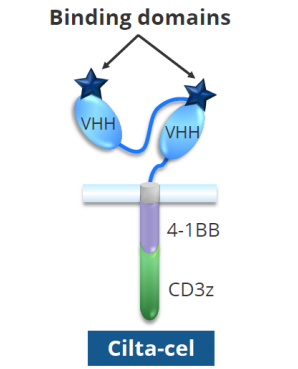
CART - cells

CARTITUDE 1



2 BCMA-targeting single-domain antibodies designed to confer avidity

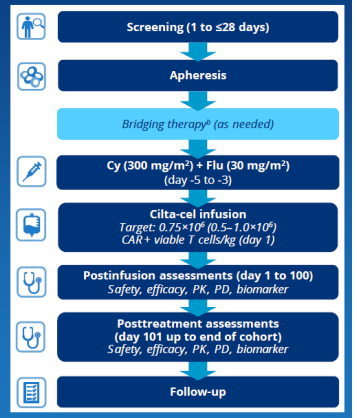
Primary objectives

- Phase 1b: Characterize the safety of cilta-cel and confirm the recommended phase 2 dose
- Phase 2: Evaluate the efficacy of cilta-cel

Key eligibility criteria

- Progressive MM per IMWG criteria
- ECOG PS ≤1
- Measurable disease
- ≥3 prior therapies or double refractory
- Prior PI, IMiD, anti-CD38 antibody exposure

Median administered dose:
0.71x10^6 (range 0.51–0.95x10^6) CAR+ viable T cells/kg



[a]NCT03548207; [b]Treatment with previously used agent resulting in at least stable disease.
CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; Cy, cyclophosphamide; ECOG PS, Eastern Cooperative Oncology Group performance status; Flu, fludarabine; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MM, multiple myeloma; PD, pharmacodynamics; PI, proteasome inhibitor; PK, pharmacokinetics

Patient characteristics

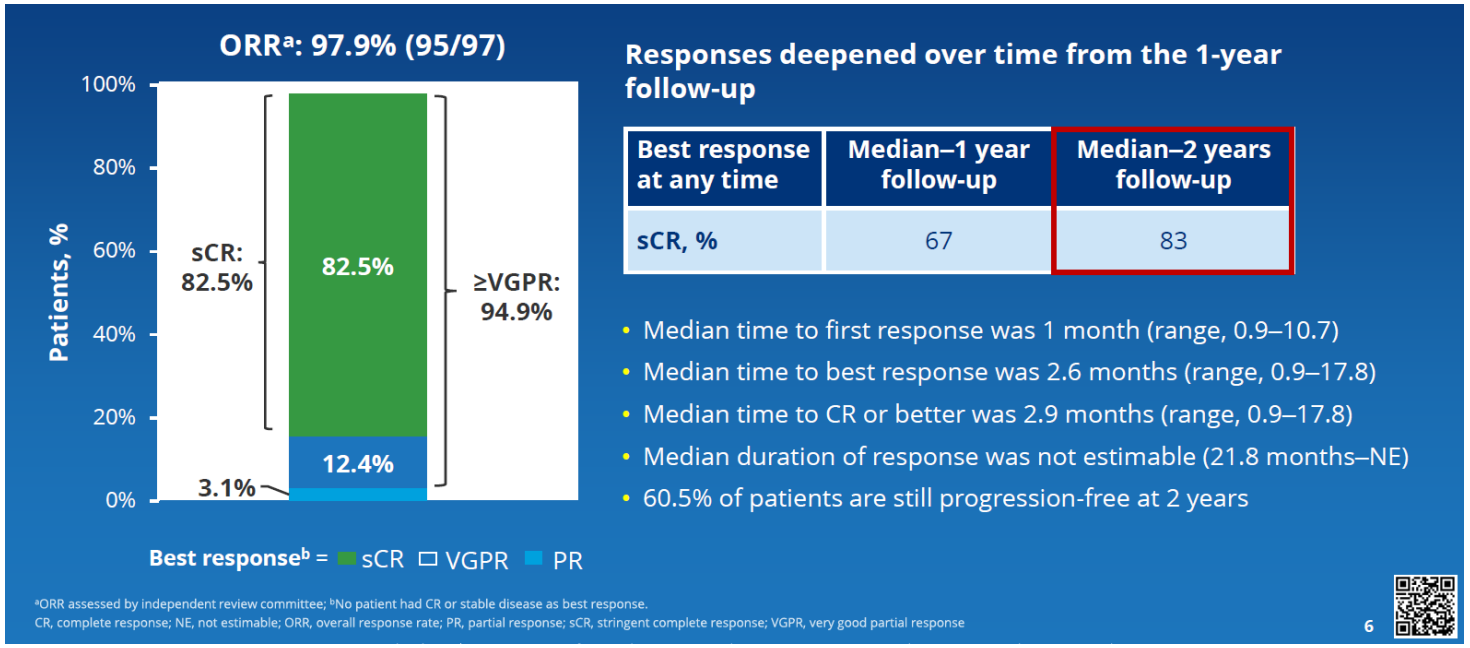
Characteristics	N=97
Age, median (range) years	61.0 (43–78)
Male, n (%)	57 (58.8)
Black/African American, n (%)	17 (17.5)
All plasmacytomas,[a] n (%)	19 (19.6)
Extramedullary plasmacytomas, n (%)	13 (13.4)
Bone-based plasmacytomas, n (%)	6 (6.2)
Bone marrow plasma cells ≥60%, n (%)	21 (21.9)
High-risk 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)[a]

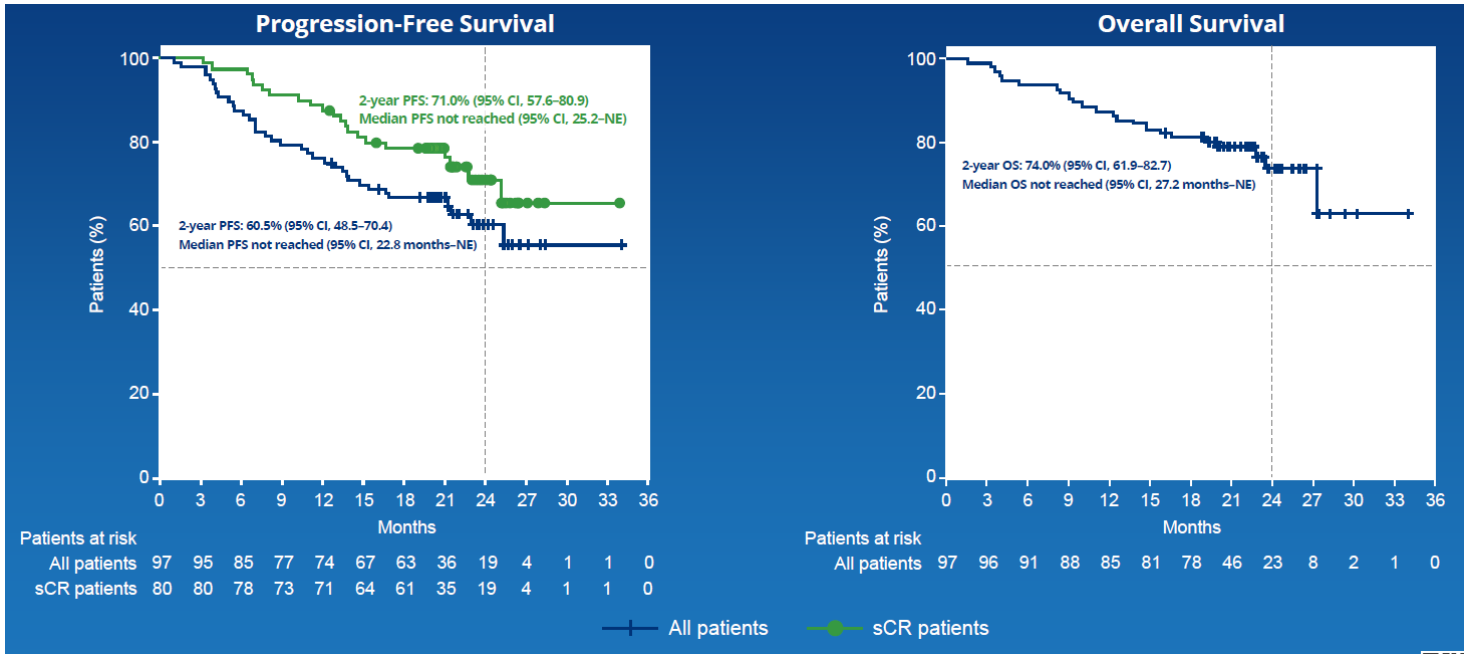
Characteristics	N=97
Prior lines of therapy, median (range)	6.0 (3–18)
Prior lines of therapy, n (%)	
3	17 (17.5)
4	16 (16.5)
≥5	64 (66.0)
Previous stem cell transplantation, n (%)	
Autologous	87 (89.7)
Allogeneic	8 (8.2)
Triple-class exposed,[b] n (%)	97 (100)
Penta-drug exposed,[c] n (%)	81 (83.5)
Triple-class refractory[b]	85 (87.6)
Penta-drug refractory[c]	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)
Years since diagnosis, median (range)	5.9 (1.6–18.2)

[a]The number of evaluable samples was 62; BCMA expression detected in all evaluable samples; [b]≥1 PI, ≥1 IMiD, and 1 anti-CD38 antibody; [c]≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 antibody.
BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; PI, proteasome inhibitor

Martin T et al. ASH 2021 #549

CARTITUDE 1 – EFFICACY, PFS AND OS





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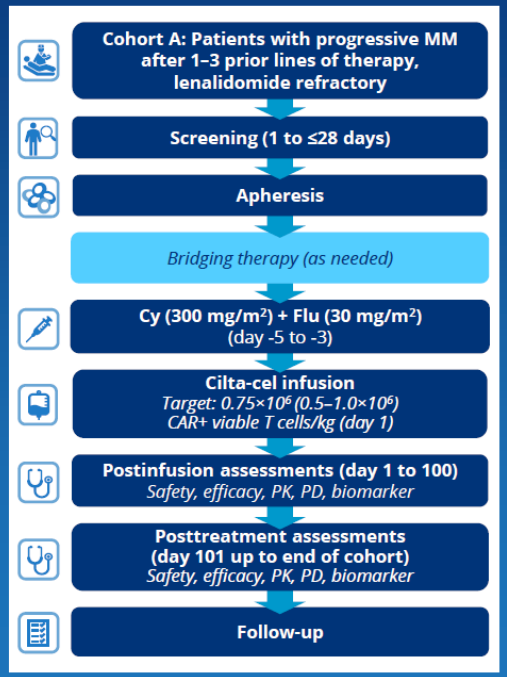
CARTITUDE-2

Primary endpoint:

- Minimal residual disease (MRD) 10^{-5} negativity
  - Assessed by next-generation sequencing

Secondary endpoints:

- ORR, per IMWG response criteria
- Duration of response
- Time and duration of MRD negativity
- Incidence and severity of AEs
  - Assessed per Common Terminology criteria for AEs version 5.0
  - Cytokine release syndrome and immune effector cell-associated neurotoxicity graded per American Society for Transplantation and Cellular Therapy criteria



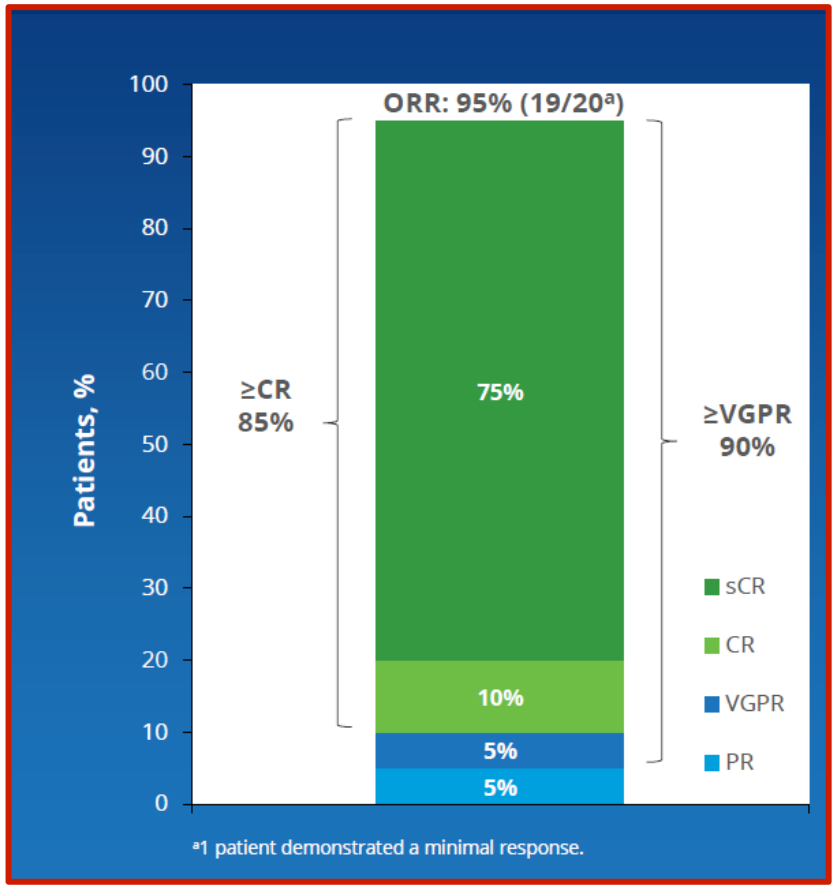
AE, adverse event; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; Cy, cyclophosphamide; Flu, fludarabine; IMWG, International Myeloma Working Group; MM, multiple myeloma; ORR, overall response rate; PD, pharmacodynamics; PK, pharmacokinetics

Characteristic	N=20
Age, years, median (range)	60 (38–75)
Male, n (%)	13 (65.0)
Extramedullary plasmacytomas ≥1, n (%)	3 (15)
Bone marrow plasma cells[a] ≥60%, n (%)	3 (15)
High-risk cytogenetic profile, n (%)	7 (35)[b]
del17p	3 (15)
t(14;16)	5 (25)
t(4;14)	0
Prior lines of therapy, median (range)	2 (1–3)
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 (%)	
Lenalidomide	20 (100)
Bortezomib	8 (40)
Carfilzomib	2 (10)
Pomalidomide	7 (35)
Daratumumab	12 (60)
Refractory to last line of therapy, n (%)	19 (95)
Years since diagnosis, median (range)	3.5 (0.7–8.0)

[a]Maximum value from bone marrow biopsy and bone marrow aspirate is selected if both results are available; [b]One patient had both del17p and t(14;16); [c]≥1 PI, ≥1 IMiD, and 1 anti-CD38 antibody; [d]≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 antibody.

Cohen Y et al. ASH 2021 #3866

CARTITUDE-2 EFFICACY AND SAFETY

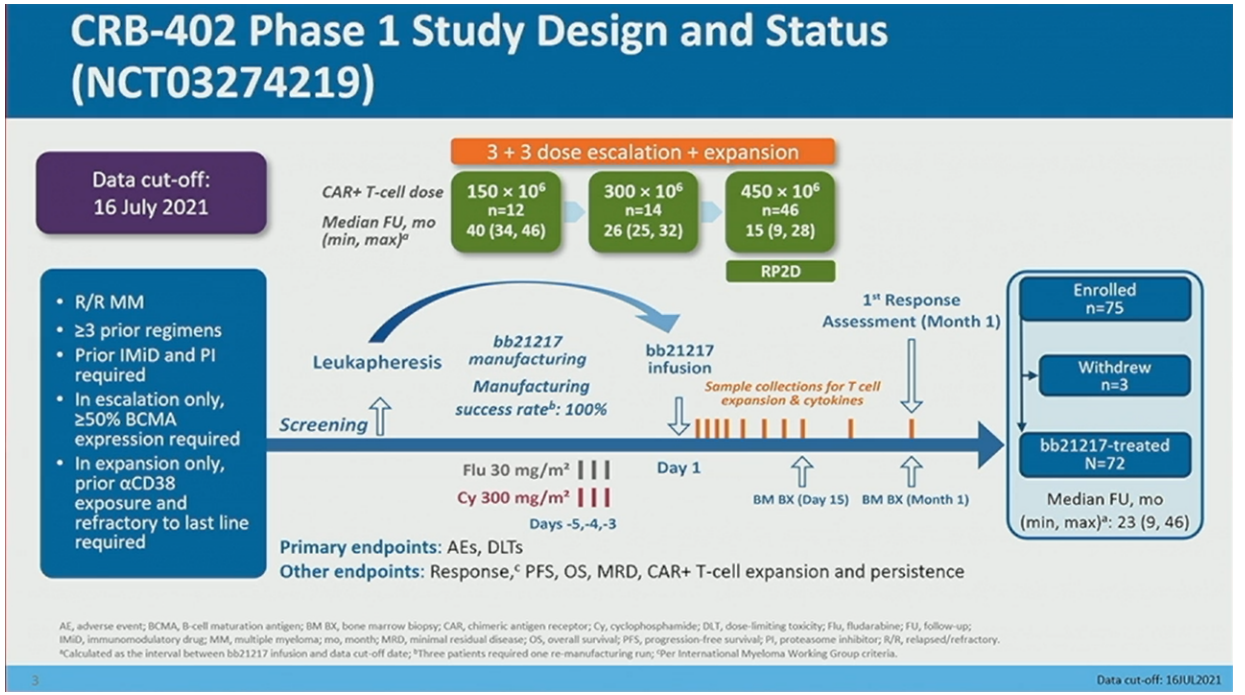


AEs ≥20%, n (%)	N=20	
	Any Grade	Grade 3/4
Hematologic		
Neutropenia	19 (95)	19 (95)
Thrombocytopenia	16 (80)	7 (35)
Anemia	15 (75)	9 (45)
Lymphopenia	13 (65)	13 (65)
Leukopenia	11 (55)	11 (55)
CAR-T–related AEs		
CRS	19 (95)	2 (10)
Neurotoxicity	4 (20)	0 (0)

Cohen Y et al. ASH 2021 #3866

BB21217

- anti-BCMA CAR T cell therapy that uses the same CAR molecule as idecabtagene vicleucel (bb2121)
- adds the PI3K inhibitor bb007 during ex vivo culture to enrich the drug product (DP) for memory-like T cells
- T cells displaying a memory like phenotype are enriched
- may result in higher persistence an longer function



Baseline Patient Characteristics and Treatment History

Baseline Characteristics	bb21217-Treated (N=72)
Age, y, median (min, max)	62 (33, 76)
Male, n (%)	44 (61)
Years since initial diagnosis, median (min, max)	6 (1, 19)
ECOG PS, n (%)	
0	26 (36)
1	41 (57)
2	5 (7)
R-ISS stage at baseline, n (%)	
I	11 (15)
II	46 (64)
III	13 (18)
Unavailable/missing	2 (3)
High-risk cytogenetics, n (%)	
del(17p), t(4;14), or t(14;16)	28 (39)
Unknown	2 (3)
Extramedullary disease, n (%)	16 (22)

Treatment History	bb21217-Treated (N=72)
No. of prior regimens, median (min, max)	6 (3, 17)
Prior autologous SCT, n (%)	61 (85)
0	11 (15)
1	46 (64)
>1	15 (21)
Prior therapy, n (%)	
Lenalidomide	71 (99)
Pomalidomide	68 (94)
Bortezomib	67 (93)
Carfilzomib	58 (81)
CD38 antibody	70 (97)
Refractory status, n (%)	
IMiD	63 (88)
Proteasome inhibitor	63 (88)
αCD38 antibodies	58 (81)
Double refractory (PI/IMiD)	59 (82)
Triple refractory (PI/IMiD/αCD38)	50 (69)

ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; R-ISS, Revised International Staging System; MM, multiple myeloma; PI, proteasome inhibitor; SCT, stem cell transplantation; y, years.

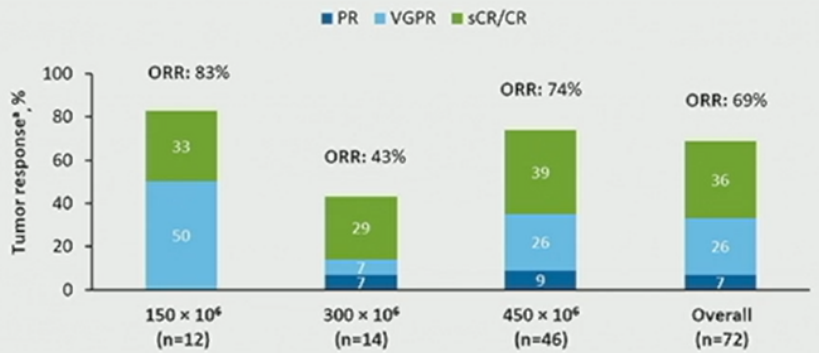
4

Data cut-off: 16JUL2021

Raje N et al. ASH 2021 #548

BB21217

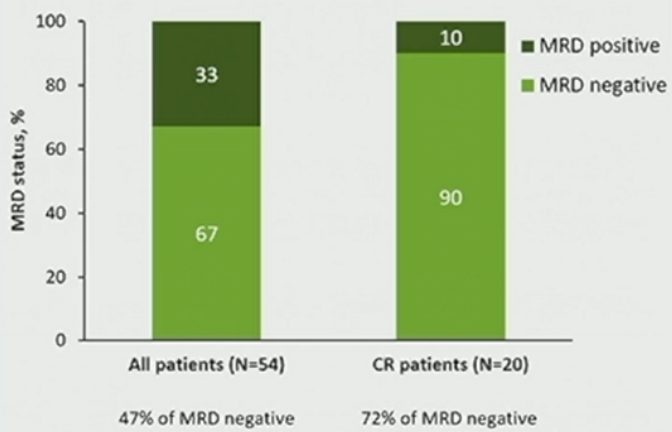
Tumor Response and MRD Status



	150 × 10⁶ (n=12)	300 × 10⁶ (n=14)	450 × 10⁶ (n=46)	Overall (n=72)
Median follow-up (min, max), mo	24.6 (4, 41)	11.9 (3, 30)	10.9 (<1, 28)	12.1 (<1, 41)
Median time to first response (min, max), mo				
≥PR	1.0 (1, 2)	1.0 (1, 1)	1.0 (1, 2)	1.0 (1, 2)
≥CR	4.4 (1, 10)	13.0 (3, 28)	3.1 (1, 15)	3.6 (1, 28)

Patients in the 450 group treated with bb21217 produced using an updated manufacturing process (n=32) had similar ORR (**81%**) and CR (**41%**) to that of the 450 group as a whole.

MRD status at 10^{-5} sensitivity[b]



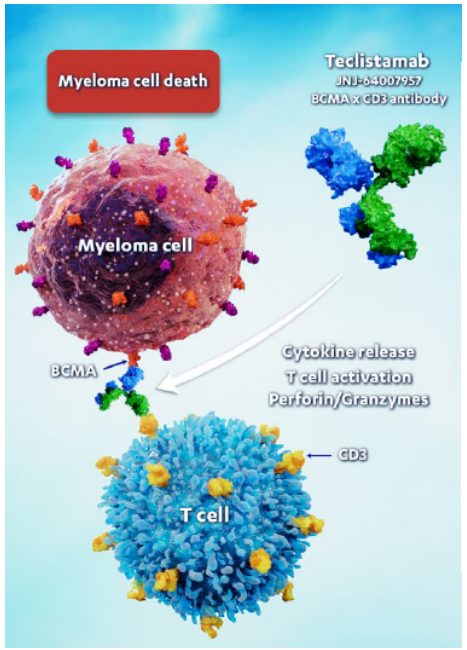
47% of MRD negative patients sustained MRD negativity at mo 9

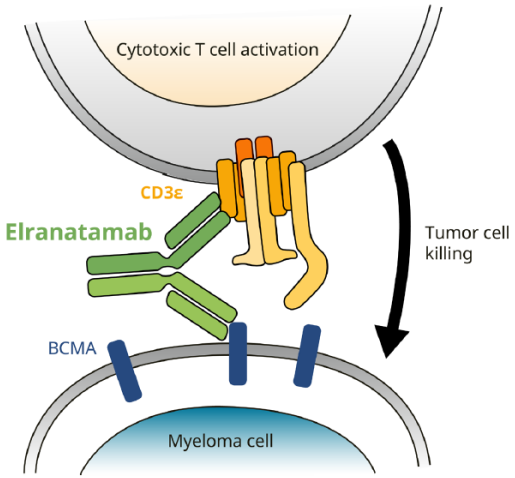
72% of MRD negative patients with CR sustained MRD negativity at mo 9

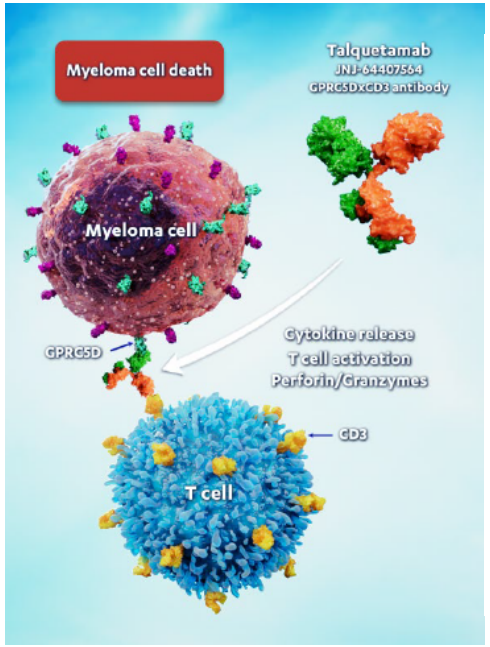
CAR, chimeric antigen receptor; CR, complete response; mo, month; MRD, minimal residual disease; ORR, objective response rate; PD, progressive disease; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
[a]Response confirmed by a consecutive response of the same category or better. Includes subjects whose response is recorded as "inevaluable" or "not done"; [b]Among evaluable patients. MRD assessment by Adaptive next-generation sequencing;

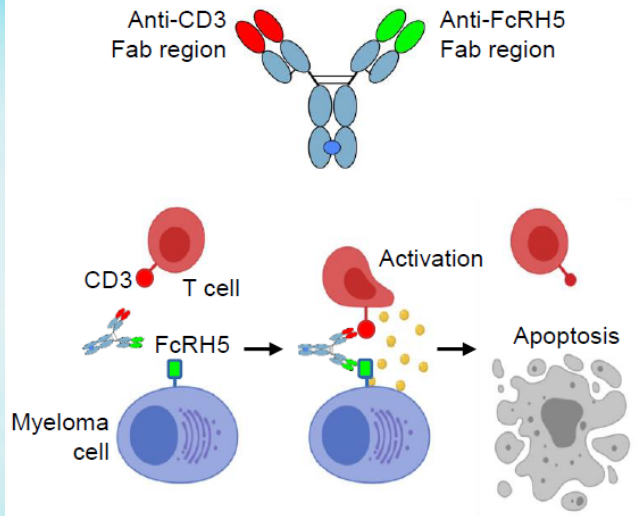
Data cut-off: 16JUL2021

Raje N et al. ASH 2021 #548









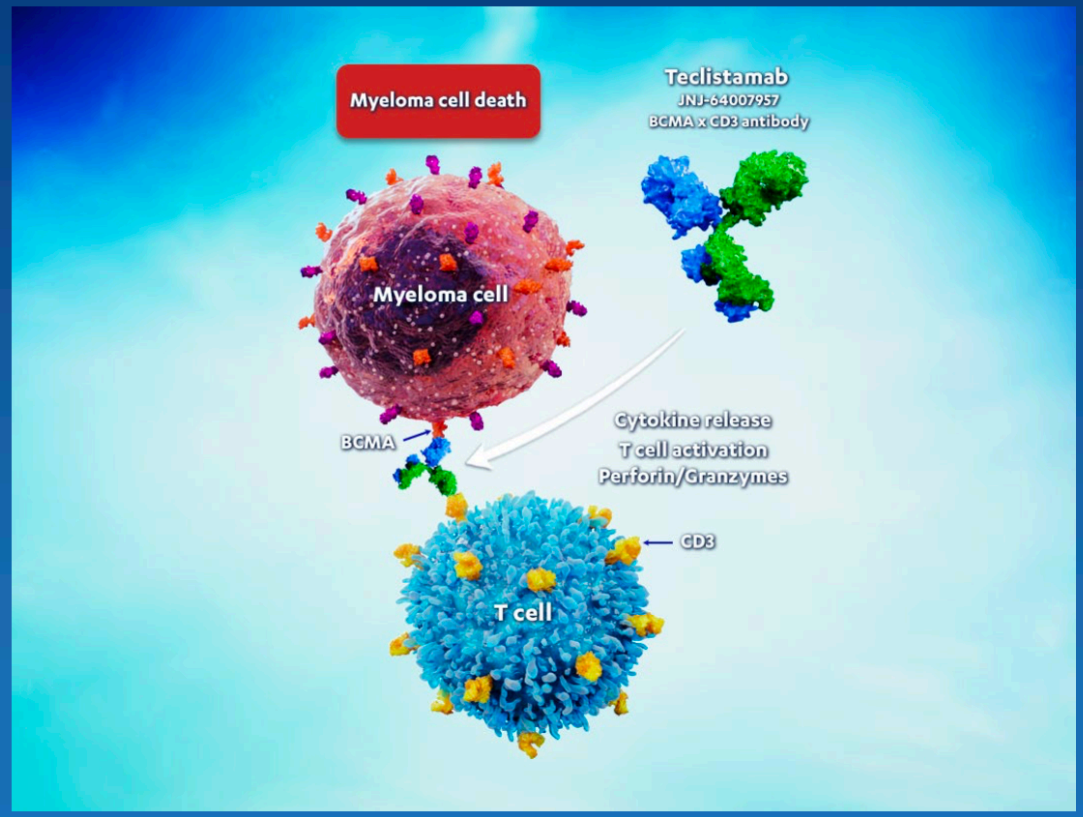
BISPEZIFISCHE ANTIKÖRPER

- Teclistamab[1] (BCMA/CD3)
- Elranatamab[2] (BCMA/CD3)
- Talquetamab[3] (GPRC5D/CD3)
- Cevostamab[4] (FcRH5/CD3)

1 Moreau P et al. ASH 2021 #896; 2 Sebag et al. ASH 2021 #895, 3 Krishnan A et al. ASH 2021 #158, 4 Trudel S et al ASH 2021 #157

Teclistamab:
A Novel BCMA × CD3 T-Cell Redirecting Bispecific Antibody

- Despite newly approved therapies for triple-class exposed patients with RRMM, unmet medical need remains high[1-2]
- Teclistamab (JNJ-64007957) is an off-the-shelf, T-cell redirecting, bispecific antibody that binds to CD3 on T cells and BCMA on plasma cells to mediate T-cell activation and subsequent lysis of BCMA-expressing MM cells
- The phase 1 portion of the MajesTEC-1 study identified the RP2D for teclistamab monotherapy: 1.5 mg/kg subcutaneous (SC) QW with step-up doses of 0.06 and 0.3 mg/kg[3]
- Here we present pivotal phase 1/2 data from the 1.5 mg/kg dose of MajesTEC-1 (NCT03145181; NCT04557098)

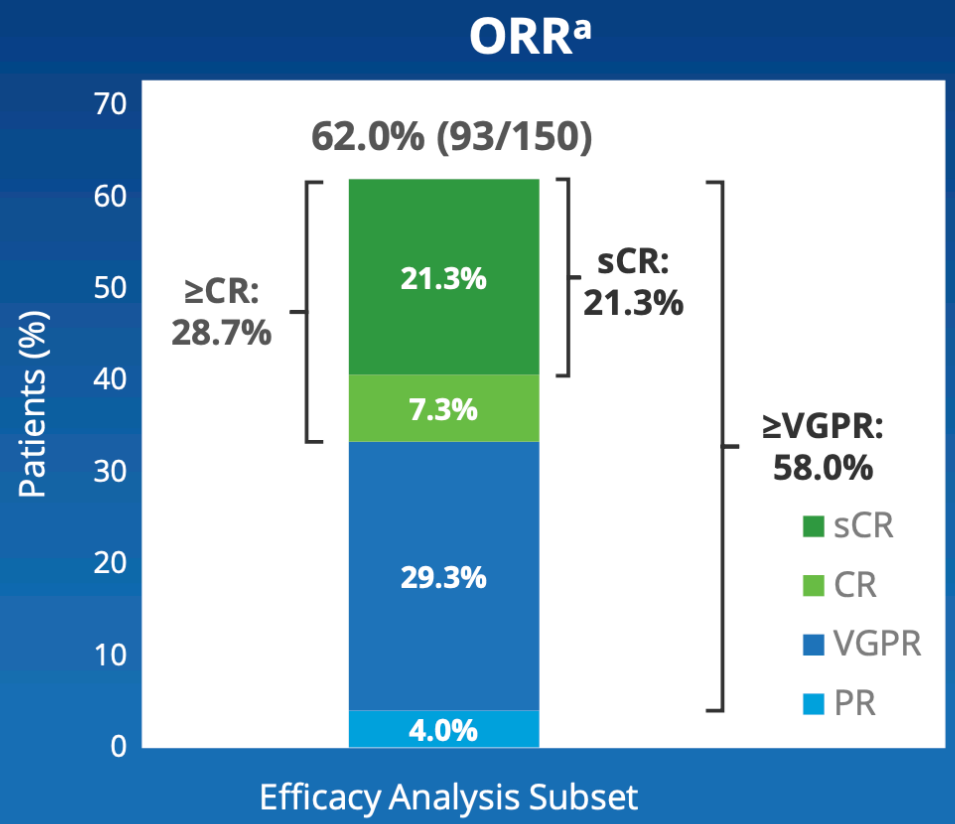


BCMA, B-cell maturation antigen; IFN, interferon; IL, interleukin; MM, multiple myeloma; QW, once weekly; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory multiple myeloma; TNF, tumor necrosis factor

1. Mateos MV, et al. *J Clin Oncol* 2021; 39 (suppl): 8041. 2. Costa L et al. *J Clin Oncol* 2021; 39 (suppl): 8030. 3. Usmani SZ, et al. *Lancet* 2021; 398(10301): 665-74.

Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual.

MajesTEC-1: Overall Response Rate for Teclistamab Monotherapy



- At a median follow-up of 7.8 months (range: 0.5+–18):
  - ORR of 62.0% (95% CI: 53.7–69.8) represents a substantial benefit for patients with triple-class exposed disease
- Median time to first response: 1.2 months (range: 0.2–5.5)
- MRD negativity rate[b]
  - 24.7% (37/150; 95% CI: 18.0–32.4) at a threshold of 10^{-5}
  - 16.7% (25/150; 95% CI: 11.1–23.6) at a threshold of 10^{-6},[c]
- In patients who achieved ≥CR, the MRD-negativity rate was 41.9%

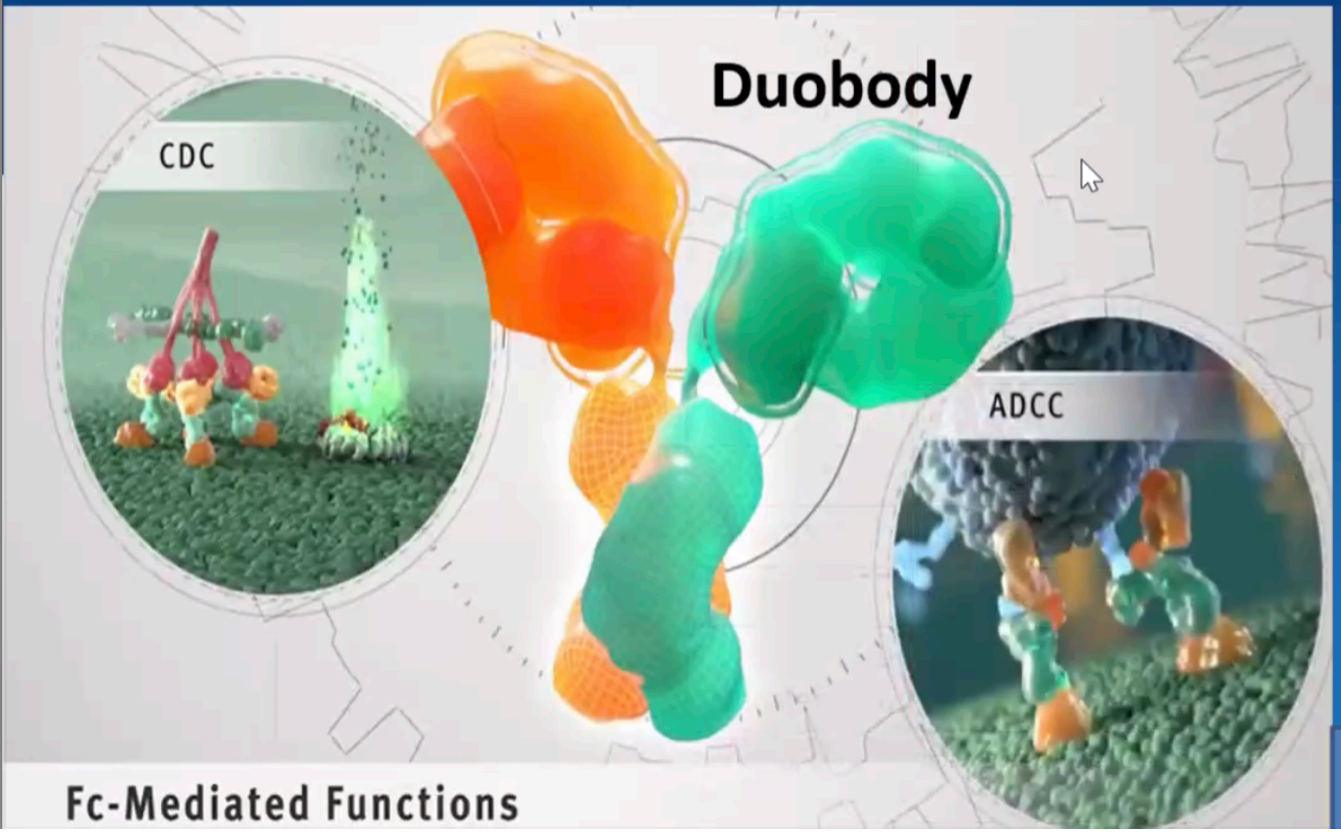
[a]PR or better, IRC assessed; ORR was assessed in efficacy analysis population, which includes all patients who received their first dose on or before March 18, 2021 (n=150); [b] Baseline clones were obtained for all patients All MRD assessments were done by next-generation sequencing; [c]Patients who were not negative at the 10^{-6} threshold were indeterminate.

CR, complete response; IRC, independent review committee; MRD, minimal residual disease; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual.

Updated Phase 1 Results From MonumenTAL-1: First-in-Human Study of Talquetamab, a G Protein-Coupled Receptor Family C Group 5 Member D x CD3 Bispecific Antibody, in Patients With RRMM

Primary goal: establish Recommended phase 2 dose



405 µg/kg SCQW dosing schedule (21-day cycle)

Step-up dosing[b]	405 µg/kg SC QW (cycle 1 and beyond)		
	Week 1	Week 1	Week 1
	⬆ Tal	⬆ Tal	⬆ Tal

800 µg/kg SCQ2W dosing schedule (28-day cycle)

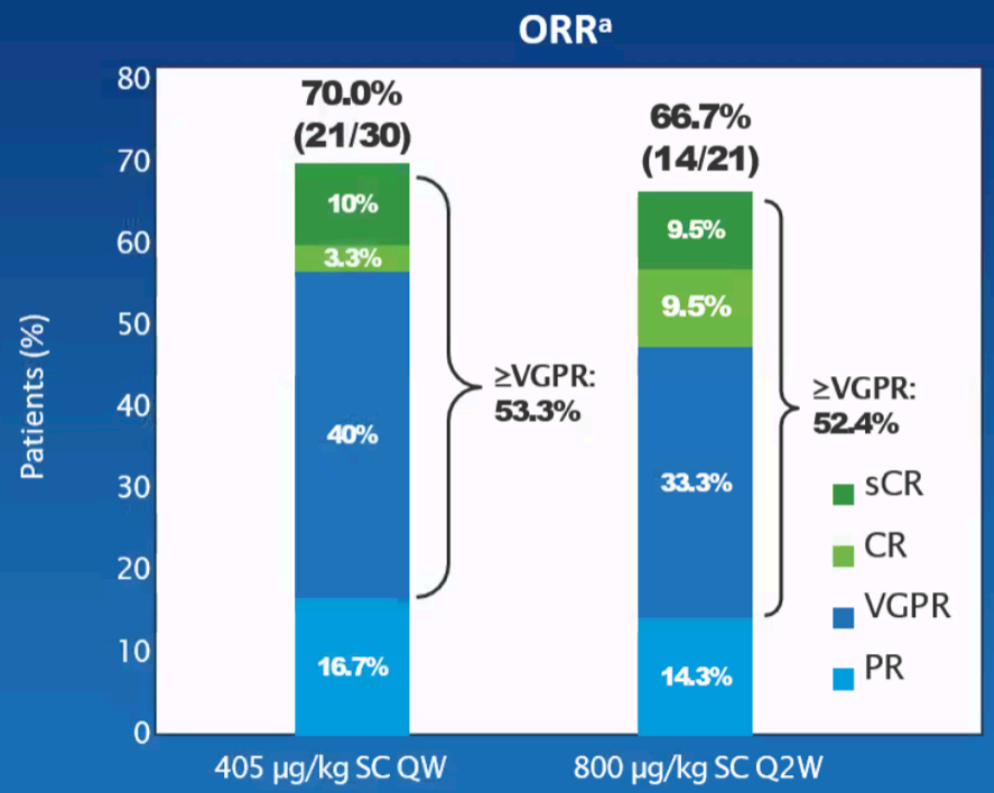
Step-up dosing[b]	800 µg/kg SC Q2W (cycle 1 and beyond)			
	Week 1	Week 2	Week 3	Week 4
	⬆ Tal		⬆ Tal	

Premedications[c] were limited to step-up doses and first full dose

No steroid requirement after the first full dose

Krishnan A et al., ASH 2021

MonumenTAL-1: Overall Response Rate



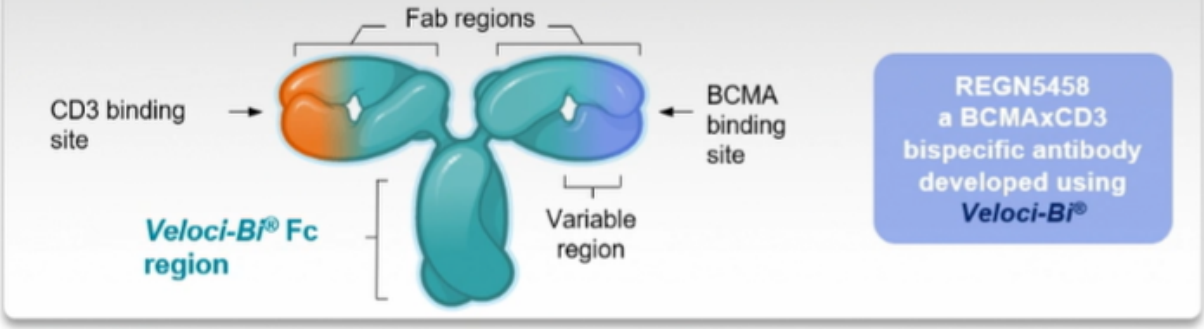
Response	405 µg/kg SC QW[b] n=30	800 µg/kg SC Q2W[b] n=25
Median follow-up (months), median (range)	9.0 (0.9–17.1)	4.8 (0.4–11.1)
Response-evaluable patients,[c] n	30	21
ORR, n (%)	21 (70.0)	14 (66.7)
ORR in triple-class–refractory patients, n/N (%)	15/23 (65.2)	12/18 (66.7)
ORR in penta-drug–refractory patients, n/N (%)	5/6 (83.3)	5/6 (83.3)
Median time to first confirmed response (months), median (range)	0.9 (0.2–3.8)	1.2 (0.2–6.8)

- ORR appears to be comparable across both RP2Ds

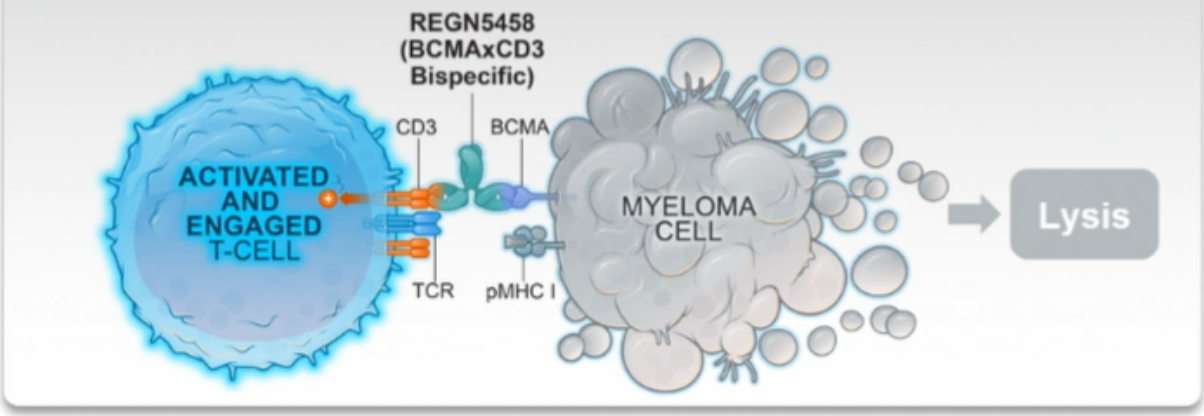
Krishnan A et al., ASH 2021

REGN5458: BCMAxCD3 Veloci-Bi® antibody

REGN5458 molecular structure



REGN5458 mechanism of action

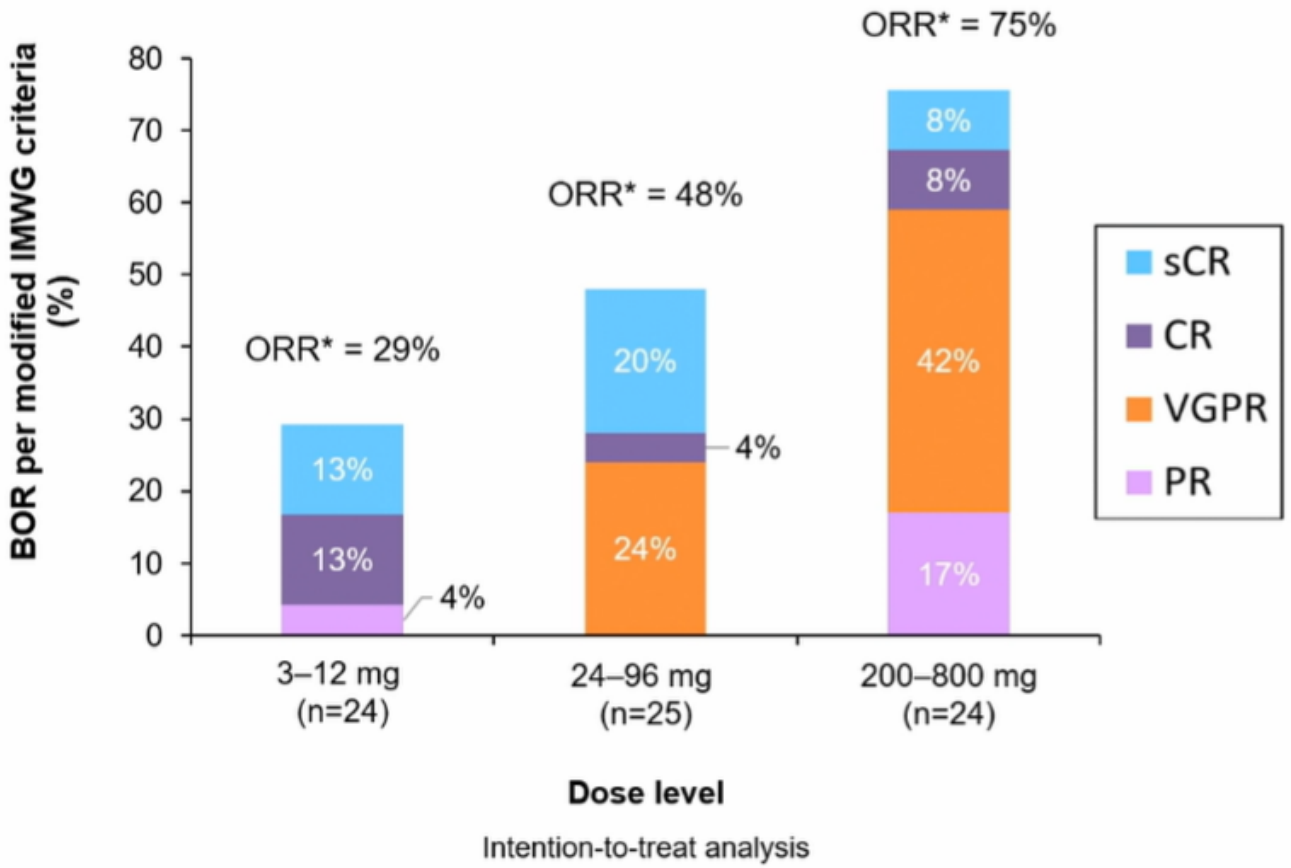


- REGN5458 is a BCMAxCD3 bispecific antibody that targets T-cell effector function to induce cytotoxicity of BCMA-expressing MM cells
- Poor outcomes are observed in patients with MM who are refractory to multiple classes of therapies, with a median PFS of ~3–5 months and OS of 6–15 months[1,2]
- Here, we report updated results from an ongoing phase 1 study of REGN5458 IV in patients with relapsed/refractory MM

The *Veloci-Bi*® platform allows for creation of bispecific antibodies that closely resemble natural human antibodies.
BCMA, B-cell maturation antigen; CD, cluster of differentiation; Fab, fragment antigen-binding; Fc, fragment crystallizable region; MM, multiple myeloma; OS, overall survival; PFS, progression-free survival; pMHC, peptide-loaded major histocompatibility complex; TCR, T-cell receptor.

1. Gandhi U, et al. *Leukemia*. 2019;33:2266–75. 2. Kumar SK, et al. *Leukemia*. 2017;31:2443–48.

Phase 1 efficacy



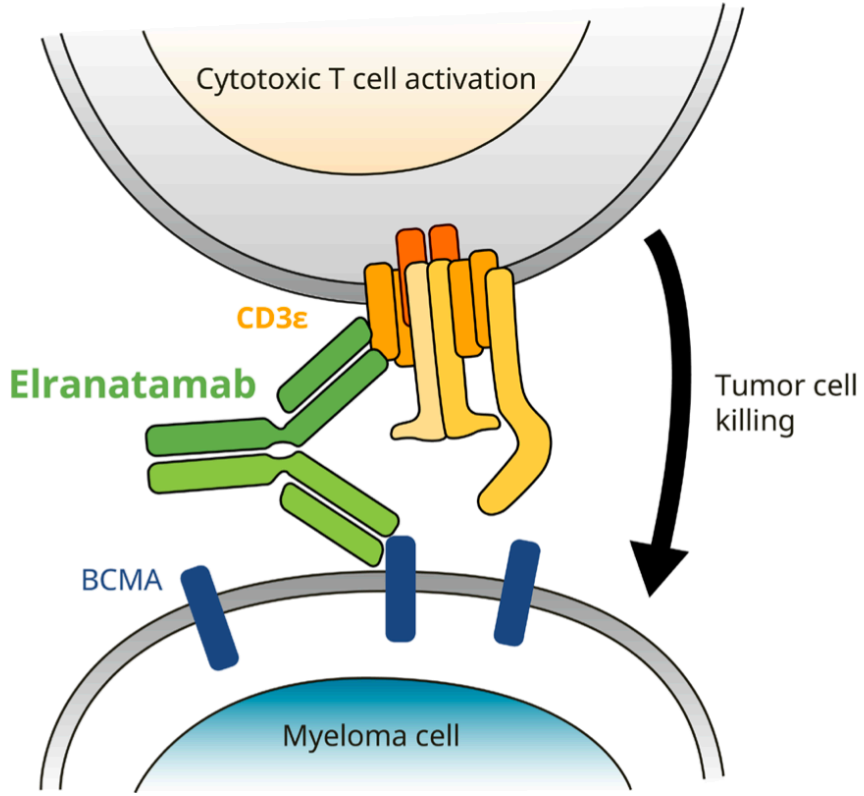
- Responses have been observed across all dose levels, with a trend for higher response rates at higher doses
  - 51% ORR among all enrolled patients*
- 75% ORR and 58% ≥VGPR with REGN5458 200–800 mg
- Among all responders, 86% achieved ≥VGPR, 43% ≥CR
- Among CR/sCR with available MRD data:
  - 4/10 MRD negative at 10^{-5}

Data cut-off: 30 September 2021. *Full analysis set - includes all patients who had opportunity for response assessment at 4 weeks.
BOR, best overall response; CR, complete response; IMWG, International Myeloma Working Group; MRD, minimal residual disease; ORR, objective response rate; PR, partial response; sCR, stringent CR; VGPR, very good partial response.

Observed median duration of follow-up (range): 3 months (0.7–22.1)

Introduction

- BCMA is a member of the TNF receptor superfamily universally expressed in MM.[1]
- Elranatamab (PF-06863135) is a humanized heterodimeric bispecific molecule that targets BCMA on MM cells and CD3 on T cells.[2]
- MagnetisMM-1 (NCT03269136), the initial study for the MagnetisMM program, is a multipart phase 1 trial designed to evaluate the safety, pharmacokinetics, pharmacodynamics, and efficacy of elranatamab for patients with RRMM.
- Here, we report results for elranatamab as a single agent from SC dose escalation (Part 1), priming cohorts (Part 1.1), and expansion (Part 2A).



1. Shah N, et al. *Leukemia* 2020;34:985. **2.** Panowski SH, et al. *Blood* 2016;128:383.
BCMA=B-cell maturation antigen ; TNF=tumor necrosis factor; MM=multiple myeloma; CD3=cluster of differentiation 3; RRMM=relapsed/refractory multiple myeloma; SC=subcutaneous.

Modakafusp alfa is a novel, first-in-class immunocytokine designed to deliver IFNα2b to CD38+ cells

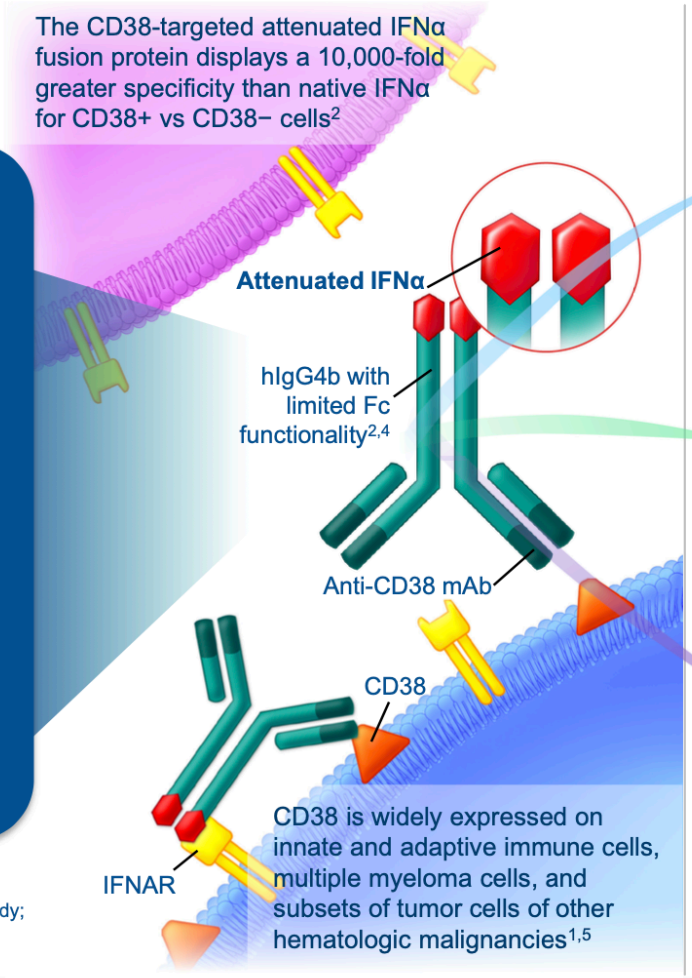
Modakafusp alfa

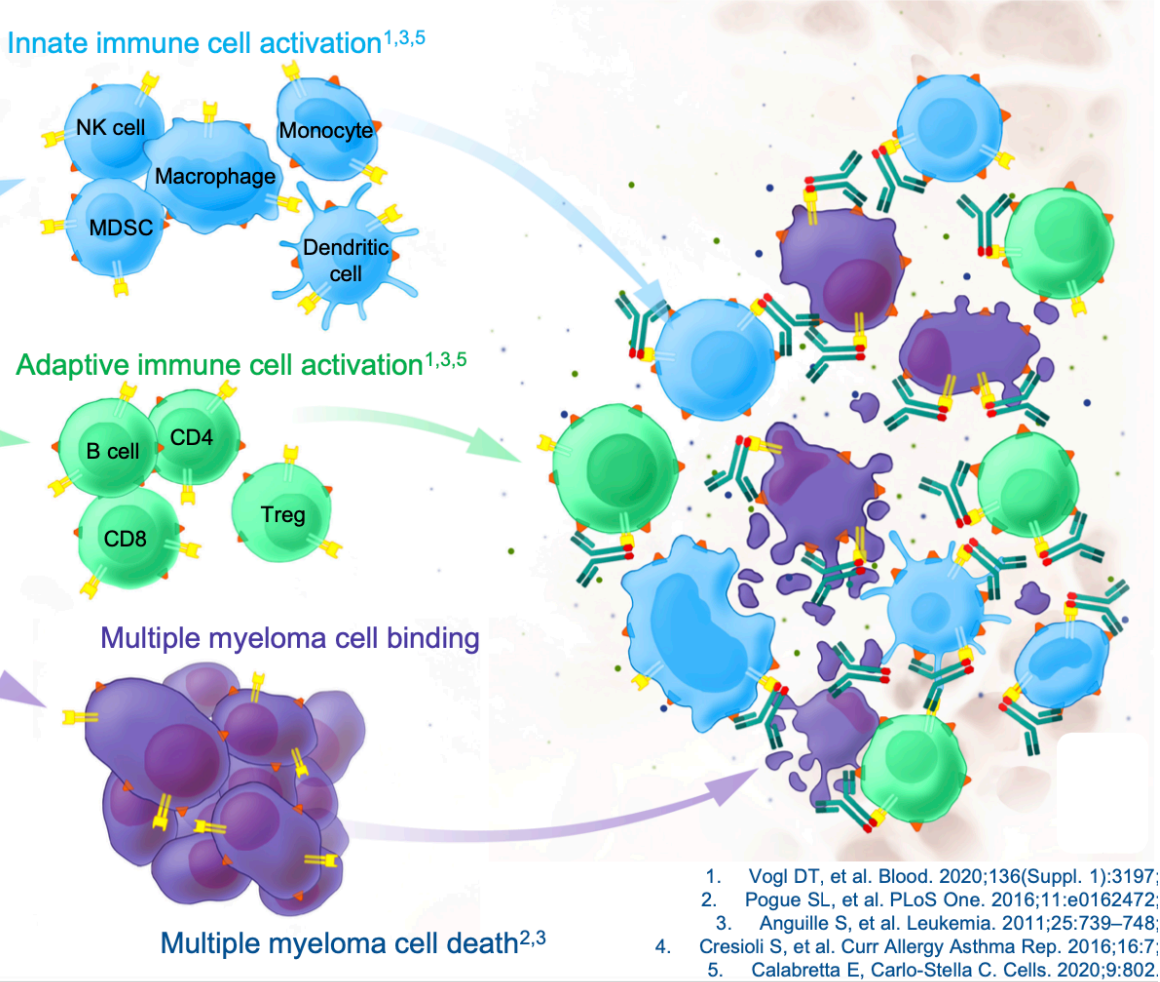
Binds with high affinity to unique epitope of CD38[1,2]

Signals through IFNAR[2] to:

- activate innate and adaptive immune cells[1]
- direct anti-proliferative/ apoptotic signals to tumor cells[2,3]

Fc, fragment crystallizable; hIgG4b, human immunoglobulin 4b; IFN, interferon; IFNAR, interferon α receptor; mAb, monoclonal antibody; MDSC, myeloid-derived suppressor cell; NK, natural killer; Treg, regulatory T cell





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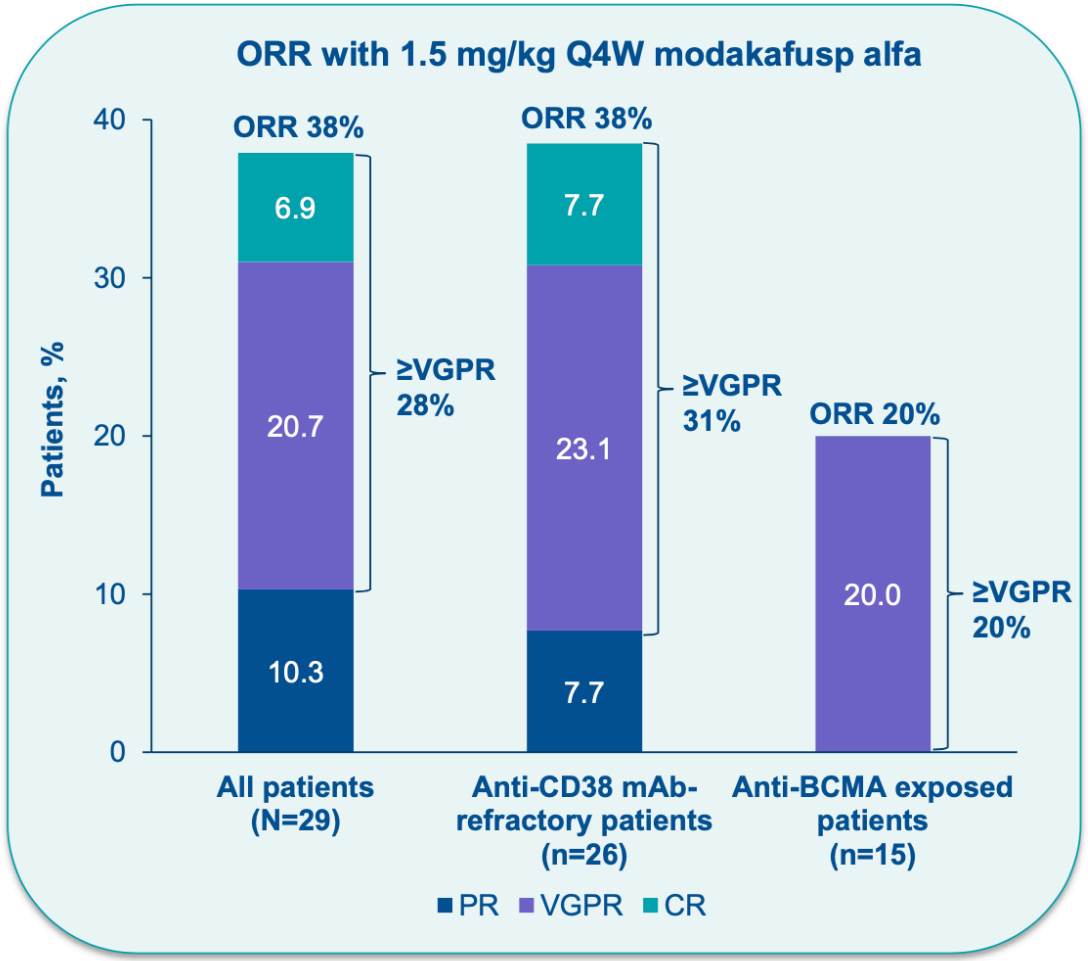
Overall response rate

- **Among 29 patients who received modakafusp alfa 1.5 mg/kg Q4W (5 in dose escalation and 24 in ongoing dose expansion):**
  - 11 patients had ≥PR (ORR 38%), including 6 with VGPR and 2 with CR (28% ≥VGPR)
- **Among 26 anti-CD38 mAb-refractory patients, ORR was also 38% (31% ≥VGPR):**
  - Among the 4 patients who received an anti-CD38 mAb in their most recent line of therapy, 1 achieved a CR, and 2 achieved a VGPR (ORR 75%)
- **Of the 15 patients with prior anti-BCMA therapy, 3 (20%) had a VGPR**



CR, complete response; PR, partial response; VGPR, very good partial response

Vogl DT, et al. Blood 2021;138(Suppl.1):898

Vielen Dank für Ihre Aufmerksamkeit!