Highlights from IMW 2021

1-2 febbraio 2022
Bologna
Royal Hotel Carlton

Giulia Perrone

Immunoterapie effettrici del MM refrattario dopo ≥3 precedenti terapie

Profili di sicurezza classe-specifici

Coordinatore Scientifico
Michele **CAVO**

Comitato Scientifico
Michele **CAVO**
Maria Teresa **PETRUCCI**

Emerging BCMA and non-BCMA targeted agents for RRMM

CAR-T cells	Bispecific T-cell Engagers	Antibody-Drug Conjugates
CILTA-CEL	TECLITASTAMAB	BELANTAMAB MAFODOTIN
IDE-CEL	ELRANATAMAB	HDP-101
CRB402	AMG701	MEDI2228
ORVA-CEL	REGN5458	
CT103A	CC93269	
CT053	***NON-BCMA***	
ALLO-CAR-T	TALQUETAMAB (GPRC5D)	
	CEVOSTAMB (FCH5)	

ANTIBODIES DRUG-CONJUGATED: SAFETY PROFILE

- Belantamab mafodotin
  - Monotherapy
    - Ocular toxicity
      - Long term analysis DREAMM-2
      - Post-hoc analysis DREAMM-2
  - Combination therapy
    - B-Pd safety analysis

Background:DREAMM-2
13 months follow up

TABLE 4. Most Common Adverse Events (Occurring in ≥15%) and Grade ≥3 Adverse Events (Occurring in ≥5%) in the Overall Population[a]

Event	Belamaf 2.5 mg/kg, N = 95: No. of Patients (%)	
	Any Grade	Grade ≥3
Any event	93 (98)	80 (84)
Eye examination finding		
Keratopathy[b]	68 (72)	44 (46)
Change in BCVA	51 (54)	29 (31)
Thrombocytopenia[c]	36 (38)	21 (22)
Anemia	26 (27)	20 (21)
Blurred vision[d]	24 (25)	4 (4)
Nausea	24 (25)	0 (0)
Pyrexia[e]	22 (23)	4 (4)
Aspartate aminotransferase increased	20 (21)	2 (2)
Infusion-related reaction[f]	20 (21)	3 (3)
Fatigue	15 (16)	2 (2)
Neutropenia[g]	14 (15)	10 (11)
Dry eye[h]	14 (15)	1 (1)
Hypercalcemia	14 (15)	7 (7)
Lymphocyte count decreased	13 (14)	12 (13)
Pneumonia	9 (9)	6 (6)

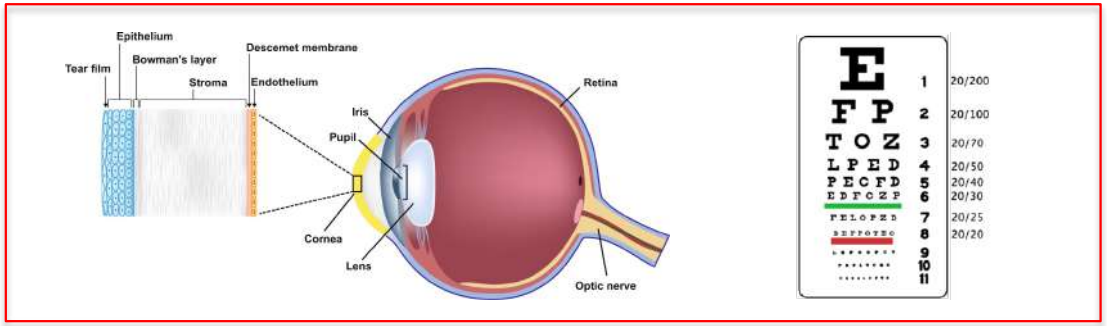


Table 1 Recommended belamaf dose modifications based on eye examination findings per the KVA scale per the US prescribing information and the EU summary of product characteristics combined[22,23].

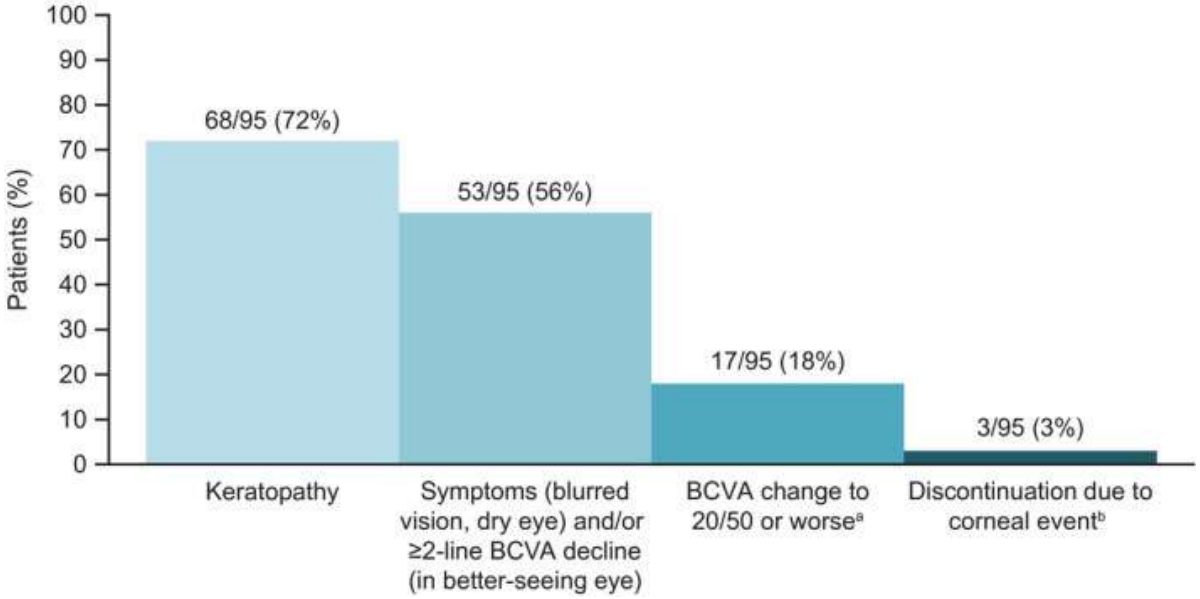
Severity[a]	Corneal examination findings[b]			Change in BCVA due to treatment-related corneal findings	Recommended dose modifications
	Description	Presentation of MECs (based on density and location)	Example schematics of MECs by severity		
Grade 1/Mild	Mild superficial keratopathy[c] (documented worsening from baseline) with or without symptoms	Mild density: non-confluent Location: predominantly (≥80%) peripheral	Cornea Limbus Pupil	Decline from baseline of 1 line on Snellen Visual Acuity	Continue treatment at current dose
Grade 2/ Moderate	Moderate superficial keratopathy[c] with or without patchy microcyst-like deposits, sub-epithelial haze (peripheral), or a new peripheral stromal opacity	Moderate density: semi-confluent Location: predominantly (≥80%) paracentral	Dots represent MECs	Decline from baseline by 2 or 3 lines (and Snellen Visual Acuity not worse than 20/200)	Withhold treatment until improvement in either exam findings or BCVA to Grade 1/ mild • Resume at a reduced dose of 1.9 mg/kg
Grade 3/ Severe	Severe superficial keratopathy[c] with or without diffuse microcyst-like deposits involving the central cornea, sub-epithelial haze (central), or a new central stromal opacity	Severe density: confluent Location: predominantly (≥80%) central		Decline from baseline of more than 3 lines (and Snellen Visual Acuity not worse than 20/200)	Withhold treatment until improvement in either exam findings or BCVA to Grade 1/ mild • Resume at a reduced dose of 1.9 mg/kg[d]
Grade 4/ Severe	Corneal epithelial defect, including corneal ulcers. These should be managed promptly and as clinically indicated by an eye care professional	Not applicable, these events are not graded based on MECs		Snellen Visual Acuity worse than 20/200	Withhold treatment until improvement in examination findings and BCVA to Grade 1/ mild. Consider treatment discontinuation based on a benefit-risk assessment. For worsening symptoms that are unresponsive to appropriate management, consider discontinuation • If continuing treatment, resume at a reduced dose of 1.9 mg/kg[d]

Lonial et al , Blood Cancer Journal 2021
Lonial et al, Cancer 2021

Background DREAMM-2
13 months follow up

Median onset of keratopathy 37 days (range, 19-143 days)
77% of patients recovered from their first keratopathy examination.
Median time to recovery 86.5 days (range, 8-358 days);

Median duration of declines in BCVA was 21.5 days (range, 7-64 days); most patients recovered after one 21-day assessment interval. No permanent complete loss of vision has been reported



Lonial et al , Blood Cancer Journal 2021
Lonial et al, Cancer 2021

Characterization of Ocular Adverse Events in Patients Receiving Belantamab Mafodotin for ≥12 Months: Post-Hoc Analysis of DREAMM-2 Study in Relapsed/Refractory Multiple Myeloma

At 13-month follow-up, the clinical benefit rate (≥minimal response) in patients receiving belamaf 2.5 mg/kg (n=97) was 36%

14 patients (15%) had received ≥12 months of treatment.

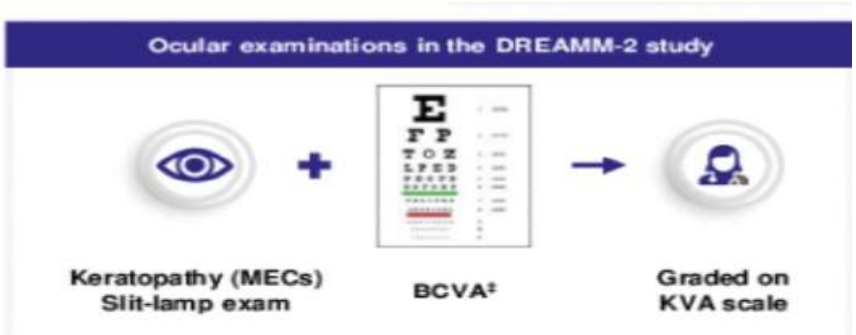


TABLE 1. Recommended Belantamab Mafodotin Dose Modifications Based on Eye Examination Findings According to the Keratopathy and Visual Acuity Scale[a]

Grading Category: US/EU	Eye Examination Findings by KVA Scale	Recommended Dose Modifications
Grade 1/mild	Corneal examination finding(s) Mild superficial keratopathy[b] Change in BCVA[c] Decline from baseline of 1 line on Snellen Visual Acuity	Continue treatment at the current dose
Grade 2/moderate	Corneal examination finding(s) Moderate superficial keratopathy[d] Change in BCVA Decline from baseline of 2 or 3 lines on Snellen Visual Acuity and ≤20/200	Withhold treatment until improvement in both corneal examination findings and change in BCVA to grade 1 (*mild*) or better and resume at the current dose; *consider resuming at a reduced dose of 1.9 mg/kg*
Grade 3/severe	Corneal examination finding(s) Severe superficial keratopathy[e] Change in BCVA Decline from baseline by more than 3 lines on Snellen Visual Acuity and not worse than 20/200[f]	Withhold treatment until improvement in both corneal examination findings and change in BCVA to grade ≥1 (*mild*) and resume at a reduced dose; *for worsening symptoms that are unresponsive to appropriate management, consider discontinuation*
Grade 4/severe	Corneal examination finding(s) Corneal epithelial defect[g] Change in BCVA Snellen Visual Acuity <20/200[f]	Consider permanent discontinuation of treatment; if continuing treatment, withhold treatment until improvement in both corneal examination findings and change in BCVA to grade ≥1 and resume at reduced a dose

Lonial et al, Abstract 1071310

Ocular events:

Table 3: Drug-related ocular events, and ocular events leading to dose modifications

	Patients with drug-related ocular adverse events n (%)	Patients with ocular adverse events leading to dose reduction n (%)	Patients with ocular adverse events leading to dose delays n (%)
Keratopathy	14 (100)	10 (71)	13 (93)
Vision blurred	8 (57)	1 (7)	3 (21)
Dry eye	5 (36)	0	1 (7)
Photophobia	3 (21)	0	0
Visual acuity reduced	3 (21)	0	0
Ocular discomfort	2 (14)	0	1 (7)
Visual impairment	2 (14)	0	0
Glaucoma	1 (7)	0	1 (7)
Retinal hemorrhage	1 (7)	0	1 (7)
Ulcerative keratitis	1 (7)	0	1 (7)
Vitreous detachment	1 (7)	0	0

- All 14 patients experienced ≥1 ocular event (maximum grade: 2 [14%]; 3 [79%]; 4 [7%]), and required ≥2 dose delays, with dose reduction to 1.92 mg/kg in 12 patients (86%).
- Dose modifications permitted ocular event recovery, so belamaf was resumed in all 14 patients.
- Patients had a mean of 3.6 dose delays (median: 3.5; range: 2–6).
- Median duration of dose delays was 41 days (range: 4–212); 10 patients (71%) had dose delays >63 days.

•Long delays did not appear to negatively impact clinical response to belamaf: 12 (86%) had a clinical response (≥partial response; 11 [79%] for ≥6 months).

•All 14 patients had keratopathy. Ocular symptoms occurred in 13 patients (93%); blurred vision 57%, dry eye 36%, visual acuity reduced 21%, and photophobia 21%. No patients had permanent complete vision loss

Lonial et al, Abstract 1071310

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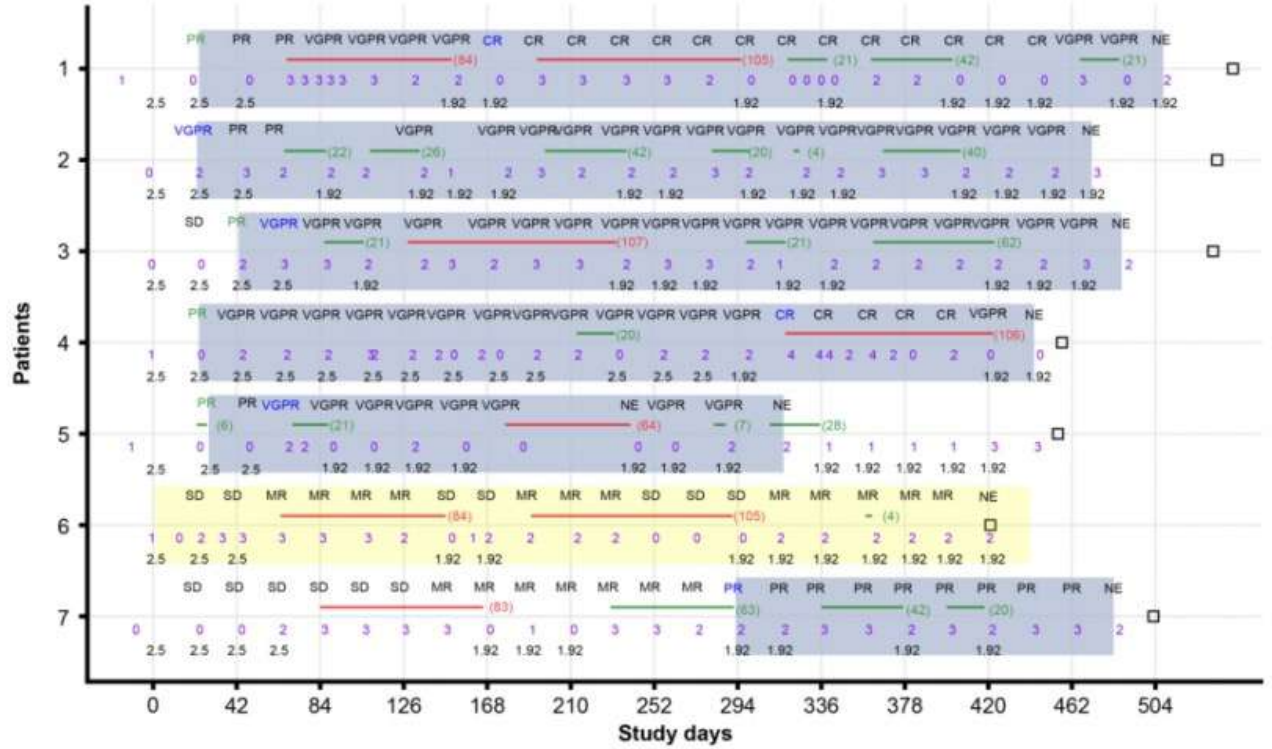
Figure 3: Profile plots of patients with corneal events graded on the KVA scale*

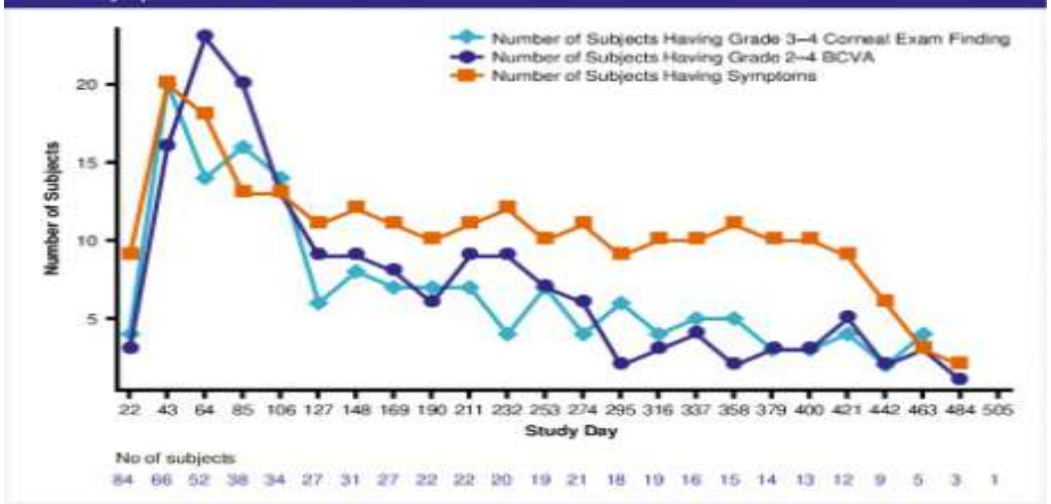


Duration of treatment
Corneal event grade (GSK scale)
≤63 day delay
>63 day delay

Lonial et al, Abstract 1071310

Relationship Between Corneal Exam Findings, Best-Corrected Visual Acuity (BCVA), and Ocular Symptoms in Patients with Relapsed or Refractory Multiple Myeloma (RRMM) Receiving Belantamab Mafodotin (GSK2857916; belamaf; BLENREP)

Figure 1: Number of Patients with GR 3–4 Keratopathy, GR 2–4 BCVA, and CTCAE-Reported Ocular Symptoms over Time



Terpos et al, Abstract 1075896

Ocular syntoms
Best corrected Visual Acuity
Corneal Exam Findings

OSDI

In only 5% of evaluations, GR 3–4 keratopathy was not associated with having an OSDI symptom or impact that was ≥ most of the time (**Table 6**).

When patients reported an ocular symptom on the OSDI that was ≥ most of the time or when that symptom occurred with GR 3–4 keratopathy or GR 0–2 keratopathy, the most frequent CTCAE-reported ocular symptoms were blurred vision (22%, 21%, and 23%, respectively) and dry eye (11%, 14%, and 10%, respectively) (**Table 7**).

Table 6: Summary of Concordance and Discordance for OSDI: 'Most of the Time' Analysis

Keratopathy and OSDI* (Total Evaluations, N = 773)	Events, n (%)
GR 0–2 Keratopathy and OSDI No Item Most of the Time	236 (31)
GR 3–4 Keratopathy and OSDI At Least One Item† ≥ Most of the Time	97 (13)
GR 0–2 Keratopathy and OSDI At Least One Item† ≥ Most of the Time	184 (24)
GR 3–4 Keratopathy and OSDI No Item Most of the Time	40 (5)
Missing Values	216 (28)

*κ = 0.1993; †OSDI Questions 1–9 only. Items 1–5 address the frequency of the following eye-related problems during the course of the prior week (Range: 'All of the time' to 'None of the time'): eyes that are sensitive to light; eyes that feel gritty; painful or sore eyes; blurred vision; and poor vision. Items 6–9 address the frequency of eye-related problems that limit performing the following tasks during the prior week: reading; driving at night; working with a computer or bank machine (ATM); and watching TV. All responses range from 'All of the time' to 'None of the time'.

Table 7: Summary of CTCAE-Reported Ocular Symptoms Detected in Evaluations with OSDI Positive*, Evaluations with OSDI Positive* plus GR 3–4 Keratopathy, and Evaluations with OSDI Positive* plus GR 0–2 Keratopathy

Ocular Symptoms (Preferred Term)	Evaluations with OSDI Positive (n = 281)	Evaluations with OSDI Positive and GR 3–4 Keratopathy (n = 97)	Evaluations with OSDI Positive and GR 0–2 Keratopathy (n = 184)
Any event	135 (48)	51 (53)	84 (46)
Vision blurred, n (%)	63 (22)	20 (21)	43 (23)
Dry eye, n (%)	32 (11)	14 (14)	18 (10)
Ocular discomfort, n (%)	19 (7)	3 (3)	16 (9)
Photophobia, n (%)	16 (6)	13 (13)	3 (2)
Eye irritation, n (%)	15 (5)	3 (3)	12 (7)
Visual acuity reduced, n (%)	10 (4)	2 (2)	8 (4)
Diplopia, n (%)	6 (2)	2 (2)	4 (2)
Visual impairment, n (%)	5 (2)	1 (1)	4 (2)
Eye pain, n (%)	1 (<1)	0	1 (<1)
Eye pruritus, n (%)	1 (<1)	0	1 (<1)

*OSDI Questions 1–9 only.

Terpos et al, Abstract 1075896

Conclusions

In evaluations with no/mild (≤GR 1) BCVA changes and no ocular symptoms, GR 3-4 keratopathy was rarely observed (only 7.5% of the time [58/773]).

In evaluations where frequent (≥ most of the time) ocular symptoms were not reported (based on OSDI questionnaire questions 1-9), GR 3-4 keratopathy was rarely observed (only 5% of the time).

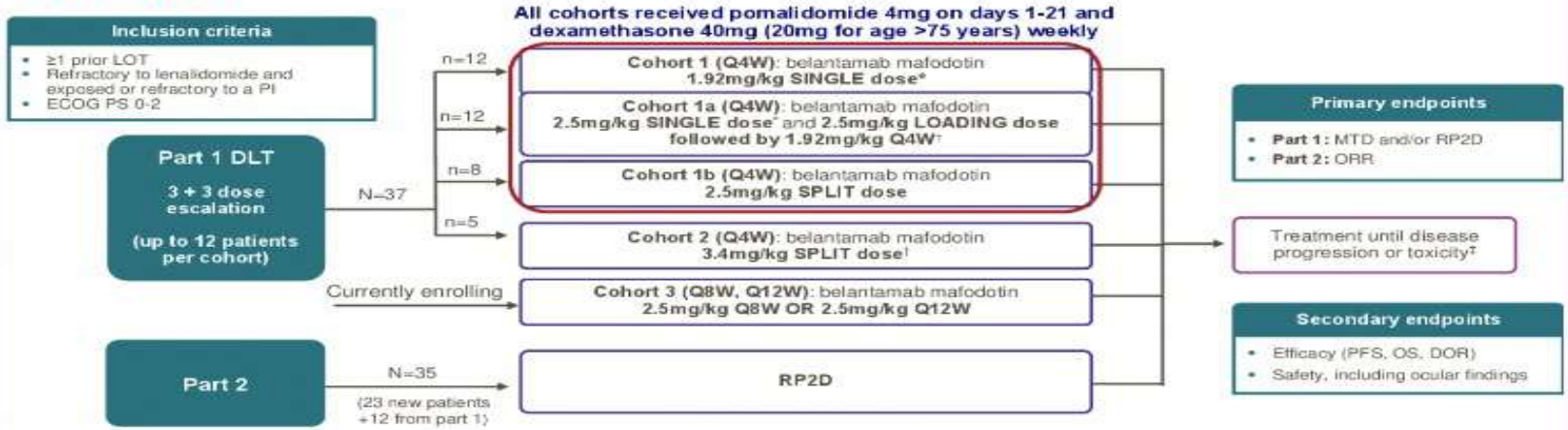
These results suggest that to determine dose modifications and patient management:

- BCVA and CTCAE-reported ocular symptoms should be further investigated to determine whether they may represent surrogates of corneal alterations.
- The OSDI questionnaire, which asks patients to report their ocular symptoms and vision-related functioning, should be further investigated to determine whether it can become a surrogate for corneal alterations.

Terpos et al, Abstract 1075896

EXTENDED FOLLOW-UP SAFETY AND EFFICACY RESULTS OF BELANTAMAB MAFODOTIN (BELAMAF) 1.92 MG/KG OR 2.5 MG/KG COMBINED WITH POM AND DEX FOR THE TREATMENT OF RELAPSED/REFRACTORY MULTIPLE MYELOMA (Abstract ID: 1082298)

METHODS



- Here we report updated tolerability and efficacy data for pts treated at each cycle with belamaf, 1.92 mg/kg (Cohort 1; n=12) or 2.5 mg/kg (Cohorts 1a and 1b; n=20) in combination with Pd

Trudel et al, Abs 1082298

Results and conclusion

- The ORR/=>VGPR rates for the 1.92 and 2.5 mg/kg cohorts, were 81.8%/63.6% and 95%/85%, respectively. The median PFS was 16.2 months for the 1.92 mg/kg cohort and 25.3 months for the 2.5 mg/kg group.

***Table 3**: Most frequent non-corneal AEs*

AE	1.92 mg/kg (Cohort 1) N=12		2.5 mg/kg (Cohorts 1a-b) N=20	
AEs ≥25%	**Any Gr**	**≥Gr 3**	**Any Gr**	**≥Gr 3**
Thrombocytopenia	7 (58.3%)	5 (41.7%)	9 (45%)	4 (20%)
Neutropenia	7 (58.3%)	6 (50%)	13 (65%)	10 (50%)
Dyspnea	3 (25%)	3 (25%)	5 (25%)	3 (15%)
Lung infection	3 (25%)	3 (25%)	5 (25%)	1 (5%)
Fever	7 (58.3%)	0 (0%)	8 (40%)	0 (0%)
Constipation	6 (50%)	0 (0%)	5 (25%)	0 (0%)
Fatigue	6 (50%)	0 (0%)	13 (65%)	0 (0%)
Nausea	3 (25%)	0 (0%)	4 (20%)	0 (0%)
Cataract	4 (33.3%)	0 (0%)	7 (35%)	0 (0%)

***Table 4**: Most frequent corneal AEs and resulting dose modifications*

Corneal AEs (Total)	1.92 mg/kg (Cohort 1) N=12		2.5 mg/kg (Cohorts 1a-b) N=20	
n(%)	**Any Gr**	**≥Gr 3**	**Any Gr**	**≥Gr 3**
Keratopathy	11 (91.7%)	5 (41.7%)	20 (100%)	14 (70%)
Blurred vision	10 (83.3%)	4 (33.4%)	18 (600%)	9 (45%)
Dose holds	7 (58.3%)		20 (100%)	
Median dose holds (range)	6 (1-8)		5 (1-16)	
Dose delays/ reductions	2 (16.7%) / 0 (0%)		4 (20%) / 11 (55%)	
Corneal AEs (12 months)	**N=7**		**N=15**	
Keratopathy	7 (100%)	3 (42.9%)	15 (100%)	15 (100%)
Blurred vision	7 (100%)	2 (28.6%)	14 (93.3%)	5 (33.3%)

- **The safety profile of B-Pd is consistent with that observed for Pd or Belamaf individually**.
- Both dose cohorts demonstrate deep and durable responses however the 2.5 mg/kg dose appears to have better efficacy.

Trudel et al, Abs 1082298

CAR-T anti BCMA: SAFETY PROFILE

- *Cilta-cell*
  - CARTITUDE-1 update follow up 18months -> ASH 2021 follow up 24 mesi
  - CARTITUDE-2 subgroup analysis choort A
  - CARTITUDE-2 neurotoxicity sub analysis

- *Ide-cell*
  - KARMMA-1 update follow up 18 months
  - Quality of life

Background CARTITUDE-1

Baseline Characteristics

	Phase 1b (n=29)	Phase 2 (n=68)	Total (N=97)
Median age, years	60·0 (57–67)	62·0 (55–70)	61·0 (56–68)
Sex			
Male	14 (48%)	43 (63%)	57 (59%)
Female	15 (52%)	25 (37%)	40 (41%)
Median time since diagnosis, years	5·1 (3·5–7·8)	6·7 (4·6–8·5)	5·9 (4·4–8·4)
ECOG performance status			
0	12 (41%)	27 (40%)	39 (40%)
1	14 (48%)	40 (59%)	54 (56%)
2	3 (10%)	1 (2%)	4 (4%)
Median previous therapies for multiple myeloma	5·0 (4·0–8·0)	6·0 (4·0–8·0)	6·0 (4·0–8·0)
Previous stem-cell transplantation			
Autologous	26 (90%)	61 (90%)	87 (90%)
Allogeneic	0	8 (12%)	8 (8%)
Previous anti-CD38 monoclonal antibodies			
Daratumumab			
Exposed	27 (93%)	67 (99%)	94 (97%)
Refractory	27 (93%)	67 (99%)	94 (97%)*
Penta-drug exposed†	22 (76%)	59 (87%)	81 (84%)
Triple-class refractory‡	25 (86%)	60 (88%)	85 (88%)
Penta-drug refractory†	9 (31%)	32 (47%)	41 (42%)
Refractory to last line of therapy	28 (97%)	68 (100%)	96 (99%)

(Table 1 continues in next column)

Adverse event

	Any grade	Grade 3–4
Any adverse event	97 (100%)	91 (94%)
Haematological*	97 (100%)	96 (99%)
Neutropenia	93 (96%)	92 (95%)
Anaemia	79 (81%)	66 (68%)
Thrombocytopenia	77 (79%)	58 (60%)
Leukopenia	60 (62%)	59 (61%)
Lymphopenia	51 (53%)	48 (50%)
Metabolism and nutrition disorders*	67 (69%)	16 (16%)
Hypocalcaemia	31 (32%)	3 (3%)
Hypophosphataemia	30 (31%)	7 (7%)
Decreased appetite	28 (29%)	1 (1%)
Hypoalbuminaemia	27 (28%)	1 (1%)
Hyponatraemia	22 (23%)	4 (4%)
Hypokalaemia	20 (21%)	2 (2%)
Gastrointestinal*	62 (64%)	4 (4%)
Diarrhoea	29 (30%)	1 (1%)
Nausea	27 (28%)	1 (1%)
Constipation	21 (22%)	0
Other*		
Fatigue	36 (37%)	5 (5%)
Cough	34 (35%)	0
Aspartate aminotransferase increased	28 (29%)	5 (5%)
Alanine aminotransferase increased	24 (25%)	3 (3%)
Chills	20 (21%)	0
Pyrexia	20 (21%)	0
Cytokine release syndrome*	92 (95%)	4 (4%)
Neurotoxicities*†	20 (21%)	9 (9%)

Berdeja et al, Lancet 2021

Background CARTITUDE-1

	All grade	Gr. 3-4	Description
Infections	56 (58%)	19 (20%)	Most common upper respiratory tract infection (15pt [16%]: 1pt gr3) Most common gr 3–4 pneumonia (8 [8%]) and sepsis (4 [4%]).
Secondary primary malignancies	7pt		Unrelated to cilta-cel treatment by the investigator five cases of myelodysplastic syndrome, two of acute myelogenous leukaemia, and one case each of prostate cancer and basal cell carcinoma
Cytokine release syndrome	92(95%)	3 (3%) gr 3, 1(1%) gr4-5	Onset 7 days (IQR 5–8) Median duration 4 days (IQR 3–6) 88 (91%) of 97 patients received supportive measures: tocilizumab (67 [69%] of 97 patients; four patients received ≥3 doses), corticosteroids (21 [22%]), and anakinra (18 [19%]). CRS resolved in 91 (99%) of 92 patients; The patient with grade 5 CRS and MAS died on day 99 subsequent to sequelae of prolonged grade 4 cytokine release syndrome

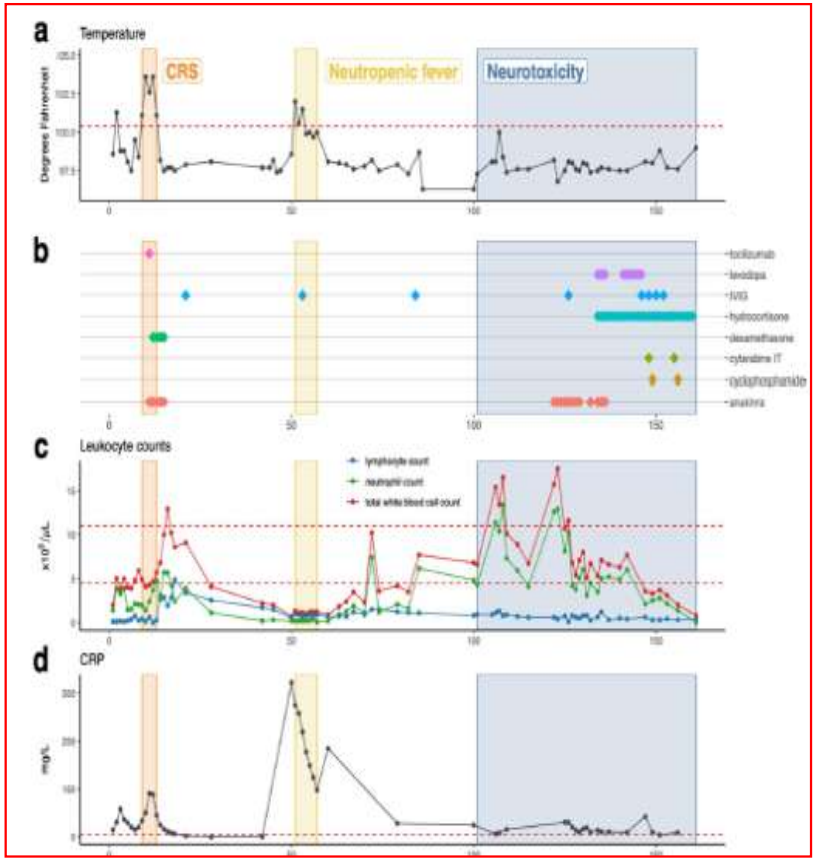
Berdeja et al, Lancet 2021

Background CARTITUDE-1

	All grade	Gr. 3-4	Description
Neurotoxicity	20 (21%)	9(9%)	
• ICANS	16 (17%)	1 (1%) gr 3 1(1%) gr 4 1(1%) gr 5	Median time onset 8 days (IQR 6·0–8·0) Median duration 4 days (IQR 3·0–6·5). 16 (17%) received supportive measures for ICANS, including corticosteroids (nine [9%]), tocilizumab (four [4%]), and anakinra (three [3%]). ICANS resolved in all 16 patients
• Other neurotoxicities	12 (12%)	7 (7%) gr 3 1(1%) gr 4 1(1%) gr 5	All had previous cytokine release syndrome, and eight (8%) had previous ICANS. Median onset 27 days (IQR 16·0–73·0). Symptoms: variable and wide-ranging, with five patients having a **cluster of movement and neurocognitive** treatment-emergent adverse events. Other neurotoxicities resolved in six (50%) of 12 patients and median time to recovery was 74·5 days (IQR 28·0–159·0). Other neurotoxicities did not resolve in the remaining six patients, of which one had ongoing symptoms, one died from grade 5 neurotoxicity on day 247 while receiving hospice care, and four died due to other reasons and, therefore, the neurotoxicity outcome could not be further evaluated.

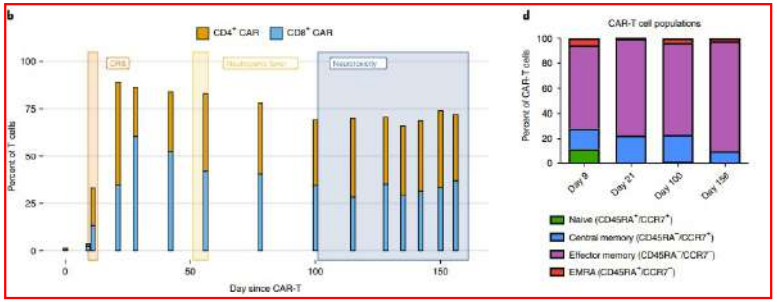
Berdeja et al, Lancet 2021

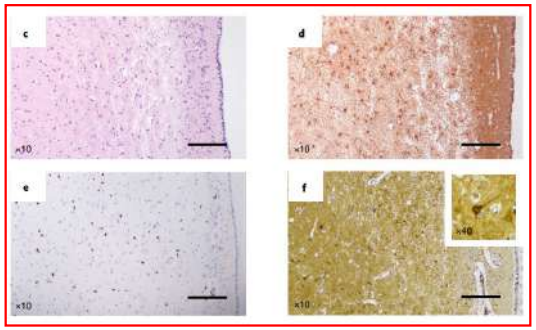
Background CARTITUDE-1



nature medicine
BRIEF COMMUNICATION
https://doi.org/10.1038/s41591-021-01564-7
Check for updates

Neurocognitive and hypokinetic movement disorder with features of parkinsonism after BCMA-targeting CAR-T cell therapy





Berdeja et al, Lancet 2021
Van Oekelen et al, Nature medicine 2021

UPDATED RESULTS FROM CARTITUDE-1: CILTACABTAGENEAUTOLEUCEL, A B-CELL MATURATION ANTIGEN–DIRECTED CHIMERIC ANTIGENRECEPTOR T (CAR-T) CELL THERAPY, IN RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM)

Updated results longer follow up 18months

CARTITUDE-1: Baseline Characteristics

Characteristic	
Age, median (range) years	61.0 (43–78)
Male, n (%)	57 (58.8)
Black/African American, n (%)	17 (17.5)
All plasmacytomas,[a] n (%)	19 (19.6)
Extramedullary plasmacytomas, n (%)	13 (13.4)
Bone-based plasmacytomas, n (%)	6 (6.2)
Bone-marrow plasma cells ≥60%, n (%)	21 (21.9)
Years since diagnosis, median (range)	5.9 (1.6–18.2)
High-risk cytogenetic profile, n (%)	23 (23.7)
del17p	19 (19.6)
t(14;16)	2 (2.1)
t(4;14)	3 (3.1)
Tumor BCMA expression ≥50%, n (%)	57 (91.9)[b]

Characteristic	
Prior lines of therapy, median (range)	6.0 (3–18)
Prior lines of therapy, n (%)	
3	17 (17.5)
4	16 (16.5)
≥5	64 (66.0)
Previous stem-cell transplantation, n (%)	
Autologous	87 (89.7)
Allogeneic	8 (8.2)
Triple-class exposed,[c] n (%)	97 (100)
Penta-drug exposed,[d] n (%)	81 (83.5)
Triple-class refractory,[c] n (%)	85 (87.6)
Penta-drug refractory,[d] n (%)	41 (42.3)
Refractory status, n (%)	
Carfilzomib	63 (64.9)
Pomalidomide	81 (83.5)
Anti-CD38 antibody	96 (99.0)
Refractory to last line of therapy, n (%)	96 (99.0)

BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; PI, proteasome inhibitor.
[a]All plasmacytomas include extramedullary and bone-based plasmacytomas. [b]Denominator n=62, the number of evaluable samples; BCMA expression detected in all evaluable samples. [c]At least 1 PI, at least 1 IMiD, and 1 anti-CD38 antibody. [d]At least 2 PIs, at least 2 IMiDs, and 1 anti-CD38 antibody.

Presented By: **Sundar Jagannath**

Jagannath et al,IMWG 2021

CARTITUDE-1: Safety

No new safety signals with longer follow-up

	N=97	
	Any grade	Grade 3/4
Hematologic AEs ≥25%, n (%)		
Neutropenia	93 (95.9)	92 (94.8)
Anemia	79 (81.4)	66 (68.0)
Thrombocytopenia	77 (79.4)	58 (59.8)
Leukopenia	60 (61.9)	59 (60.8)
Lymphopenia	51 (52.6)	48 (49.5)
Nonhematologic AEs ≥25%, n (%)		
Metabolism and nutrition disorders		
Hypocalcemia	31 (32.0)	3 (3.1)
Hypophosphatemia	30 (30.9)	7 (7.2)
Decreased appetite	28 (28.9)	1 (1.0)
Hypoalbuminemia	27 (27.8)	1 (1.0)
Gastrointestinal		
Diarrhea	29 (29.9)	1 (1.0)
Nausea	27 (27.8)	1 (1.0)
Other		
Fatigue	36 (37.1)	5 (5.2)
Cough	34 (35.1)	0
AST increased	28 (28.9)	5 (5.2)
ALT increased	24 (24.7)	3 (3.1)

CRS	N=97
Patients with a CRS event,* n (%)	92 (94.8)
Time to onset, median (range) days	7 (1–12)
Duration, median (range) days	4 (1–97)†

Of 92 patients with CRS, majority (94.6%) were grades 1/2
CRS resolved in 91 (98.9%) patients within 14 days of onset

	N=97
Total CAR T-cell neurotoxicities, n (%)	
Any Grade	20 (20.6)
Grade ≥3	10 (10.3)
ICANS, n (%)	
Any Grade	16 (16.5)
Grade ≥3	2 (2.1)
Other neurotoxicities,* n (%)	
Any Grade	12 (12.4)
Grade ≥3	9 (9.3)

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ASTCT, American Society for Transplantation and Cellular Therapy; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; HLH, hemophagocytic lymphohistiocytosis; ICANS, immune effector cell-associated neurotoxicity syndrome. *CRS was graded using Lee et al. (Blood 2014) in the phase 1b portion of the study and ASTCT in phase 2; in this combined analysis, Lee et al. criteria were mapped to ASTCT criteria for patients in the phase 1b portion. †The patient with 97-day duration died due to CRS/HLH. ‡Events not reported as ICANS (ie, onset after a period of recovery from CRS and/or ICANS).

Presented By: **Sundar Jagannath**

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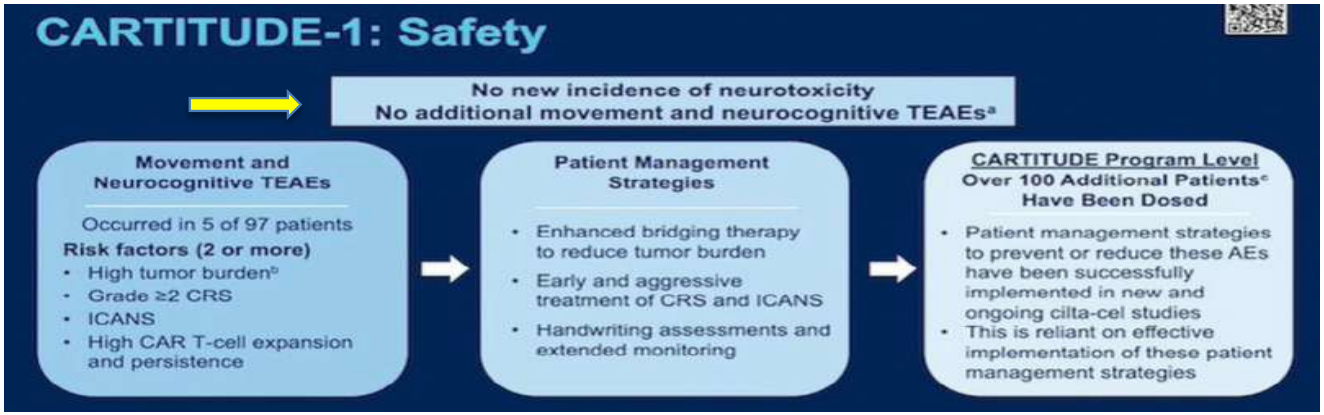


- **At a longer median follow-up of 18 months, a single dose of cilta-cel led to early, deep, and durable responses in heavily pretreated patients with MM**
  - ORR: 98%; sCR: 80%; MRD 10^{-5} negativity: 92% in evaluable patients
  - 18-month PFS rate: 66%; OS rate: 81%
- **Cilta-cel has a manageable safety profile consistent with its mechanism of action; no new safety signals were observed with longer follow-up**
  - Successful new patient management strategies have been implemented in the CARTITUDE program to prevent and reduce the incidence of neurotoxicity
- **Cilta-cel is being investigated in the ongoing phase 2 CARTITUDE-2[a] and phase 3 CARTITUDE-4[b] studies in earlier line settings**

Jagannath et al, IMWG 2021

CARTITUDE-2: Phase 2 Multi-Cohort Study in Various MM Settings

Screening (1 to ≤28 days)

- **Cohort A (n=40)**: Progressive disease after 1–3 lines of MM therapy and lenalidomide refractory
- **Cohort B (n=20)**: Early relapse: <12 months after frontline therapy or <12 months after ASCT
- **Cohort C (n=20)**: RRMM after PI, IMiD, anti-CD38, and BCMA-targeting therapy[a]
- **Cohort D (n=20)**: <CR after ASCT with or without consolidation in NDMM + len
- **Cohort E (n=20)**: NDMM with no prior therapy and high-risk per ISS stage III criteria

Induction if applicable

Cohort E D-VRd

Apheresis

Lymphodepletion Cy/Flu (Day -5 to -3)

Cilta-cel infusion (Target: 0.75×10⁶ CAR+ T cells/kg)

T-cell transduction and expansion to manufacture cilta-cel

Bridging therapy as needed

Follow-up

Consolidation

Cohort D + Len (2 years)

Cohort E + Len Dara (2 years)

[a]Excluding prior BCMA-targeting cellular therapy.

ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; CR, complete response; Cy, cyclophosphamide; Dara, daratumumab; D-VRd, daratumumab, bortezomib, lenalidomide, and dexamethasone; Flu, fludarabine; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; ISS, International Staging System; Len, lenalidomide; MM, multiple myeloma; NDMM, newly diagnosed multiple myeloma; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma

Presented by: **Adam Cohen**

Choen et al, IMWG 2021

CARTITUDE-2 Baseline Characteristics

Characteristic	N=20
Male, n (%)	13 (65)
Years since diagnosis, median (range)	3.5 (0.7–8.0)
Age, years, median (range)	60 (38–75)
Extramedullary plasmacytomas ≥1, n (%)	3 (15)
Bone-marrow plasma cells[a] ≥60%, n (%)	3 (15)
Prior lines of therapy, median (range)	2 (1–3)
Number of prior lines of therapy, n (%)	
<3 prior lines	12 (60)
3 prior lines	8 (40)
High-risk cytogenetic profile, n (%)	7 (35)[b]
del17p	3 (15)
t(14;16)	5 (25)
t(4;14)	0

Characteristic	N=20
Previous stem-cell transplantation, n (%)	
Autologous	17 (85)
Allogeneic	0
Triple-class exposed,[c] n (%)	13 (65)
Triple-class refractory,[c] n (%)	8 (40)
Penta-drug exposed,[d] n (%)	4 (20)
Penta-drug refractory,[d] n (%)	1 (5)
Refractory status, n (%)	
Bortezomib	8 (40)
Carfilzomib	2 (10)
Pomalidomide	7 (35)
Daratumumab	12 (60)
Refractory to last line of therapy, n (%)	19 (95)

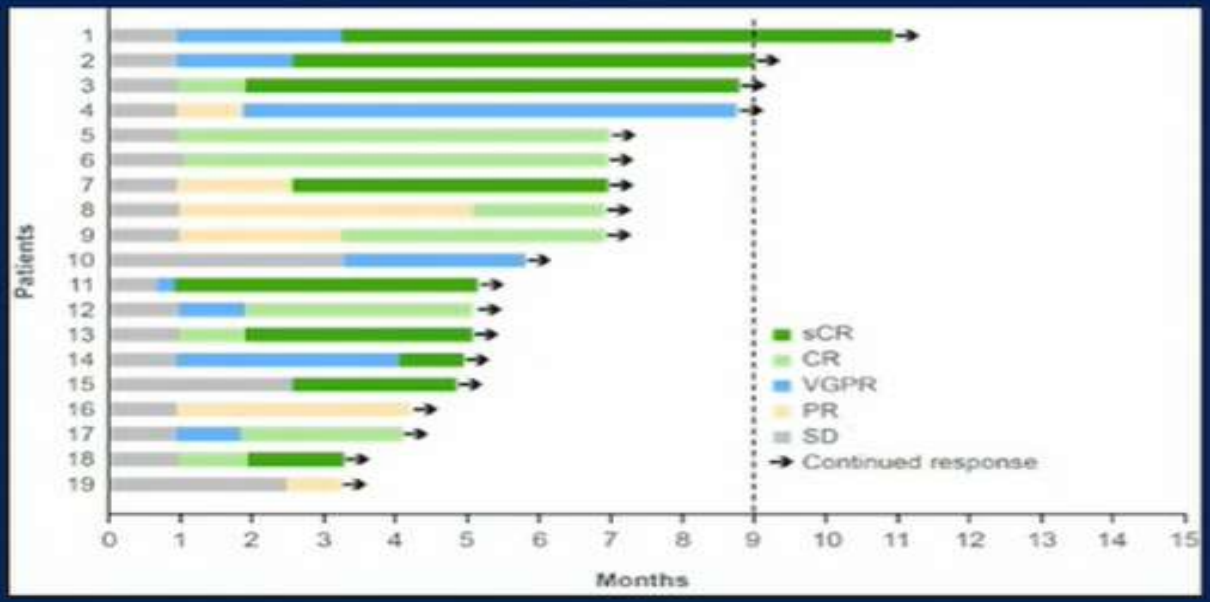
- All patients were refractory to lenalidomide
- All patients were exposed to a PI, an IMiD, and dexamethasone
- 95% were exposed to alkylating agents and 65% to daratumumab

Presented by: **Adam Cohen**

[a]Maximum value from bone marrow biopsy and bone marrow aspirate is selected if both results are available. [b]One patient had both del(17p) and t(14;16). [c]≥1 PI, ≥1 IMiD, and 1 anti-CD38 antibody. [d]≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 antibody.
IMiD, immunomodulatory drug; PI, proteasome inhibitor

Choen et al, IMWG 2021

CARTITUDE-2: Duration of Response



- Responses deepened over time
- No progression of disease at median follow-up of 5.8 months

Presented by: **Adam Cohen**

CR, complete response; PR, partial response; sCR, stringent complete response; PR, partial response; SD, stable disease; VGPR, very good partial response

Choen et al, IMWG 2021

CARTITUDE-2: Safety

Nonhaematologic AEs ≥20%, n (%)	N=20	
	Any grade	Grade 3/4
Metabolism and nutrition disorders		
Hypokalaemia	8 (40)	0
Hypocalcaemia	7 (35)	3 (15)
Hypophosphataemia	7 (35)	3 (15)
Hypomagnesaemia	6 (30)	0
Decreased appetite	5 (25)	3 (15)
Gastrointestinal		
Diarrhoea	9 (45)	3 (15)
Nausea	5 (25)	0
Constipation	4 (20)	0
Vomiting	4 (20)	0
Other		
Fatigue	9 (45)	1 (5)
Back pain	5 (25)	2 (10)
Pyrexia	5 (25)	0
Arthralgia	4 (20)	0
Renal impairment	4 (20)	0

Haematologic AEs ≥20%, n (%)	N=20	
	Any grade	Grade 3/4
Neutropaenia	19 (95)	18 (90)
Thrombocytopaenia	16 (80)	7 (35)
Anaemia	13 (65)	8 (40)
Lymphopaenia	12 (60)	11 (55)
Leukopaenia	11 (55)	11 (55)

- Incidence of prolonged Grade 3/4 cytopaenias beyond Day 60:
  - Neutropaenia: 25%
  - Thrombocytopaenia: 0%
  - Lymphopaenia: 45%

Presented by: **Adam Cohen**

AE, adverse event

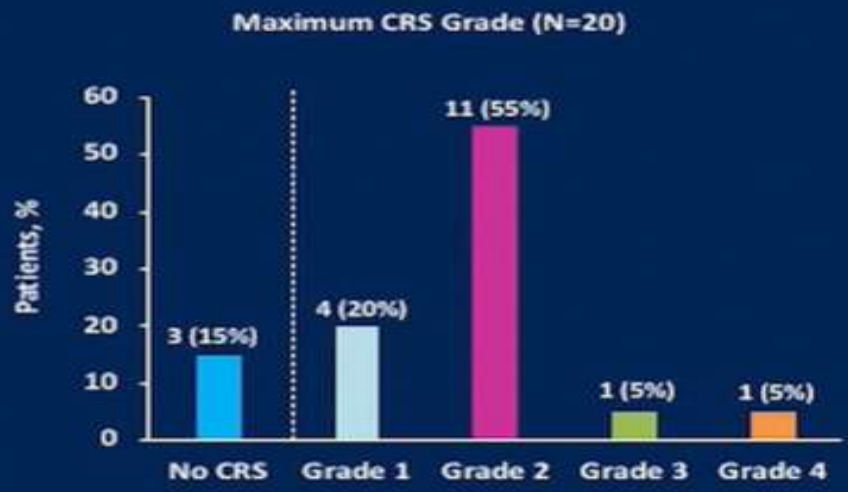
Choen et al, IMWG 2021

CARTITUDE-2: Safety

CRS	N=20
Patients with a CRS event, n (%)	17 (85)
Time to onset, days, median (range)	7 (5–9)
Duration, days, median (range)	3.5 (2–11)
Supportive measures,[a] n (%)	
Tocilizumab	14 (70)
Corticosteroids	6 (30)
IV fluids	6 (30)
Oxygen	4 (20)
Anakinra	1 (5)
Vasopressor	1 (5)
CRS resolved or recovered in 94% of patients at the time of data cut-off	

Neurotoxicity	N=20
ICANS, n (%)	3 (15)
Median time to onset, days (range)	8 (7–11)
Median duration, days (range)	2 (1–2)

All ICANS were grades 1/2
No cases of movement and neurocognitive TEAEs



- 1 death occurred on Day 100 after infusion due to COVID-19, and was assessed as treatment-related by the investigator

Presented by: **Adam Cohen**

[a]Includes supportive measures to treat CRS events and symptoms. Data cut-off date: Jan 2021
AE, adverse event; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity; IV, intravenous; TEAE, treatment-emergent adverse event

Choen et al, IMWG 2021

CARTITUDE-2 Program: Safety

No movement and neurocognitive TEAEs were observed in patients of Cohort A in CARTITUDE-2

Movement and Neurocognitive TEAEs[a]

Risk factors (2 or more)

- High tumour burden[b]
- Grade ≥2 CRS
- ICANS
- High CAR T-cell expansion and persistence

Patient Management Strategies

- Enhanced bridging therapy to reduce tumour burden
- Early and aggressive treatment of CRS and ICANS
- Handwriting assessments and extended monitoring

CARTITUDE Program Level >100 additional patients have been dosed[c]

- Patient management strategies to prevent or reduce these AEs have been successfully implemented in new and ongoing cilta-cel studies
- This is reliant on effective implementation of these patient management strategies

Presented by: **Adam Cohen**

[a]As observed in 5 of 97 patients in CARTITUDE-1. [b]Defined as high tumour burden when any of the following parameters were met: bone marrow plasma cell ≥80%, serum M-spike ≥5 g/dL, serum free light chain ≥5000 mg/L. [c]Included patients treated in earlier- and later-line settings across the CARTITUDE program.
AE, adverse event; cilta-cel, ciltacabtagene autoleucel; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event

Choen et al, IMWG 2021

CARTITUDE-2: Conclusions

- A single infusion of cilta-cel led to early and deep responses in patients with MM who received 1–3 prior lines of therapy and were lenalidomide refractory
  - ORR was 95%, with 75% of patients achieving CR or better and 85% achieving VGPR or better
  - Responses deepened over time and follow-up is ongoing
- The safety profile was manageable
  - CRS was mostly grades 1/2; median time to CRS onset was 7 days (range, 5–9)
  - No incidence of movement and neurocognitive TEAEs with this patient management strategy
- Cilta-cel is being evaluated in the phase 3 CARTITUDE-4[a] study in patients with 1–3 prior lines of therapy versus D-Pd or PVd

Presented by: **Adam Cohen**

[a]ClinicalTrials.gov: NCT04181827.
Cilta-cel, ciltacabtagene autoleucel; CAR, chimeric antigen receptor CR, complete response; CRS, cytokine release syndrome; D-Pd, daratumumab, pomalidomide, and dexamethasone; MM, multiple myeloma; ORR, overall response rate; PVd, pomalidomide, bortezomib, and dexamethasone; TEAE, treatment-emergent adverse event; VGPR, very good partial response

Choen et al, IMWG 2021

Highlights from IMW 2021

1-2 Febbraio 2022
Bologna
Royal Hotel Carlton

Incidence, Mitigation, and Management of Neurologic Adverse Events in CARTITUDE-2, a Phase 2 Study of Ciltacabtagene Autoleucel (cilta-cel) in Patients with Multiple Myeloma

Hermann Einsele[1], Samir Parekh[2], Deepu Madduri[3], Bianco Santomasso[3], Jaime Gállego Pérez-Larraya[4], Niels WCJ van de Donk[5], Bertrand Arnulf[6], Maria-Victoria Mateos[7], Kevin C De Bregeon[8], Helen Varsos[8], Marlene J Carrasco-Alfonso[8], Muhammad Akram[8], Nikoletta Lendvai[9], Carolyn C Jackson[10], Yuru Olyslager[10], Enrique Zudaire[11], Claire Li[12], Gong Geng[8], Andrzej Jakubowiak[13], Adam Cohen[14]

[1]Universitätsklinikum Würzburg, Medizinische Klinik und Poliklinik II, Würzburg, Germany; [2]Mount Sinai Medical Center, New York, NY, USA; [3]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [4]Clínica Universidad de Navarra, CIMA IDI, 31008, Pamplona, Spain; [5]Department of Hematology Cancer Center Amsterdam, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [6]Saint-Louis University Hospital AP-HP, Paris, France; [7]Institute of Cancer Molecular and Cellular Biology, University Hospital of Salamanca, Salamanca, Spain; [8]Janssen Research & Development, Raritan, NJ, USA; [9]Legend Biotech USA, Inc, Piscataway, NJ, USA; [10]Janssen Research & Development, Beerse, Belgium; [11]Janssen Research & Development, Spring House, PA, USA; [12]University of Chicago, Chicago, IL, USA; [13]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; *Current is employed with Janssen Research & Development
**Employed with Legend Biotech at the time the study was conducted

Treatment-emergent neurotoxicities are known side effects of CAR-T therapies and can be mild to life threatening, requiring careful monitoring and management[3-5]

- Movement and neurocognitive treatment-emergent adverse events (TEAEs) were observed in 5 of 97 patients treated with cilta-cel in the CARTITUDE-1 study[6]
- Grade 3 Parkinsonism has been reported in a study with another anti-BCMA CAR-T therapy, idecabtagene vicleucel[7]

Here, we describe the patient management strategies implemented to identify and reduce the incidence of neurologic AEs in patients from CARTITUDE-2 who had progressive MM after 1–3 prior lines of therapy

Table 1. Neurologic AEs

Neurotoxicities	Grade 1/2	Grade ≥3
ICANS, n (%)	3 (15)	0
Other neurotoxicities,* n (%)	1 (5)	0

*Events not reported as ICANS (ie, onset after a period of recovery from CRS and/or ICANS). AEs, adverse events; ICANS, immune effector cell–associated neurotoxicity syndrome.

Figure 2. Patient Management Strategies for Neurologic AEs in CARTITUDE-2

Movement and Neurocognitive TEAEs Risk Factors (2 or more)
- High tumor burden*
- Grade ≥2 CRS
- ICANS
- High CAR T cell expansion and persistence

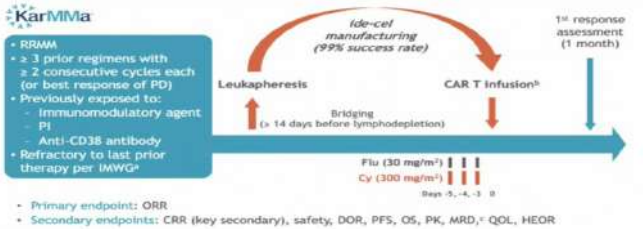
Implementation of Patient Management Strategies
- More effective bridging therapy to reduce tumor burden
- Early and aggressive treatment of CRS and ICANS
- Handwriting assessments and extended monitoring

CARTITUDE Program Level
More Than 100 Patients Have Been Dosed
- Patient management strategies to prevent or reduce these AEs have been successfully implemented in new and ongoing cilta-cel studies
- This strategy is reliant on effective implementation of these patient management strategies

*Defined as high tumor burden when any of the following parameters were met: bone marrow plasma cell ≥50%, serum M-spike ≥5 g/dL, serum free light chain ≥5000 mg/L. AEs, adverse events; CAR T, chimeric antigen receptor T cell; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; TEAE, treatment-emergent AE.

Einsele et al, IMWG 2021

Idecabtagene vicleucel (ide-cel, bb2121), a BCMA-directed CAR T cell therapy, for the treatment of patients with relapsed and refractory multiple myeloma: updated results from KarMMa



Baseline demographics and clinical characteristics

Characteristics	Prior line of therapy		All ide-cel treated (N = 128)
	3 (n = 15[a])	≥ 4 (n = 113)	
Age, median (range), years	58 (38-74)	61 (33-78)	61 (33-78)
Male sex, %	80	57	59
ECOG PS (0 / 1 / 2), %	40 / 60 / 0	45 / 52 / 3	45 / 53 / 2
R-ISS Stage (I / II / III), %	7 / 87 / 7	12 / 68 / 18	11 / 70 / 16
High risk cytogenetics,[b] %	47	34	35
High tumor burden,[c] %	47	51	51
Tumor BCMA expression ≥ 50%,[d] %	87	85	85
Extramedullary disease, %	47	38	39
Time since initial diagnosis, median (range), years	4 (2-7)	7 (1-18)	6 (1-18)
Prior anti-myeloma regimens, median (range)	3 (3-3)	6 (4-16)	6 (3-16)
Prior autologous SCT (any / > 1), %	87 / 0	95 / 39	94 / 34
Any bridging therapies for multiple myeloma, %	87	88	88
Refractory status, %			
Anti-CD38 antibody-refractory	100	93	94
Triple-refractory[e]	93	83	84
Penta-refractory[f]	27	26	26

Anderson et al,IMWG 2021

Background Ide-Cel KaRMMA-1: Safety

Table 2. Adverse Events, Cytokine Release Syndrome, and Neurotoxic Effects in the 128 Patients Who Received Ide-Cel.

Variable	Any Grade	Grade 3 or 4
	no. of patients (%)	
Adverse event*		
Any	128 (100)	127 (99)
Hematologic		
Neutropenia	117 (91)	114 (89)
Anemia	89 (70)	77 (60)
Thrombocytopenia	81 (63)	67 (52)
Leukopenia	54 (42)	50 (39)
Lymphopenia	35 (27)	34 (27)
Febrile neutropenia	21 (16)	20 (16)
Gastrointestinal		
Diarrhea	45 (35)	2 (2)
Nausea	37 (29)	0
Constipation	20 (16)	0
Other		
Hypokalemia	45 (35)	3 (2)
Fatigue	43 (34)	2 (2)
Hypophosphatemia	38 (30)	20 (16)
Hypocalcemia	34 (27)	10 (8)
Pyrexia	32 (25)	3 (2)
Hypomagnesemia	30 (23)	0
Decreased appetite	27 (21)	1 (<1)
Headache	27 (21)	1 (<1)
Hypogammaglobulinemia	27 (21)	1 (<1)
Cough	26 (20)	0
Hyponatremia	24 (19)	7 (5)
Hypoalbuminemia	22 (17)	4 (3)
Aspartate aminotransferase level increased	21 (16)	2 (2)
Hypotension	21 (16)	1 (<1)
Cytokine release syndrome†	107 (84)	7 (5)
Neurotoxic effect‡	23 (18)	4 (3)

Infections :69%; grade 3 or 4 in 28 (22%).

CRS *84%, mostly grade 1 or 2 .*
Five patients (4%) had grade 3 cytokine release syndrome, 1 (<1%) had grade 4, and 1 (<1%) had grade 5 (300×10^6 dose level).
Median time onset CRS 1 day (range, 1 to 12), median duration of 5 days (range, 1 to 63).
Management of CRS involved the use of tocilizumab in 67 of 128 (52%) patients, but only 19 of 128 (15%) patients required glucocorticoids

ICANS *23 patients (18%), of whom 4 (3%) had grade 3 events; no grade 4 or 5.*
Median time onset neurotoxic effect 2 days (range, 1 to 10), and the median duration was 3 days (range, 1 to 26).

A total of 44 treated patients (34%) died during the study, with most deaths (27) attributed by the investigator to complications of myeloma progression.
*Three patients (2%) died within 8 weeks after ide-cel infusion from ide-cel–related adverse events (**bronchopulmonary aspergillosis, gastrointestinal hemorrhage, and cytokine release syndrome**). One patient (1%) died between 8 weeks and 6 months from an ide-cel–related adverse event (**cytomegaloviral pneumonia**). Five patients (4%) died after 6 months from unrelated adverse events, and an additional 8 patients (6%) died after disease progression.*

Munshi at al, N Engl J Med 2021

Background Ide-Cel KaRMMA-1: Neurotoxicity

Characteristics of neurotoxicity associated with idecabtagene vicleucel (ide-cel, bb2121) in patients with relapsed and refractory multiple myeloma (RRMM) in the pivotal phase II KarMMa study.

Conclusion: *All NT occurred in the proximity of cytokine release syndrome (CRS) events with the start date of NT events either overlapping with or occurring within 1 wk of the start of a CRS event*

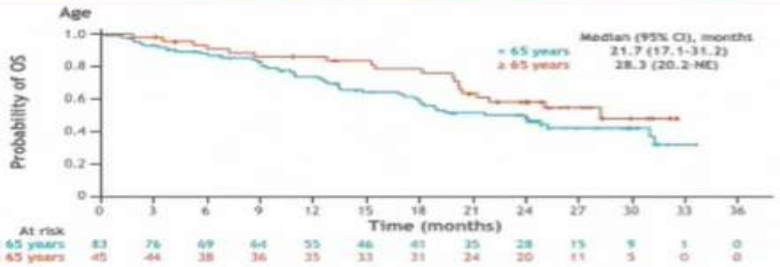
NT events	Gr 1 (n = 12)	Gr 2 (n = 7)	Gr 3 (n = 4)	Any gr (n = 23)
Time to onset, median (range), d	2 (1-10)	2 (1-4)	3 (1-4)	2 (1-10)
No. of events	13	7	4	24
Duration/event, %				
1-5 d	69	43	25	54
6-10 d	31	29	0	25
>10 d	0	14	75	17
Ongoing	0	14	0	4
Median (range), d[a]	3 (1-9)	6 (1-26)	14 (2-22)	3 (1-26)
CS / Toci / ANR, %	17 / 8 / 0	57 / 0 / 0	100 / 50 / 25	43 / 13 / 4

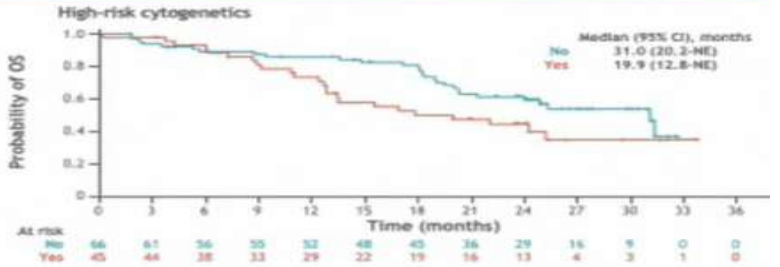
Efficacy	No NT (n = 105)	NT, any gr (n = 23)
Response, % (95% CI)		
ORR	73 (64.9-81.8)	74 (56.0-91.9)
CRR	35 (26.1-44.4)	22 (4.9-38.6)
PFS, median (95% CI), mo	8.9 (5.7-11.9)	6.1 (3.0-11.1)
DOR,[b] median (95% CI), mo	11.0 (8.0-11.3)	10.0 (4.0-NE)
OS, median (95% CI), mo	19.4 (18.0-NE)	NE (12.3-NE)

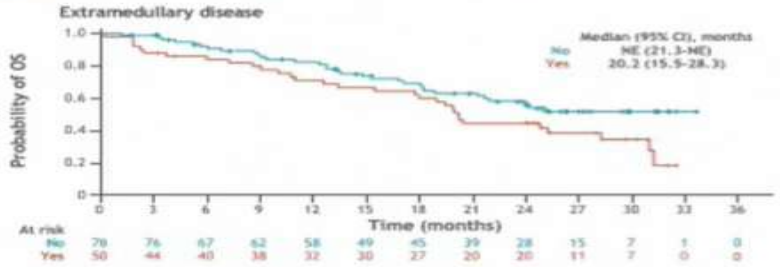
Data cutoff: 14 Jan 2020. NE, not estimable. [a]Ongoing NT excluded. [b]Among responders.

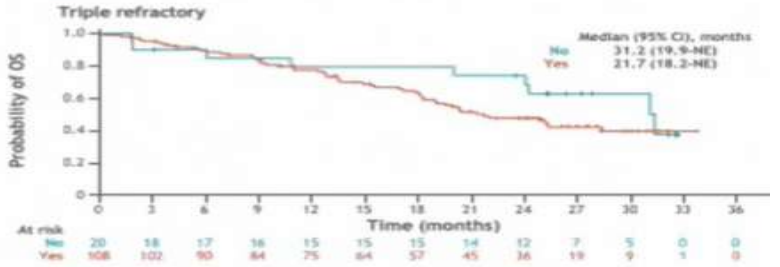
Manier S, et al. **J. Clin. Oncol.** 39(Suppl. 15), 8036–8036 (2021).

Overall survival in high-risk patient subgroups









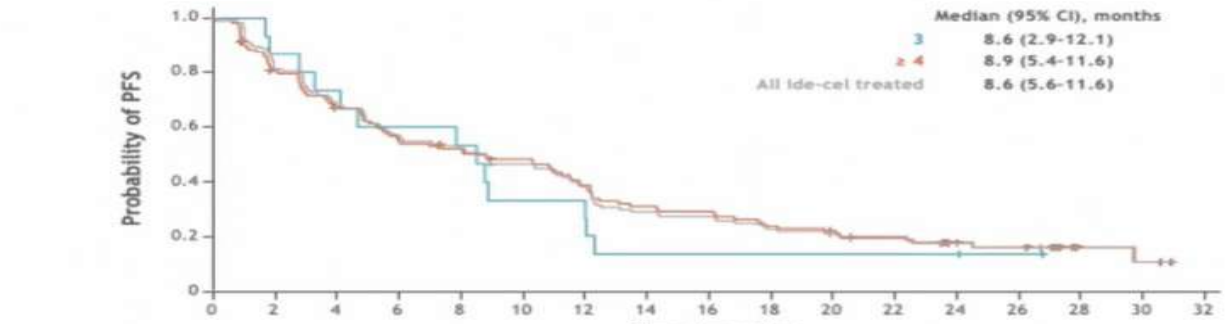
- Median OS was > 20 months in several key high-risk subgroups, including age (≥ 65 years), extramedullary disease, and triple-refractory status

1

Anderson LD, et al. IMW 2021 [presentation #OA827]

Anderson et al,IMWG 2021

PFS by number of prior lines of therapy and in all ide-cel treated patients



- Median PFS was 8.6 months in all ide-cel treated patients and was similar in patients with 3 and ≥ 4 prior lines of therapy

9

Anderson LD, et al. IMW 2021 [presentation #OA827]

Anderson et al,IMWG 2021

Incidence of CRS and neurotoxicity

	Prior line of therapy		All ide-cel treated (N = 128)
	3 (n = 15)	≥ 4 (n = 113)	
≥ 1 CRS event, n (%)	13 (87)	94 (83)	107 (84)
Maximum grade,[a] n (%)			
1/2	12 (80)	88 (78)	100 (78)
3	1 (7)	4 (4)	5 (4)
4	0	1 (< 1)	1 (< 1)
5	0	1 (< 1)	1 (< 1)
Median onset (range), days	1 (1-2)	1 (1-12)	1 (1-12)
Median duration (range), days	4 (1-63)	6 (2-28)	5 (1-63)
≥ 1 NT event, n (%)	2 (13)	21 (19)	23 (18)
Maximum grade,[b] n (%)			
1	1 (7)	10 (9)	11 (9)
2	0	7 (6)	7 (5)
3	1 (7)	4 (4)	5 (4)[c]
Median onset (range), days	3 (1-5)	2 (1-10)	2 (1-10)
Median duration (range), days	3 (2-5)	3 (1-26)	3 (1-26)

- Incidences of CRS and NT were similar in patients who received 3 or ≥ 4 prior lines of therapy and were mostly low grade

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Adverse events of interest

Adverse events of interest, n (%)	Prior line of therapy				All ide-cel treated (N = 128)	
	3 (n = 15)		≥ 4 (n = 113)			
	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Hematologic						
Neutropenia	14 (93)	13 (87)	103 (91)	101 (89)	117 (91)	114 (89)
Anemia	10 (67)	5 (33)	80 (71)	73 (65)	90 (70)	78 (61)
Thrombocytopenia	11 (73)	8 (53)	71 (63)	59 (52)	82 (64)	67 (52)
Leukopenia	7 (47)	6 (40)	47 (42)	44 (39)	54 (42)	50 (39)
Lymphopenia	7 (47)	7 (47)	29 (26)	28 (25)	36 (28)	35 (27)
Nonhematologic						
Infections	12 (80)	2 (13)	78 (69)	32 (28)	90 (70)	34 (27)
SPM[a]	0	0	9 (8)	3 (3)	9 (7)	3 (2)
HLH/MAS	1 (7)	1 (7)	3 (3)	1 (1)	4 (3)	2 (2)

- With longer follow-up, similar rates of infections and SPMs, as well as no unexpected gene therapy-related toxicities were observed
- Median time to recovery of grade ≥ 3 neutropenia and thrombocytopenia was 2 months for 3 and ≥ 4 prior lines of therapy subgroups and in all treated patients

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Conclusions

- Long term results from the KarMMa trial continue to demonstrate frequent, deep, and durable responses in heavily pretreated patients with RRMM
  - ORR, CRR, DOR, and PFS were consistent with previous reports[1,2] and patients received similar benefit regardless of number of prior lines of therapy
  - With longer follow-up, efficacy remains greatest with the highest target dose (450 × 10^6 CAR+ T cells)
  - Median OS was 24.8 months in all ide-cel treated patients and > 20 months in several high-risk subgroups
- The safety profile of ide-cel was consistent with previous reports across all groups
  - The frequencies of CRS and NT remain consistent with previous reports[1,2]
  - Similar rates of infections and SPMs, and no unexpected gene therapy-related toxicities were observed with longer follow-up
- The favorable benefit-risk profile of ide-cel regardless of the number of prior lines of therapy supports its role as a treatment option for heavily pretreated RRMM

Ide-cel is being explored in ongoing clinical trials: KarMMa-2 KarMMa-4 KarMMa-3 KarMMa-7

1. Munshi NC, et al. *N Engl J Med* 2021;384:705-716; 2. Munshi NC, et al. Poster presentation at the 2020 ASCO Annual Meeting; May 29-31, 2020; Virtual. Abstract 8503.

Anderson LD, et al. IMW 2021 [presentation #OA827]

Anderson et al,IMWG 2021

Health-Related Quality of Life (HRQoL) Among Real-World Ide-Cel-Eligible Patients (pts) With Relapsed/Refractory Multiple Myeloma (RRMM): Results From the Connect® MM Registry

Lynne I. Wagner,[1] Rafat Abonour,[2] Sikander Ailawadhi,[3] Brian G.M. Durie,[4] Cristina J. Gasparetto,[5] James W. Hardin,[6] Hans C. Lee,[7] Mohit Narang,[8] Robert M. Rifkin,[9] Howard Terebelo,[10] Kathleen Toomey,[11] Prashant Joshi,[12] Amit Agarwal,[13] Julia Braverman,[14] Devender Dhanda,[15] Mia He,[15] and Sundar Jagannath[15] on behalf of CONNECT MM Registry Investigators

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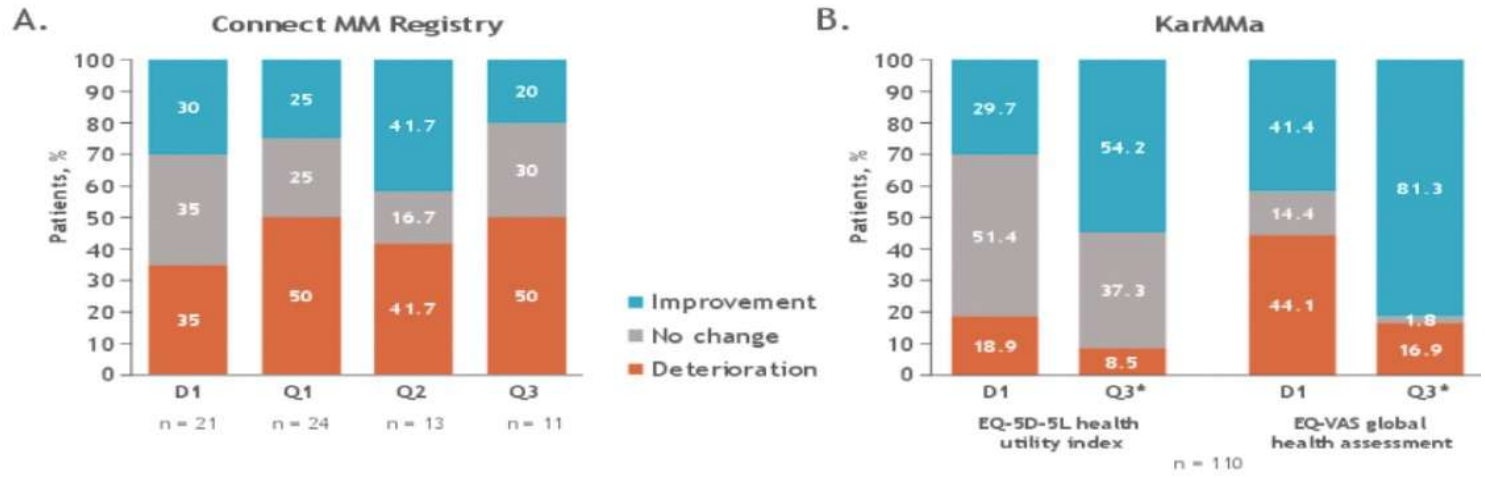
Results (cont.)

Figure 5. Proportion of responders with meaningful change from baseline in the (A) Connect MM Registry (EQ-5D) and (B) KarMMa trial (EQ-5D and EQ-VAS)



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Conclusions

- By Q3 posttreatment initiation, a substantial proportion of ide-cel-eligible real-world patients with RRMM from the CONNECT MM Registry who received various alternate (non-CAR T cell therapy) MM regimens experienced meaningful deterioration of HRQoL (measured by EQ-5D-3L and FACT-MM) from D1 over time
- In the context of the KarMMa trial, it was observed that a higher proportion of patients on ide-cel experienced meaningful improvement in HRQoL (measured by EQ-5D-5L) and fewer patients experienced deterioration by Q3 after treatment[3]
- Limitations of this analysis include small sample size and use of different versions of EQ-5D assessments (eg, 3L vs 5L)
- HRQoL remains an important goal of MM treatment, and therapies that improve HRQoL should be developed explicitly
- These results support the need for replication of this analysis in a larger patient sample and to complement clinical trial findings as well as to utilize HRQoL to inform development of therapeutic strategies in myeloma management

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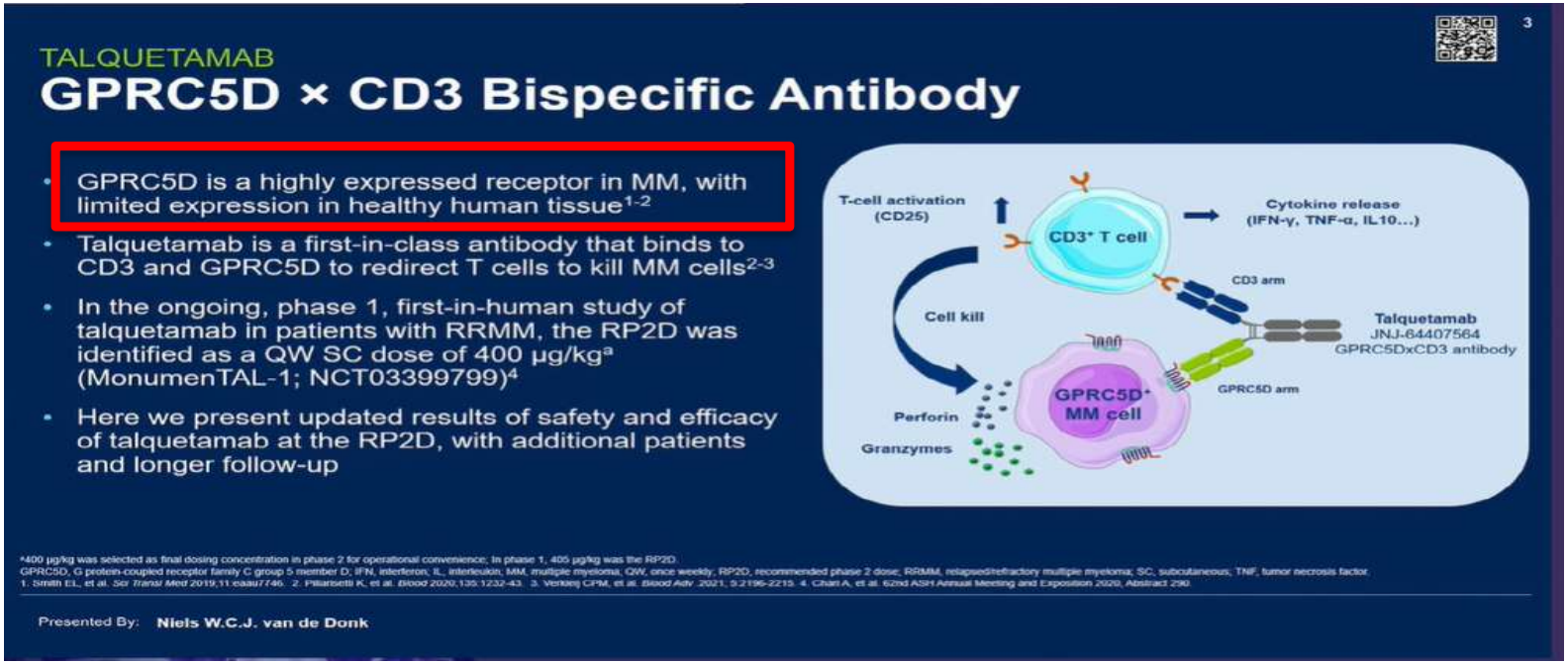
BISPECIFIC T-cell ANTIBODY: SAFETY PROFILE

- *BCMA*
  - ELRANATAMAB->MagnetisMM Ph1
- *GPRC5D*
  - TALQUETAMAB->MonoumenTAL Ph1
- *FcRH5*
  - No data

TALQUETAMAB, A G PROTEIN-COUPLED RECEPTOR FAMILY C GROUP 5 MEMBER D (GPRC5D) × CD3 BISPECIFIC ANTIBODY, IN RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM): UPDATED RESULTS OF A PHASE 1, FIRST-IN-HUMAN STUDY



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TALQUETAMAB

MonumenTAL-1 Study Design

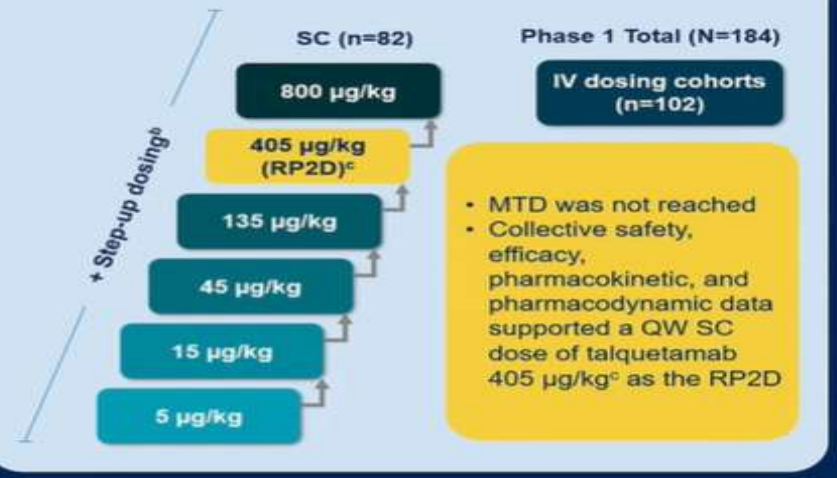
Key Objectives
- Part 1: Identify RP2D
- Part 2: Safety and tolerability at RP2D
- Antitumor activity, pharmacokinetics, pharmacodynamics

Key Eligibility Criteria
- Adults with measurable MM
- R[illegible]or intolerant to established MM therapies
- Hemoglobin ≥8 g/dL, platelets ≥50×10⁹/L, ANC ≥1.0×10⁹/L
- Prior BCMA-targeted therapy allowed

Dosing Schedule at RP2D

Step-up doses of 10 µg/kg and 60 µg/kg	405 µg/kg SC (cycle 1 and beyond)		
Week −1	Week 1	Week 2	Week 3
	Tal	Tal	Tal

- Premedications[a] were limited to step-up doses and first full dose
  - No steroid requirement after first full dose



- The data cut-off date for these analyses was April 18, 2021

[a]Glucocorticoid, antihistamine, and antipyretic; [b]1-3 step-up doses given within 1 week before a full dose; [c]Step-up doses of 10 and 60 µg/kg.
ANC, absolute neutrophil count; BCMA, B-cell maturation antigen; IV, intravenous; MM, multiple myeloma; MTD, maximum tolerated dose; QW, every week; RP2D, recommended phase 2 dose; RR, relapsed/refractory; SC, subcutaneous.

Presented By: **Niels W.C.J. van de Donk**

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TALQUETAMAB

Patient Demographics and Disease Characteristics

Characteristic	SC Total n=82	RP2D (405 µg/kg SC QW)[a] n=30
Age, years, median (range)	63.0 (42–80)	61.5 (46–80)
Age ≥70 years, n (%)	22 (27)	7 (23)
Sex, n (%)		
Male	47 (57)	19 (63)
Female	35 (43)	11 (37)
Years since diagnosis, median (range)	5.9 (1–20)	5.6 (2–20)
Extramedullary plasmacytomas ≥1, n (%)[b]	27 (33)	10 (33)
Bone marrow plasma cells ≥60%, n (%)[c]	13 (17)	6 (21)
ISS stage, n (%)[d]		
I	26 (32)	12 (40)
II	36 (44)	13 (43)
III	13 (16)	3 (10)
Prior transplantation, n (%)	71 (87)	27 (90)

Characteristic	SC Total n=82	RP2D (405 µg/kg SC QW)[a] n=30
Prior lines of therapy, n, median (range)	6.0 (2–17)	6.0 (2–14)
Exposure status, n (%)		
Prior BCMA therapy[e]	20 (24)	8 (27)
Triple-class[f]	81 (99)	30 (100)
Penta-drug[g]	64 (78)	24 (80)
Refractory status, n (%)		
PI[h]	69 (84)	25 (83)
Carfilzomib	54 (66)	19 (63)
IMiD[i]	76 (93)	28 (93)
Pomalidomide	67 (82)	26 (87)
Anti-CD38 mAb[j]	77 (94)	30 (100)
BCMA[e]	14 (17)	5 (16)
Triple-class[f]	62 (76)	23 (77)
Penta-drug[g]	23 (28)	6 (20)
To last line of therapy	69 (84)	26 (87)

[a]Step-up doses of 10 µg/kg and 60 µg/kg; [b]Soft-tissue component of a bone-based plasmacytoma not included; [c]Percentages calculated from n=76 for SC total and n=29 at RP2D; [d]Percentages calculated from n=66 for SC total and n=27 at RP2D; [e]BCMA CAR-T therapy or BCMA non-CAR-T therapy; [f]≥1 PI, ≥1 IMiD, and 1 anti-CD38 mAb; [g]≥2 PI, ≥2 IMiD, and 1 anti-CD38 mAb; [h]Bortezomib, carfilzomib, and/or ixazomib; [i]Thalidomide, lenalidomide, and/or pomalidomide; [j]Daratumumab and/or isatuximab.
BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; IMiD, immunomodulatory drug; ISS, International Staging System; mAb, monoclonal antibody; PI, proteasome inhibitor; QW, weekly; RP2D, recommended phase 2 dose; SC, subcutaneous.

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TALQUETAMAB

Safety Profile

AE (≥20% of total SC), n (%)	SC Total n=82		RP2D (405 µg/kg SC QW)[a] n=30	
	Any grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic				
Neutropenia	47 (57)	40 (49)	20 (67)	18 (60)
Anemia	37 (45)	23 (28)	17 (57)	8 (27)
Thrombocytopenia	23 (28)	15 (18)	10 (33)	6 (20)
Leukopenia	21 (26)	16 (20)	11 (37)	8 (27)
Lymphopenia	19 (23)	19 (23)	9 (30)	9 (30)
Nonhematologic				
CRS	55 (67)	1 (1)	22 (73)	1 (2)
Dysgeusia	38 (46)	NA	18 (60)	NA
Fatigue	26 (32)	0	9 (30)	0
Pyrexia	23 (28)	1 (1)	7 (23)	1 (2)
Dry mouth	22 (27)	0	8 (27)	0
Dysphagia	21 (26)	0	11 (37)	0
Headache	19 (23)	1 (1)	7 (23)	0
Diarrhea	18 (22)	0	7 (23)	0
Nausea	18 (22)	0	7 (23)	0

[a]Step-up doses of 10 µg/kg and 60 µg/kg. [b]Includes skin exfoliation, pruritis, rash, and nail disorders. [c]Includes nail disorders, onychomadesis, and nail dystrophy.
AE, adverse event; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; NA, not applicable; RP2D, recommended phase 2 dose; SC, subcutaneous.

- Talquetamab has a tolerable safety profile at the RP2D of 405 µg/kg SC
  - No DLTs at the RP2D
  - Cytopenias mostly confined to step-up doses and cycles 1/2
  - Neutropenias generally resolved within a week and were limited to cycles 1/2
- Infections in 37% of SC and RP2D patients (grade 3/4: 9% for SC total, 3% for RP2D)
- Neurotoxicities (all grade 1/2) in 4 patients with SC dosing; 2 patients (7%) at RP2D
- Injection-site reactions in 17% of SC patients (including RP2D) were mild and manageable (all grade 1/2)
- Skin-related AEs[b] in 67% of SC patients; 77% at RP2D (majority grade 1/2)
  - Nail disorders[c] in 21% of patients; 27% at RP2D
- No deaths due to AEs at the RP2D

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TALQUETAMAB

Cytokine Release Syndrome

Parameter	SC Total n=82	RP2D (405 µg/kg SC QW)[a] n=30
Patients with CRS, n (%)	55 (67)	22 (73)
Time to onset, days,[b] median (range)	2 (1–22)	2 (1–22)
Duration, days, median (range)	2 (1–7)	2 (1–3)
Supportive measures, n (%)[c]	55 (67)	22 (73)
Tocilizumab[d]	43 (52)	18 (60)
Steroids	5 (6)	1 (3)
Low-flow oxygen by nasal cannula	6 (7)	1 (3)
Vasopressor	2 (2)	1 (3)

- CRS was generally confined to step-up and first full doses
- Across all SC cohorts, CRS was limited to grade 1/2 in all patients, with the exception of 1 patient with grade 3 CRS
  - Majority of patients only had 1 dose of tocilizumab as a supportive measure for CRS

[a]Step-up doses of 10 µg/kg and 60 µg/kg; [b]Relative to the most recent dose; [c]A patient could receive >1 supportive therapy; [d]Tocilizumab was allowed for all CRS events; [e]Graded according to Lee et al. *Blood* 2014;124:188.
CRS, cytokine release syndrome; QW, weekly; RP2D, recommended phase 2 dose; SC, subcutaneous.

Presented By: **Niels W.C.J. van de Donk**

VanDe Donk et al, IMWG 2021

TALQUETAMAB

Conclusions

- Talquetamab is an off-the-shelf T-cell redirecting, GPRC5D targeting agent that requires limited steroid use and has a manageable safety profile at a dose of 405 µg/kg SC QW
- Additional patients and longer follow-up support the RP2D
  - A high response rate (70% ORR) was observed
  - High response rate was maintained in triple-refractory and penta-refractory patients (65% and 84%, respectively)
  - Responses were durable and continued to deepen over time
  - Pharmacokinetic and pharmacodynamic data continue to support the RP2D
- Talquetamab showed encouraging efficacy in heavily pretreated patients with RRMM
  - A phase 2 expansion study of talquetamab at the RP2D[a] is in progress (NCT04634552)

[a]400 µg/kg selected as final dosing concentration in phase 2 for operational convenience.
GPCR5D, G protein–coupled receptor family C group 5 member D; ORR, overall response rate; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous; QW, weekly.

Presented By: **Niels W.C.J. van de Donk**

VanDe Donk et al, IMWG 2021

Characterization and Management of Oral and Dermatological Toxicities in Patients Receiving the CD3 X GPRC5D Bispecific Antibody Talquetamab (JNJ-64407564) for the Treatment of Relapsed and/or Refractory Multiple Myeloma

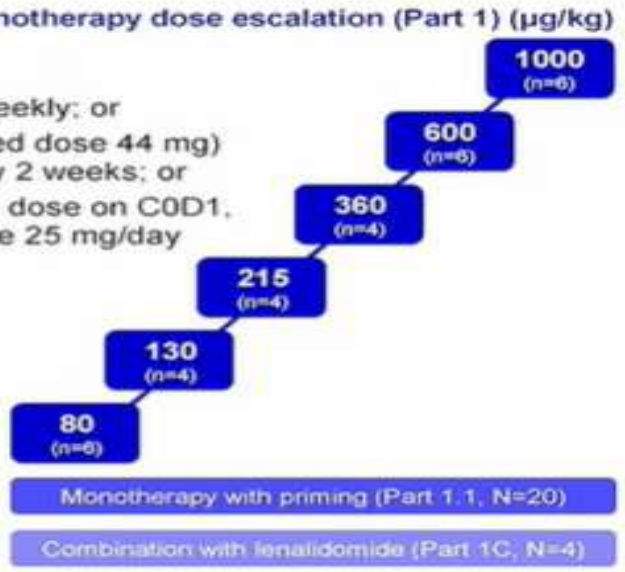
Stefania Stefania Mancia, Annamaria Farrell, Karen Louw, Erika Florendo, Elizabeth Aronson, Kiah Purcell, Donna D Catamero, Juliet Escalon, Joanne Thomas, Annel Aponte, Angela Lamb, Diana Kirke, Aimee Lucas, Sundar Jagannath, Hearn Jay Cho, Samir Parekh, Joshua Richter, Larysa Sanchez, Ajai Chari

In collaboration with dermatology consultation, the management of palmar/plantar desquamation, nail disorders, and injection site reaction has been ammonium lactate 12% cream, triamcinolone 0.1% cream, along with plain Vaseline and Vanicream products applied twice daily.
Of the 11 pts with systemic rash, 10 were at or above a dose of 405 µg /kg. Five pts had grade 3 rash requiring dose hold and systemic steroids in conjunction with topical medications. All pts have resumed dosing without recurrence of grade 3 rash. Four of these pts were at a dose level of 800 µg/kg SC. Grade 1-2 rash did not require dose hold and was managed with early intervention of the 3 topical treatments applied to affected areas twice daily.
In addition to the above described dermatologic AEs, treatment emergent oral AEs were observed in 38 (48.7%) pts, all grade 1-2. 42 pts developed dysgeusia (53.8%), 16 developed dry mouth (20.5%), and 17 developed dysphagia (21.8%).
Dysgeusia resulted in 3 pts requiring drug interruption. 1 pt requiring dose reduction, and 1 discontinued treatment. The average time to onset for dysgeusia was 26.5 days. Dry mouth resulted in no drug interruptions, reductions, or discontinuations, and had an average onset of 6.7 days.
Dysphagia also ranged from grades 1-2, with 3 pts requiring drug interruption. There were no dose reductions or treatment discontinuation. The average time to onset was 41.5 days. Dry mouth, dysgeusia, and dysphagia were more prevalent with higher doses.
Along with GI and nutrition consultation, oral AEs have been successfully managed with saliva substitute sprays and rinses. These supportive interventions are instituted promptly at time of onset of symptoms.

Mancia et al, ASH 2021

MagnetisMM-1 Study of Elranatamab (PF-06863135), a B-Cell Maturation Antigen (BCMA) Targeted CD3-Engaging Bispecific Molecule, for Patients With Relapsed or Refractory Multiple Myeloma

- Patients with RRMM received:
  - Monotherapy (Part 1, N=30): elranatamab 80, 130, 215, 360, 600, or 1000 µg/kg weekly; or
  - Monotherapy with priming (Part 1.1, N=20): a single priming dose (600 µg/kg or fixed dose 44 mg) followed 1 week later by full dose (1000 µg/kg or fixed dose 76 mg) weekly or every 2 weeks; or
  - Combination therapy with lenalidomide (Part 1C, N=4): elranatamab 32 mg priming dose on C0D1, followed 1 week later by elranatamab 44 mg weekly beginning C1D1 + lenalidomide 25 mg/day orally on D1–21 of a 28-day cycle, beginning with C1
- Safety assessments
  - TEAEs were graded by CTCAE version 4.03
  - CRS was graded by ASTCT criteria[1]
  - DLT was monitored to the end of C1
- PK, pharmacodynamics, and immunogenicity were evaluated
- Response was assessed by IMWG criteria[2]
- Data cutoff was June 7, 2021



Dholaria et al, IMWG 2021

Monotherapy (Part 1, N=30) – Patient and Disease Characteristics

- 30 patients had received elranatamab SC by the data cutoff
  - 80 (n=6), 130 (n=4), 215 (n=4), 360 (n=4), 600 (n=6), and 1000 (n=6) µg/kg weekly

Characteristics	SC dosing total (N=30)
Gender, n (%)	
Female	17 (56.7)
Median age, y (range)	63.0 (46–80)
≥65 y, n (%)	12 (40.0)
R-ISS stage at initial diagnosis, n (%)	
Stage I	6 (20.0)
Stage II	12 (40.0)
Stage III	7 (23.3)
Not reported	5 (16.7)
Cytogenetic risk	
High	7 (23.3)
Standard	19 (63.3)
Unknown	4 (13.3)

Data cutoff was June 7, 2021.
R-ISS=Revised International Staging System; SC=subcutaneous.
Definition of high cytogenetic risk includes t(4;14), t(14;16), del(17p), and del(13q).

Dholaria et al, IMWG 2021

Monotherapy (Part 1, N=30) – Treatment-Emergent Adverse Events (All Causality) Occurring in ≥1/3 of Patients

Adverse event, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Total (N=30)
Hematologic					
Lymphopenia	0	0	7 (23.3)	19 (63.3)	26 (86.7)
Anemia	1 (3.3)	4 (13.3)	18 (60.0)	0	23 (76.7)
Thrombocytopenia	4 (13.3)	2 (6.7)	5 (16.7)	6 (20.0)	17 (56.7)
Neutropenia	0	0	6 (20.0)	10 (33.3)	16 (53.3)
Leukopenia	1 (3.3)	3 (10.0)	7 (23.3)	1 (3.3)	12 (40.0)
Non-hematologic					
CRS	16 (53.3)	6 (20.0)	0	0	22 (73.3)
Injection site reaction	14 (46.7)	2 (6.7)	0	0	16 (53.3)
Nausea	4 (13.3)	6 (20.0)	2 (6.7)	0	12 (40.0)
Increased AST	5 (16.7)	3 (10.0)	3 (10.0)	0	11 (36.7)
Increased ALT	5 (16.7)	2 (6.7)	3 (10.0)	0	10 (33.3)
Diarrhea	5 (16.7)	4 (13.3)	1 (3.3)	0	10 (33.3)

- No DLT was observed

Dholaria et al, IMWG 2021

Monotherapy (Part 1, N=30) – Cytokine Release Syndrome

- Patients did not receive premedication or priming/step-up dosing to mitigate CRS
  - Overall incidence of CRS was 73.3%
- CRS was limited to Grade 1 or 2, with no events >Grade 2
  - Median (range) time to onset was 1 (1–3) day
  - Median (range) duration was 3 (1–10) days
  - 9 (30%) patients received tocilizumab and 3 (10%) received steroid treatment for CRS
  - No permanent treatment discontinuations, dosing interruptions, or dose reductions occurred due to CRS

Patients with CRS, n (%)	80 µg/kg (n=6)	130 µg/kg (n=4)	215 µg/kg (n=4)	360 µg/kg (n=4)	600 µg/kg (n=6)	1000 µg/kg (n=6)	Total (N=30)
Overall	2 (33.3)	2 (50.0)	3 (75.0)	3 (75.0)	6 (100.0)	6 (100.0)	22 (73.3)
Grade 1	1 (16.7)	2 (50.0)	2 (50.0)	2 (50.0)	5 (83.3)	4 (66.7)	16 (53.3)
Grade 2	1 (16.7)	0	1 (25.0)	1 (25.0)	1 (16.7)	2 (33.3)	6 (20.0)

Dholaria et al, IMWG 2021

Monotherapy With Priming (Part 1.1, N=20) – Treatment-Emergent Adverse Events (All Causality) Occurring in >1/3 of Patients

- 20 patients received monotherapy with priming
  - 7 patients received elranatamab 1000 µg/kg weekly
  - 13 patients received elranatamab 1000 µg/kg every 2 weeks
- Patients did not receive premedication to mitigate CRS

Adverse event, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Total (N=20)
CRS	10 (50.0)	10 (50.0)	0	0	20 (100.0)
Neutropenia	0	2 (10.0)	7 (35.0)	7 (35.0)	16 (80.0)
Anemia	1 (5.0)	5 (25.0)	9 (45.0)	0	15 (75.0)
Thrombocytopenia	2 (10.0)	4 (20.0)	2 (10.0)	5 (25.0)	13 (65.0)
Injection site reaction	10 (50.0)	2 (10.0)	0	0	12 (60.0)
Fatigue	3 (15.0)	6 (30.0)	0	0	9 (45.0)
Hypomagnesemia	8 (40.0)	0	0	0	8 (40.0)
Hypophosphatemia	0	3 (15.0)	5 (25.0)	0	8 (40.0)
Decreased appetite	6 (30.0)	1 (5.0)	0	0	7 (35.0)
Diarrhea	5 (25.0)	2 (10.0)	0	0	7 (35.0)
Lymphopenia	0	0	0	7 (35.0)	7 (35.0)
Vomiting	5 (25.0)	2 (10.0)	0	0	7 (35.0)

- CRS was limited to Grade 1 or 2, with no events >Grade 2
- Median (range) duration of CRS was 3 (2–7) days

Data cutoff was June 7, 2021. Reporting of TEAEs based on CTCAE version 4.03, except for CRS (Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625).
CRS=cytokine release syndrome; CTCAE=Common Terminology Criteria for Adverse Events; TEAE=treatment-emergent adverse event

Dholaria et al, IMWG 2021

Combination Therapy With Lenalidomide (Part 1C, N=4)

- 4 patients received elranatamab + lenalidomide
- All 4 patients were triple-class refractory (PI, IMiD, and anti-CD38)
- All 4 patients had previously received both lenalidomide and pomalidomide

Treatment-emergent adverse events (all causality) occurring in >1/3 of patients

Adverse event, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Total (N=4)
Hematologic					
Lymphopenia	0	0	1 (25.0)	2 (50.0)	3 (75.0)
Neutropenia	0	0	1 (25.0)	2 (50.0)	3 (75.0)
Leukopenia	0	0	2 (50.0)	0	2 (50.0)
Non-hematologic					
Injection site reaction	4 (100.0)	0	0	0	4 (100.0)
Headache	3 (75.0)	0	0	0	3 (75.0)
CRS	0	2 (50.0)	0	0	2 (50.0)
Decreased appetite	2 (50.0)	0	0	0	2 (50.0)
Hypokalemia	0	1 (25.0)	1 (25.0)	0	2 (50.0)
Hypophosphatemia	0	0	2 (50.0)	0	2 (50.0)
Nausea	2 (50.0)	0	0	0	2 (50.0)
Pneumonia	0	0	2 (50.0)	0	2 (50.0)

Efficacy

IMWG response, n (%)	Total (N=4)
Stringent complete response	1 (25.0)
Complete response	1 (25.0)
Very good partial response	1 (25.0)
Partial response	0
Minimal response	0
Stable disease	1 (25.0)
Progressive disease	0
Objective response rate	**3 (75.0)**

- No drug–drug interaction was observed between elranatamab and lenalidomide
- Treatment-emergent peripheral neuropathy was not observed

Data cutoff was June 7, 2021. Reporting of TEAEs based on CTCAE version 4.03, except for CRS (Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625).
PI=proteasome inhibitor; IMiD=immunomodulatory drug; CRS=cytokine release syndrome; IMWG=International Myeloma Working Group; CTCAE=Common Terminology Criteria for Adverse Events; TEAE=treatment-emergent adverse event

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Conclusions

- Elranatamab given either weekly or every 2 weeks had a manageable safety profile for patients with RRMM
- Safety, PK, pharmacodynamics, and efficacy support the RP2D
- At doses ≥215 µg/kg, elranatamab demonstrated ORR of 70.0% and sCR/CR rate of 30.0%
  - 3 of 4 patients with prior BCMA-directed therapy achieved response (1 sCR and 2 VGPR)
  - All 4 patients assessed with CR or sCR achieved MRD negativity by IMWG criteria (1×10^{-5})
- At RP2D of 1000 µg/kg, ORR was 83.3%
- For patients with triple-class refractory MM who received elranatamab + lenalidomide, ORR was 75.0%
- These results support further development of elranatamab both as monotherapy and in combination with other agents

Data cutoff was June 7, 2021.
BCMA=B-cell maturation antigen; CR=complete response; ORR=objective response rate; PK=pharmacokinetics; RP2D=recommended phase 2 dose; RRMM=relapsed/refractory multiple myeloma; sCR=stringent complete response; VGPR=very good partial response

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Discussion Topics

- How will the numerous BCMA bsAbs agents and CAR-T in development be differentiated from one another?
- Patient (disease status),considerations for using T-cell engager vs. CAR-T (*assuming both options are commercially available*)
- How do frailty and comorbidities influence the choice of CAR-T vs. bispecific antibodies vs. ADC?
- Will community hematologists/oncologists prefer bsAbs or ADCs over CAR-T?
- How do non-BCMA targeted bsAbs potentially factor into sequencing approaches with BCMA-targeted CAR-Ts or bsAbs?