CAMK1D gene, which has been identified as a crucial regulator of tumor-intrinsic immune resistance, showed differential 5hmC level between cases and controls, highlighting a vital connection between epigenetic modifications and immune evasion mechanisms in MM. **Conclusions:** Leveraging a state-of-the-art technique, we identified novel epigenetic modifications and pathways in the risk of MM. This approach establishes a solid foundation for further investigating etiology of MM, deepening our understanding of the disease, and advancing the discovery of biomarkers, which could potentially guide preventive strategies. Research Sponsor: U.S. National Institutes of Health; R01CA223662; U.S. National Institutes of Health; R56CA282891.

Exploring T cell subsets as predictors of response to BCMA targeting bispecific antibody therapy in multiple myeloma.

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Background: BCMA targeting bispecific Antibody (bsAb) therapy has shown unprecedented response and survival rates in patients with relapsed/refractory multiple myeloma (MM). The clinical activity of bsAb therapy has been shown to depend on T-cell function, yet clinical parameters, such as absolute lymphocyte count (ALC) have not been found to be associated with response to bsAbs. The aim of the present study was to elucidate whether distinct T cell subsets, such as CD4 and CD8 counts as well as their proportion within the ALC are associated with outcome of BCMA targeting bsAb therapy. **Methods:** We retrospectively collected data on 79 patients who had been treated with at least one full dose of a BCMA targeting bsAb. T cell subsets, including ALC, total CD3, CD4 and CD8, were measured from peripheral blood within 7 days prior to bsAb therapy initiation. Statistical analysis was performed with SAS version 9.4 using univariate and multivariate logistic regression models. **Results:** Median age of the patient cohort was 72 (31-84) years with 40/79 (51%) being male and 15/79 (19%) being African American. Median lines of therapy was 5 (2-12) with 78/79 (99%) patients being triple class refractory and 50/79 (63%) being penta-drug refractory. 59/79 (75%) of patients had at least one prior stem cell transplant (SCT) with 35/79 (44%) having had at least two SCTs. 26/79 (33%) patients had prior exposure to BCMA targeting therapy, with 18/79 (23%) and 8/79 (10%) previously having received belantamab mafodotin or BCMA targeting Car-T cell therapy respectively. Cytokine release syndrome (CRS) occurred in 38/79 (48%) of patients with the majority (92%) being grade 1 with the remainder being grade 2. Median ALC was 1.02 (0.25-5) $x10^3$/mL, median CD4 count was 0.27 (0.04-1.13) $x10^3$/mL while median CD8 count was 0.5 (0.07-2.97) $x10^3$/mL. Overall response (OR) rate of the whole cohort was 82% (69/79) with best responders (^{3}very good partial response) comprising 51% (40/79). While total ALC, CD4 and CD8 counts did not appear to impact response to BCMA targeting bsAb therapy, the ratio of CD4 to ALC proved to be significantly associated with OR (univariate p=0.04) and best response (univariate p= 0.004, multivariate p=0.01) . The CD8 to ALC ratio had no significant impact in this patient population. The only other factor to show a significant association with response was the number of prior lines of therapy with higher numbers being associated with worse response (p=0.046). **Conclusions:** Our study suggests that an increased proportion of CD4 cells within the ALC is significantly associated with better response to BCMA targeting bsAb. While future studies are needed to elaborate on CD4 function in bsAB therapy, our findings imply that therapeutic strategies to increase the CD4 proportion could lead to improved bsAb therapy effectiveness. Research Sponsor: None.

Unveiling consistency: A large-scale analysis of conference proceedings and subsequent publications in oncology clinical trials using large language models.

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Background: Conference abstracts serve as pivotal sources for sharing initial clinical trial findings, and influencing clinical decisions.Yet, concerns persist regarding the impact of unpublished conference abstracts on ultimate conclusions and the potential for inconsistency in result reporting. We aim to assess the feasibility of large-scale analysis, examining the consistency between initial conference results and subsequent reporting in published articles, specifically focusing on treatment efficacy and safety in oncology clinical trials using a large language model (LLM) pipeline. **Methods:** We collected clinical trial abstracts (2012-2023) from the American Society of Clinical Oncology conference (ASCO) conference and PubMed, encompassing both solid and hematopoietic cancer treatments. Utilizing a GPT-4-based LLM model, we extracted study details, treatment safety, and efficacy outcomes. Performance evaluation was conducted on manually annotated gold standards, including 100 multiple myelomas, 25 leukemia, 25 lymphomas, 30 breast cancer, and 35 lung cancer studies. To assess the consistency between reported outcome values in earlier conference abstracts and final published articles, we conducted a two-proportional Z-test. The test factored in cohort size and outcome values at each time point for selected efficacy outcomes, with p-values exceeding 0.05 suggesting a consistent pattern. **Results:** Our LLM pipeline achieved high performance with precision, recall (sensitivity), and F1 scores in the ranges of 0.958-0.986, 0.944-0.969, and 0.951-0.976, respectively, across diverse cancer types. While challenges arose in comparing outcomes between initial and final reporting in phase 1 dose-escalation studies due to variations in reported dosage groups, consistency prevailed when focusing on the recommended phase 2 dosage (RP2D) cohort in phases 1/2 and 2 studies. As part of the feasibility test, we analyzed outcomes from conference abstracts and final published data (with 1-2y differences) for the most common efficacy-safety measures in multiple myeloma studies. Results showed consistency with p-values ranging for Overall Response Rate (0.618-1), Complete Response (0.072-0.844), Very Good Partial Response (0.525), Minimal Residual Disease Negative (0.074), Neutropenia (0.212), Thrombocytopenia (0.372-0.422), Cytokine Release Syndrome (0.113-1), and Neurotoxicity (0.308-1). **Conclusions:** Our LLM model enables large-scale dataset analysis and facilitates effective outcome comparison among diverse sources and time points. The analysis of frequently appearing treatment outcomes showed no significant differences between earlier and final time points in the fixed dosage studies across therapies, despite variations in cohort sizes and follow-up times. Research Sponsor: None.

7569 Poster Session

Exploring the role of the combination of FDG-PET plus whole body MRI for staging patients with high-risk smoldering myeloma: A prospective trial.

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Background: According to IMWG criteria, Smoldering Multiple Myeloma (SMM) is an asymptomatic stage characterized by M-spike < 3 g/dl serum and/or bone marrow plasma cells infiltration between 10-59% in absence of myeloma-defining events and organ damage. In SMM setting, it is really important to differntiate high risk SMM (HR-SMM), in which treatment could be available thanks to clinical trials. 2016 IMWG criteria state that detection of bone lesions is mandatory for diagnosis of multiple myeloma and essential for diagnosis of SMM. It is really important to clarify in SMM the best imaging analysis in order to perform a correct diagnosis, and particularly it is necessary to define if the combination of FDG-PET/TC and WB-MRI could improve the assessment of lytic lesions and so the discrimination between high risk SMM and symptomatic MM. **Methods:** In our Institution we conducted a prospective trial, based on integrated new generation imaging, aiming to improve patients' stadiation and to define its prognostic implications. From January 2021 to January 2024, we performed a prospective trial enrolling 26 consecutive newly diagnosed high risk SMM, according to IMWG, in which WB-MRI was performed according to MY-RADS criteria in combination with FDG PET-CT (median age 56; range 36-85). **Results:** Our comparison between WB-MRI and FDG PET-CT, showed a discordance between the two imaging modalities in 4/26 (15%) cases. In particular, in 3/26 (12%) cases WB-MRI showed bone lesions that have lead to symptomatic MM diagnosis according to IMWG criteria, while PET-CT was negative. In one case, PET-CT showed a diffuse uptake, not diagnostic for MM, while WB-MRI was negative. WB-MRI showed a 100% of accuracy in detecting SMM and MM. Therefore, WB-MRI has lead to a modification of the prognosis and treatment approach (observation in SMM vs treatment in symptomatic MM) in 3/26 patients (11%) (i.e. Figure 1, with DWI of C2 lesion). Furthermore, in 5/23 (22%) cases of confirmed SMM WB-MRI showed a slight diffuse alteration pattern of bone marrow without any overt lytic bone lesion, which could be a potential prognostic evidence. **Conclusions:** Our results support a fundamental role of WB-MRI in combination with FDG PET/CT in the stadiation of patients with newly diagnosed high risk SMM, which could modify prognosis and treatment, improving the differentiation with symptomatic MM. In particular, combination of WB-MRI plus FDG PET/CT could be more accurate in the detection of bone lesions than FDG PET/CT alone, being able to anticipate symptomatic MM diagnosis and consequently its treatment. Moreover, a diffuse pattern of marrow involvement could be detected in some HR-SMM patients without any overt lytic lesions: it is questionable if this group of patients is associated with a rapid progression in lytic lesions and so in symptomatic MM diagnosis. Prospective data on evolution of these patients are pending. Research Sponsor: None.

Clinical outcomes of retreatment with daratumumab-based regimens in anti-CD38 refractory multiple myeloma.

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Background: Daratumumab (Dara)-based regimens have resulted in deep responses and improved outcomes in newly diagnosed (NDMM) and relapsed/refractory multiple myeloma (RRMM). As the use of dara has increased in both settings, understanding the utility of retreating patients (pts) with dara-based therapy is important. Our prior work showed that pts treated with dara-based induction can derive benefit from dara-based retreatment. Herein, we examined outcomes of dara-based retreatment (D2) in pts with RRMM. **Methods:** We conducted a retrospective study of pts with RRMM who received D2 at Memorial Sloan Kettering from 1/1/2015 to 12/31/2021. Cutoff date for analysis was 1/9/2024. Pts who received ³1 cycle of dara-based therapy as the initial dara-based regimen (D1) and D2 were included. Response was assessed by IMWG response criteria. Discrete pt characteristics were summarized by frequency (%) and continuous characteristics were summarized by median (Interquartile Range, IQR). Progression-free survival (PFS) and overall survival (OS) were evaluated by Kaplan-Meier method. **Results:** In 128 RRMM pts who received D2, median age at start of D2 was 66 (IQR 59-73); 50% male; 17% Black; ISS Stage I 45%, II 35%, III 19%; and 44% had high-risk cytogenetics (gain/amp 1q, t(4;14), t(14;16), t(14;20), del(17p)). Median prior lines of therapy (LOT) at D1 was 3 (range 2-10) and at D2 was 5 (3-14). Median time between end of D1 and start of D2 was 7.3 months (IQR 3-15.6). Of 119 pts with dara-refractory status, 100 were dara-refractory at D2. Overall response rate (ORR) was 54% for D1 and 51% for D2 for response-evaluable pts. Median duration of therapy for D2 was 4.7 months (1.8-11.3) and median time to next treatment for D2 was 8.2 months (5.8-11.4). After a median follow-up (mFU) of 56.4 months from start of D2, median PFS (mPFS) for D2 was 8.2 months (95%CI 5.3-11.2) and median OS was 43 months (35.8-60.3). Subgroup analysis based on retreatment interval of 180 days (>180 days N=74) demonstrated no significant difference in PFS between pts who received D2 ≤180 days or >180 days from D1. Median PFS from start of D2 was 8.2 months (95%CI 3.9-19.3) for ≤180-days cohort and 7.6 months (5.3-11.5) for >180-days cohort (P=0.35). When comparing outcomes of pts who received D2 as ≤4 LOTs and >4 LOTs, the mPFS for pts who received D2 as >4 LOTs was 5.4 months compared to 13.9 months for pts who received D2 as ≤4 LOT (P=0.002). **Conclusions:** In this retrospective study, dara retreatment yielded similar ORR compared to initial dara-based therapy in RRMM, despite a large proportion of pts being dara-refractory prior to D2. Our findings suggest that retreatment with dara in combination with other active MM agents can generate responses in pts with RRMM who are dara-refractory. Research Sponsor: Janssen Scientific Affairs.

Dara-based therapy for D1 and D2.

Agents - n (%)	D1	D2
Dara	41 (32)	8 (6)
Dara/PI	22 (17)	31 (24)
Dara/IMiD	58 (45)	70 (55)
Dara/IMiD/PI	1 (1)	10 (8)
Dara + other	6 (5)	9 (7)

7571 Poster Session

1p and 1q: Partners in crime in multiple myeloma.

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Background: Cytogenetic abnormalities in multiple myeloma (MM) highly influence the disease course, response to treatment and survival. Trisomies and immunoglobulin H chain translocations are primary CA while del(17p), gain(1q), del(1p) among others are secondary CA. Gain (3 copies) and amplification (>3 copies) 1q have been recognized as adverse prognostic markers and incorporated into the second revision of the International Staging System (R2-ISS). However, the role of del(1p) is less well defined, especially in the era of novel therapies. We aimed to analyze the outcomes of newly diagnosed MM (NDMM) patients with chromosome 1 abnormalities, mainly del 1p, treated with autologous stem cell transplant (ASCT) consolidation at our institution. **Methods:** We conducted a retrospective study of all NDMM patients who were treated with ASCT from 1/1/2015-2/13/2019 (n=511). High-risk cytogenetics (HRC) were defined by the presence of del(17p), t(4;14), or t(14;16) similar to R-ISS; standard-risk cytogenetics (SRC) were defined as the absence of HRC. Modified HR cytogenetics (mHRC) included gain/amp 1q and/or t(14;20) in addition to HRC, while ultra high-risk (uHRC) included 2 or more mHRC CA. **Results:** Of 511 pts transplanted, 453 had cytogenetic data at the time of diagnosis. SRC were seen in 353 pts (77.9%), while 100 (22.1%) had HRC, 156 (34.4%) had mHRC, and 43 (9.5%) had uHRC. Thirty-two (7.1%) pts had del(1p) while 105 (23.2%) had gain 1q and 30 (6.6%) had amplification 1q. As expected, compared to SRC pts, pts with HRC, mHRC and uHRC had higher risk of relapse or death. Patients with gain and amp 1q had inferior outcomes in terms of progression-free survival (PFS) (HR 1.35; 95% CI 1.06-1.73, p=0.016), time to next treatment (TTNT) (HR 1.84; 95% CI 1.40-2.42, p<0.001) and overall survival (OS) (HR 1.47; 95% CI 1.06-2.02, p=0.02) compared to those without, consistent with published literature. The median PFS, TTNT and OS from ASCT in pts with gain/amp 1q were 3.17 years (y), 3.95y and 7.13y, respectively, compared to 4.01y, 7.60y and 8.21y in pts without gain/amp 1q. Pts with del(1p) had inferior PFS (median 2.43y versus 3.98y; HR 1.75; 95% CI 1.16-2.64, p=0.008), TTNT (median 2.72y versus 6.17y; HR 1.96; 95% CI 1.22-3.14, p=0.005) and OS (median 4.11y versus 8.38y; HR 2.19; 95% CI 1.34-3.58, p=0.002) from the time of ASCT compared to those without del(1p). **Conclusions:** In our study of NDMM patients that underwent AHCT, del(1p) at diagnosis was an independent predictor of shorter PFS, TTNT and OS. Despite induction therapy involving novel drugs and ASCT consolidation, patients with del(1p) at diagnosis continue to have inferior outcomes. Larger analyses are needed to validate the prognostic value of del(1p) and investigate its role in predicting outcomes in MM. Research Sponsor: None.

Long-term outcomes after cardiac transplantation in AL amyloidosis.

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Background: Systemic AL amyloidosis can lead to progressive multi-organ dysfunction including advanced heart failure which may require orthotopic heart transplantation (OHT). Hematologic outcomes of AL amyloidosis post-OHT are not well described. **Methods:** We report outcomes for patients with AL amyloidosis with cardiac involvement post-OHT from Nov 2008 - Jun 2023 at Vanderbilt University Medical Center. Hematologic response was graded per the ISA guidelines. **Results:** Fourteen pts underwent OHT of whom 13 had lambda light chain disease. Three (21%) pts had isolated AL amyloidosis (AL) without myeloma (MM), while 11 (79%) also had MM: 6 with bone marrow plasma cells (BMPCs) 10-19% (AL-PCMM-10) and 5 with BMPC ≥20% (AL-PCMM-20). One each with AL-PCMM-10 and AL-PCMM-20 had lytic lesions (AL-CRAB). Median age at OHT was 55.5 yrs (range 37-74). Median time from diagnosis to OHT was 18 mo (range 3-62). Five (35%) pts had biopsy-proven extracardiac amyloid involvement. Median difference in serum free light chains at first evaluation was 70 mg/dL (range 9-289). Three pts were Mayo 2012 stage II, 4 stage III, and 7 stage IV. Four pts had t(11; 14) and 1 had 1q gain. Ten (71%) pts received triplet therapy (VCd or VRd) and 3 (21%) received quadruplet therapy (Dara-VCd or Isa-VCd) pre-OHT. Six (43%) pts had autologous stem cell transplantation (ASCT); 1 pre-OHT and 5 post-OHT. Of ASCT pts, 1 pt achieved CHR, 1 VGPR, 2 PR, and 1 had PD pre-ASCT. Pre-OHT, 4 pts achieved CHR, 6 VGPR, 3 PR, and 1 had PD. Eleven pts (79%) received maintenance therapy post-OHT (5 proteosome inhibitors, 6 anti-CD38). At last follow-up, 8 pts were in CHR, 3 in VGPR, 1 in PR, and 2 had PD. Four (29%) pts died post-OHT: 2 from AL recurrence (1 each with AL and AL-PCMM-10), 1 from cardiac allograft vasculopathy (AL-CRAB), and 1 from renal failure (AL-CRAB). Three (21%) pts had hematologic relapse 5, 21 and 48 mo post-OHT, and of those, 2 had recurrent cardiac amyloid in graft 37 and 71 mo post-OHT. Of those with hematologic relapse, 2 had AL-PCMM-10 and 1 had AL. One pt had post-transplant lymphoproliferative disorder 126 mo post-OHT, requiring treatment. Median follow-up and survival of the cohort post-OHT was 2.25 yrs (range 0.5-13.8). **Conclusions:** In this single-center analysis of pts undergoing OHT for cardiac AL amyloidosis, we demonstrate feasibility of excellent long-term outcomes, in predominantly high-risk AL pts where majority harbored high-risk disease with MM overlap, either by AL-CRAB or AL-BMPC. Induction alone led to ≥VGPR response in 10 (71%) pts pre-OHT and further therapy deepened this to 11 (79%) pts. Both AL-CRAB pts died during follow-up, highlighting the overall poor prognosis in this specific subgroup. In our cohort, non-relapse related mortality was seen in only 2 (14%) pts, demonstrating acceptable post-OHT risk and overall ability to achieve far improved outcomes in the high-risk cardiac AL amyloidosis patient population that otherwise suffers from rapid and universal mortality. Research Sponsor: None.

Long term follow up of monoclonal gammopathy of undetermined significance (MGUS) in US Veterans: Racial differences and associations with other malignancies.

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Background: Monoclonal gammopathy of undetermined significance (MGUS) is associated with lymphoid malignancies such as lymphoma and myeloma, but the association with other malignancies has not been described in the US veteran population. **Methods:** Veterans diagnosed with MGUS from 1991-2023 were identified from the US Veteran Affairs Central Cancer Registry (VACCR). Age at the diagnosis of MGUS was divided into four categories of <60, 60-69, 70-79, 80+. Variables collected included demographic factors and the diagnosis of other cancers. Differences were analyzed using the Chi Square test. **Results:** There were 3975 veterans who met the criteria. Most patients were male (96.7%) with a median age at diagnosis of MGUS of 70.5 (IQR 65.4-76.0). Almost 1/3 of patients were Black and were diagnosed with MGUS at a younger age compared to White veterans (Table, $p<0.0001$). Over the 32-year period included in this study, 2/3 of patients remained with a diagnosis of MGUS (62.3%) alone whereas 29.4% had 1 additional malignancy diagnosed and 8.3% had 2 or more additional malignancies. Black veterans with MGUS were more likely to have additional malignancies than white patients (41.4% vs 35.9%, $p=0.016$). MGUS was diagnosed prior to other cancers in 52% of patients and afterward in 48%. The most common cancers diagnosed in patients with MGUS were prostate (31%), lymphomas (13%), GI (12.5%), lung (12.0%), and skin (6.8%). CLL (3.4%), LPL (3.0%). Among lymphomas, CLL (3.4%) and LPL (3.0%) were most common. Of note, multiple myeloma or plasmacytoma was diagnosed in 6.5% of patients. The proportion of patients with MGUS and additional malignancies was comparable in the 4 age cohorts ($p=0.072$), indicating that younger patients with MGUS were as likely to be diagnosed with additional malignancies as older patients. **Conclusions:** In US veterans, nearly 1/3 of those diagnosed with MGUS were Black. These patients were younger when diagnosed with MGUS and were more likely to develop additional malignancies compared to White veterans. Over the 32 years of this study, a considerable proportion of veterans with MGUS developed various solid tumors. Further investigation is warranted to understand the racial, genetic, and other factors that may be contributing to the development of cancers in patients with MGUS. Research Sponsor: VA Office of Research and Development.

Race	<60 Years, n=399	60-69 Years, n=1464	70-79 Years, n=1556	80+ Years, n=556
White, n (%)	158 (39.6)	825 (56.4)	921 (59.2)	339 (61.0)
Black, n (%)	185 (46.4)	497 (34.0)	451 (29.0)	130 (23.4)
Hispanic, n (%)	22 (5.5)	72 (4.9)	88 (5.7)	56 (10.1)
Other, n (%)	8 (2.0)	15 (1.0)	31 (2.0)	8 (1.4)
Unknown, n (%)	26 (6.5)	55 (3.8)	65 (4.2)	23 (4.1)

TPS7575 **Poster Session**

A phase III, randomized study of daratumumab, cyclophosphamide, bortezomib and dexamethasone (DARA-VCD) induction followed by autologous stem cell transplant or DARA-VCD consolidation and daratumumab maintenance in patients with newly diagnosed AL amyloidosis.

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Background: Light chain (AL) amyloidosis is a plasma cell malignancy characterized by the production of amyloidgenic clonal light chains that deposit in various tissues. The addition of daratumumab to bortezomib, cyclophosphamide and dexamethasone (Dara-VCD) has improved depth of hematologic and organ responses. However, this approach has not yet demonstrated an overall survival (OS) benefit with short follow-up. Autologous stem cell transplant (ASCT) consolidation remains safe and is associated with deep and durable hematologic responses with an 83% 2-year progression free survival (PFS) and up to 72% of patients achieving a VGPR or better, comparable to Dara-VCD (79%). In multiple myeloma, ASCT improved PFS even in patients who are MRD negative at the end of standard induction therapy. It is thus reasonable to consider that ASCT might provide similar benefits in AL patients. No randomized data exist to inform the optimal use of ASCT in the era of Dara-VCD. **Methods:** This randomized phase 3 SWOG led intergroup trial will accrue a total of 143 participants per arm and compare MOD-PFS (major organ deterioration progression free survival: defined as time from randomization to death, cardiac/renal progression, or hematologic progression) between participants receiving an ASCT with those receiving Dara-VCD consolidation following uniform Dara-VCD induction. A median MOD-PFS of 31 months is anticipated in the non-ASCT arm. This study has 90% power and a two-sided significance level of 0.05 to detect a hazard ratio of 0.62 corresponding to a MOD-PFS of 50 months in the ASCT arm. Important additional endpoints include OS, hematological PFS, cardiac and renal responses and progression, MRD negativity both by peripheral blood mass spectrometry and bone marrow next generation flow cytometry, delayed utilization of ASCT, and quality of life. This trial was activated on 12/1/2023. Funding: NIH/NCI/NCTN grants and in part by Janssen Pharmaceuticals. Clinical trial information: NCT06022939. Research Sponsor: NIH/NCI/NCTN grants; U10CA180888, U10CA180819.

S2213 study schema.

Participants with Newly Diagnosed AL Amyloidosis* **Registration Step 1**		
↓		
Induction** **Dara-VCD** **3 cycles (q28-day cycle)**		
↓		
Registration Step 2**		
↓	Randomization 1:1	
Consolidation** **Arm 1** **Dara-VCD** **3 cycles (q28-day cycle)**		Consolidation** Arm 2 Melphalan + ASCT
↓		↓
Registration Step 3		Registration Step 3
↓		↓
Maintenance **Arm 1** **Dara** **18 Cycles (q28-day cycle)**		Maintenance Arm 2 Dara 18 Cycles (q28-day cycle)
↓		↓
Endpoint **MOD-PFS**		Endpoint MOD-PFS

*1 cycle (28-day) of induction treatment is allowed prior to Registration Step 1.
** Participants must have overall response of PR or better to proceed to Registration Step 2. Patients who do not achieve a best overall response of PR or better following the completion of induction therapy will not be eligible to continue on to Registration Step 2.

TPS7576 Poster Session

Evaluation of elranatamab vs EPd, PVd, or Kd in patients with relapsed or refractory multiple myeloma and prior anti-CD38–directed therapy: MagnetisMM-32.

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Background: Elranatamab (ELRA), a humanized B-cell maturation antigen (BCMA)-CD3 bispecific antibody, has shown efficacy and manageable safety as a monotherapy in patients with relapsed or refractory multiple myeloma (RRMM). This study will evaluate ELRA monotherapy vs elotuzumab-pomalidomide-dexamethasone (EPd), pomalidomide-bortezomib-dexamethasone (PVd), or carfilzomib-dexamethasone (Kd) in patients with RRMM to determine whether ELRA can provide superior clinical benefit. **Methods:** MagnetisMM-32, a phase 3, open-label, multicenter, randomized study, will enroll ≈492 patients. Patients will receive ELRA (Arm A) or investigator's choice of EPd, PVd or Kd (Arm B), until disease progression, unacceptable toxicity, withdrawal of consent, loss to follow-up, or study termination. Patients treated with ELRA will receive 2 step-up priming doses followed by weekly doses in a 28-day cycle. Patients who achieve a PR or better for ≥2 months will be eligible for reduced dosing frequency. Patients will be randomized 1:1 (stratified by prior line of therapy [1 vs 2 vs 3/4] and International Staging System disease stage [1/2 vs 3]). Key inclusion criteria include age of ≥18 years, prior multiple myeloma diagnosis with measurable disease (per IMWG criteria), evidence of progressive disease or failure to achieve a response to last line of multiple myeloma therapy, 1 to 4 prior lines of therapy including an anti–CD38 antibody–containing regimen (for ≥2 consecutive cycles) and a lenalidomide-containing regimen (for ≥2 consecutive cycles), adequate bone marrow function, and an ECOG performance status of ≤2. Key exclusion criteria include stem cell transplant ≤12 weeks prior to enrollment; active, uncontrolled infection; prior BCMA-directed or CD3-redirecting therapy; and unable to receive EPd, PVd, or Kd. The primary and key secondary endpoints are progression-free survival (PFS) by blinded independent central review (BICR) per IMWG criteria and overall survival (OS), respectively. Other secondary endpoints include PFS by investigator, objective response rate, duration of response, time to response by BICR, PFS on next line of therapy per IMWG criteria, MRD negativity rate, safety, pharmacokinetics of ELRA, immunogenicity, and health-related quality of life outcomes. The primary endpoint and OS will be compared statistically between treatment arms by stratified log-rank tests. Clinical trial information: NCT06152575. Research Sponsor: Pfizer Inc.

TPS7577 Poster Session

MagnetisMM-30: A phase 1b, open-label study of elranatamab in combination with iberdomide in patients with relapsed or refractory multiple myeloma (RRMM).

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Background: Elranatamab (ELRA) is a humanized B-cell maturation antigen (BCMA)–CD3 bispecific antibody (BsAb). Single-agent ELRA induced deep and durable responses with a manageable safety profile in patients (pts) with RRMM enrolled in the phase 2 registrational MagnetisMM-3 study (NCT04649359; Lesokhin et al, *Nat Med* 2023). Iberdomide (IBER) is a novel CELMoD[TM] agent that induces enhanced antimyeloma tumoricidal and immunomodulatory activity in pts with RRMM (Lonial et al, *Lancet Haematol* 2022). While IBER in combination with ELRA has not been evaluated clinically, it may provide additional benefit to pts with RRMM based on the mechanisms of action of this novel combination. **Methods:** MagnetisMM-30 is a phase 1b, open-label, prospective study evaluating the safety, efficacy, and pharmacokinetics of ELRA in combination with IBER in pts with RRMM. The study has 2 parts: Part 1 for dose-escalation and Part 2, randomized for dose optimization. After 2 step-up priming doses of ELRA, pts will receive subcutaneous ELRA weekly with IBER given daily for 21 days of each 28-day cycle. After ≥6 months (cycles) of treatment, pts with a partial response or better for ≥2 months are eligible for reduced dosing frequency of ELRA. Once the 2 combination dose levels (dose levels A and B) are selected from Part 1 as the recommended phase 2 doses for ELRA and IBER, pts in Part 2 will be randomized 1:1 (stratified by the number of prior lines of therapy [LOTs; 1 vs >1]) to dose levels A and B. Key inclusion criteria are pts aged ≥18 years with a MM diagnosis per IMWG criteria, Eastern Cooperative Oncology Group performance status of 0-1, adequate organ and bone marrow function, and disease relapsed or refractory to the last antimyeloma regimen per IMWG response criteria. Pts who received 2-4 or 1-3 prior LOTs, including ≥1 immunomodulatory drug (IMiD) and ≥1 proteasome inhibitor (PI), are eligible for Parts 1 and 2, respectively. All pts must have received ≥2 consecutive cycles of an IMiD-containing regimen and ≥2 consecutive cycles of a PI or PI-containing regimen. Key exclusion criteria are pts with stem cell transplant ≤12 weeks prior to enrollment; active, uncontrolled infection; prior treatment with BCMA-directed or CD3 redirecting therapy or prior CELMoD agents (ie, IBER or mezigdomide). This study is ongoing; Part 1 and Part 2 will enroll approximately 27 and 60 pts, respectively. Study endpoints are listed in the table. Clinical trial information: NCT06215118. Research Sponsor: This study was sponsored and funded by Pfizer.

	Part 1	Part 2
Primary endpoints	Dose-limiting toxicities	AEs, lab abnormalities
Secondary endpoints	AEs, lab abnormalities	ORR
	ORR	CRR
	CRR	Time-to-event outcomes
	Time-to-event outcomes	PK
	PK	MRD negativity rate
	MRD negativity rate	Immunogenicity
	Immunogenicity	