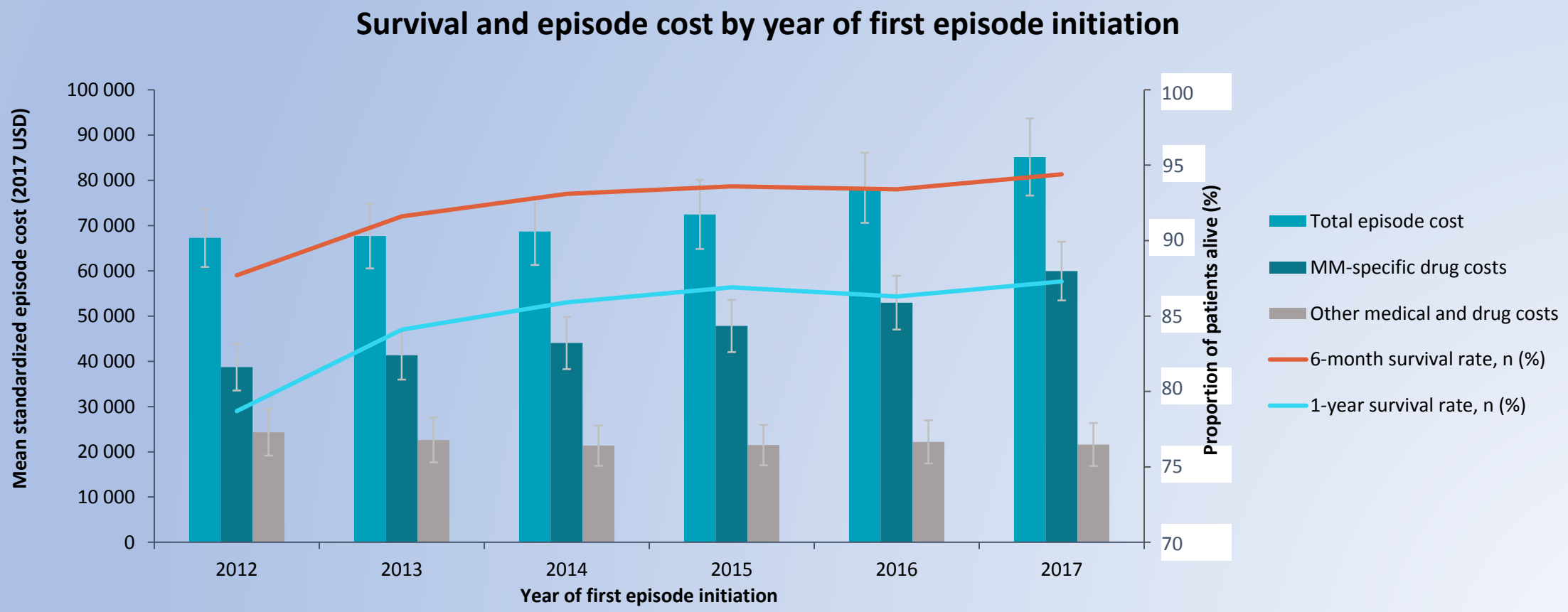
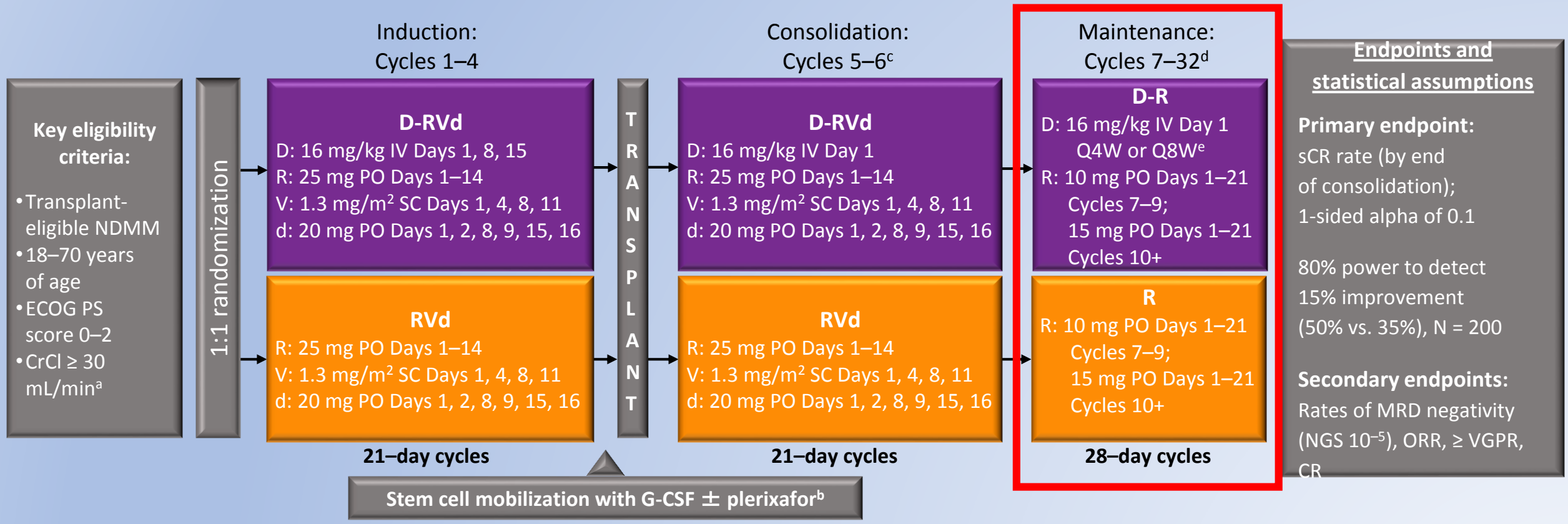
Episode costs and survival increased over time

- From 2012 to 2017, average total episode costs, MM-specific drug costs, and survival all increased
- Cost increases were primarily driven by MM-specific drug costs as new treatments became available



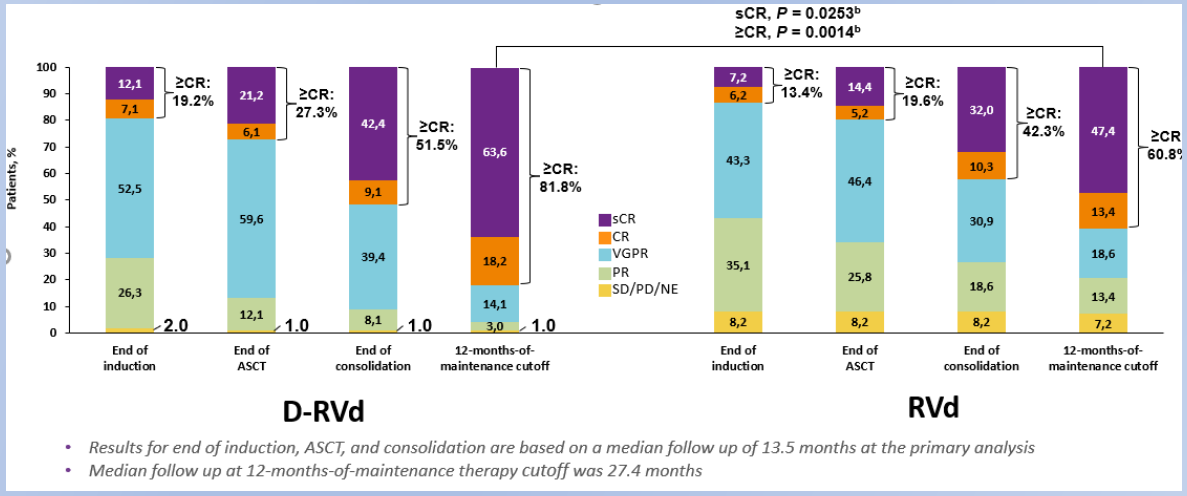
GRIFFIN: Randomized Phase 2 study

- Phase 2 study of D-RVd versus RVd in transplant-eligible NDMM, 35 sites in the United States with enrollment between December 2016 and April 2018

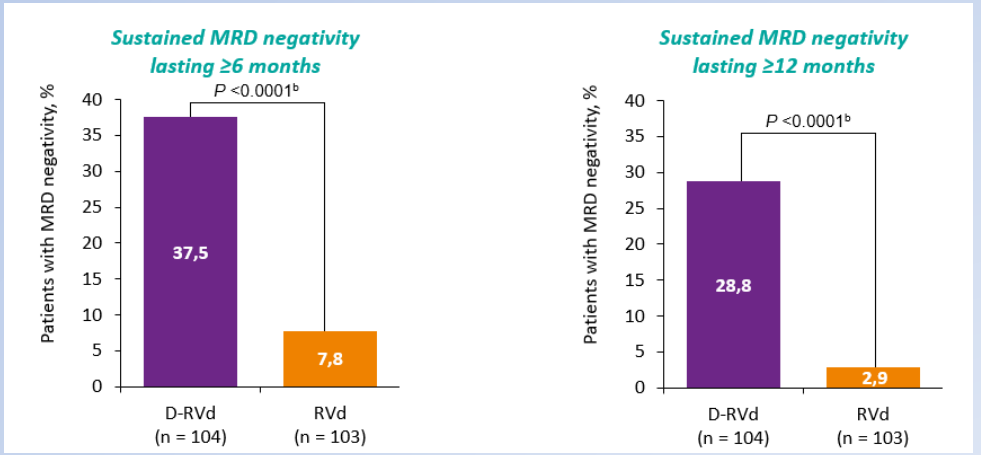


ECOG PS, Eastern Cooperative Oncology Group performance status; CrCl, creatinine clearance; IV, intravenous; PO, oral; G-CSF, granulocyte colony-stimulating factor; Q4W, every 4 weeks; Q8W, every 8 weeks; NGS, next-generation sequencing; ORR, overall response rate; VGPR, very good partial response; CR, complete response. [a]Lenalidomide dose adjustments were made for patients with CrCl ≤ 50 mL/min. [b]Cyclophosphamide-based mobilization was permitted if unsuccessful. [c]Consolidation was initiated 60 to 100 days post transplant. [d]Patients who complete maintenance cycles 7 to 32 may continue single-agent lenalidomide thereafter. [e]Protocol Amendment 2 allowed for the option to dose daratumumab Q4W, based on pharmacokinetic results from study SMM2001 (NCT02316106).

Updated analysis of GRIFFIN after 12 months of Maintenance Therapy

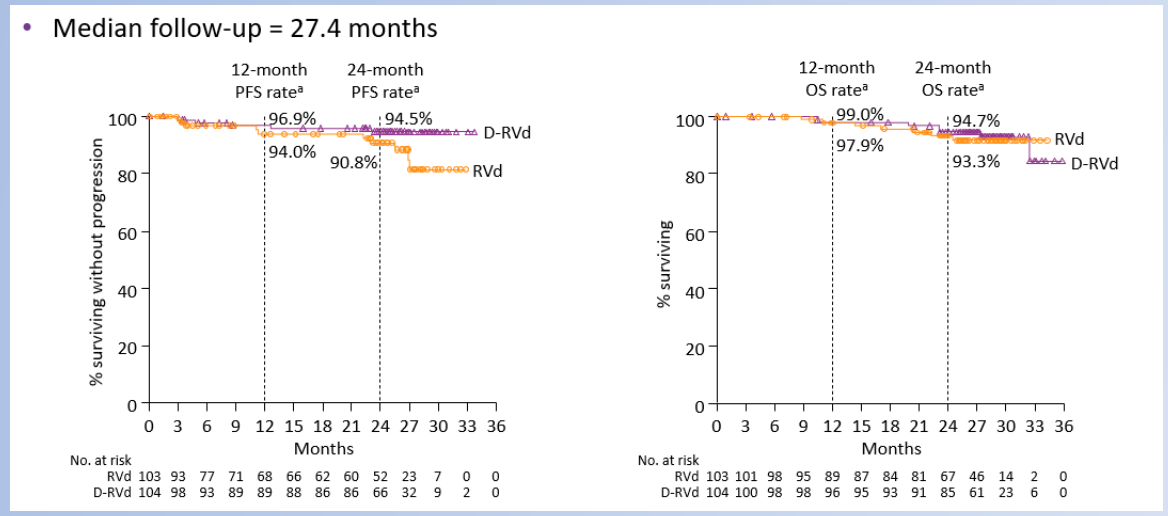


Response rates and depths were greater for DRVd at all time points



DRVd improved rates of sustained MRD negativity versus RVd

PFS and OS in the ITT population

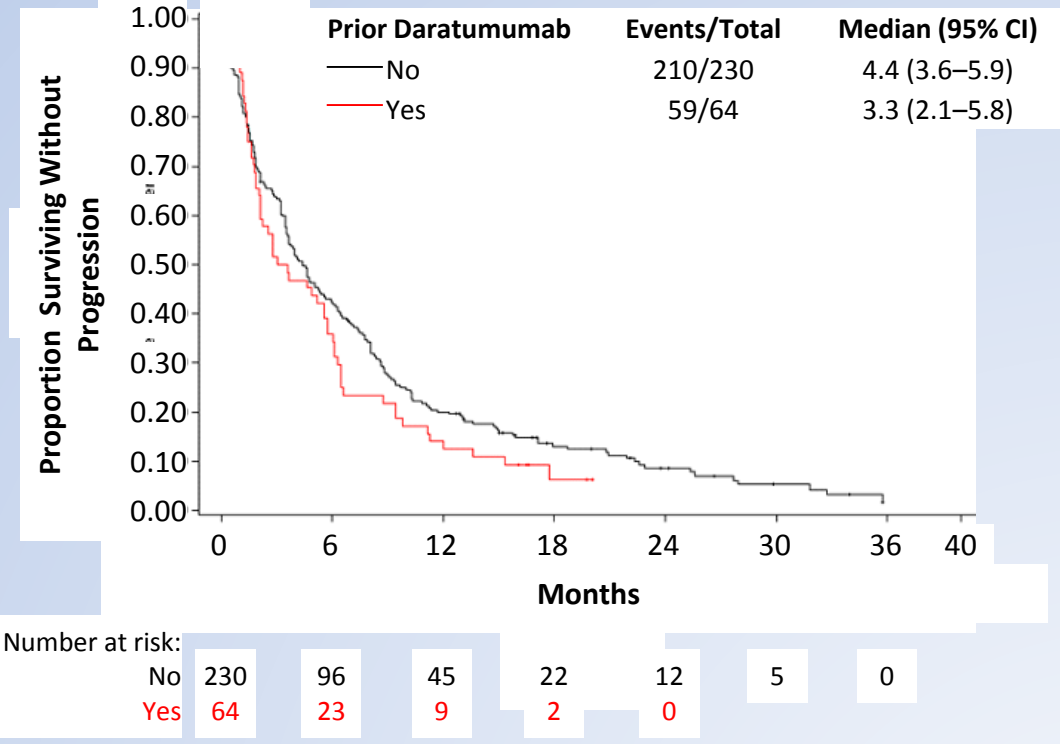


Median PFS and OS were not reached for DRVd and RVD

Clinical Characteristics and PFS

Patient Characteristics	Daratumumab Exposed (N = 141)	Daratumumab Naïve (N = 294)
Median age (SD) at index	69 (9.53)	70 (10.37)
Prior lines, n (%)		
3	36 (28)	189 (67)
4	28 (22)	56 (20)
5	28 (22)	26 (9)
6	22 (17)	6 (2)
7	14 (11)	6 (2)
Prior drug exposures, n (%)		
Bortezomib	121 (85.82)	261 (88.78)
Carfilzomib	70 (49.65)	108 (36.73)
Ixazomib	32 (22.70)	60 (20.41)
Thalidomide	6 (4.26)	11 (3.74)
Lenalidomide	117 (82.98)	230 (78.23)
Pomalidomide	97 (68.79)	109 (37.07)
Daratumumab	141 (100.00)	0 (0.00)
Elotuzumab	14 (9.93)	15 (5.10)
Selinexor	0 (0.00)	0 (0.00)
Venetoclax	2 (1.42)	0 (0.00)

PFS in Patients Receiving 4th Line Therapies by Prior Daratumumab Treatment



Short PFS was observed for RRMM patients regardless of prior daratumumab exposure; the need for effective novel classes of therapies remains high in the US community practice setting

CI, confidence interval; PFS, progression-free survival; SD, standard deviation; RRMM, relapsed or refractory multiple myeloma; US, United States.

Kim C, et al. Presented at 62nd ASH® Annual Meeting and Exposition; Dec 5–8, 2020; Virtual. Abstract 2566.

PANORAMA 3: a randomized, open-label, international, multicenter, phase 2 study

Background: In PANORAMA 1, significant PFS benefit with FVd was demonstrated compared with placebo-Vd; however, AEs were also more frequent.[1]

PANORAMA 3 aim: To optimize the FVd regimen by assessing three different doses and schedules of panobinostat, and incorporating *s. c.* bortezomib (instead of *i. v.* bortezomib, as used in PANORAMA 1).

Randomized* patients

Inclusion criteria included:
- ≥ 18 years
- RRMM (IMWG 2014 criteria[2])
- 1–4 prior lines of therapy (including an IMiD)

Exclusion criteria included:
- Refractoriness to bortezomib

1:1:1

- **Panobinostat 20 mg TIW**
- **Panobinostat 20 mg BIW**
- **Panobinostat 10 mg TIW**

For Cycles 1–4, all patients ≤ 75 years old received:
- s.c. bortezomib 1.3 mg/m^2 BIW
- oral dexamethasone 20 mg QIW

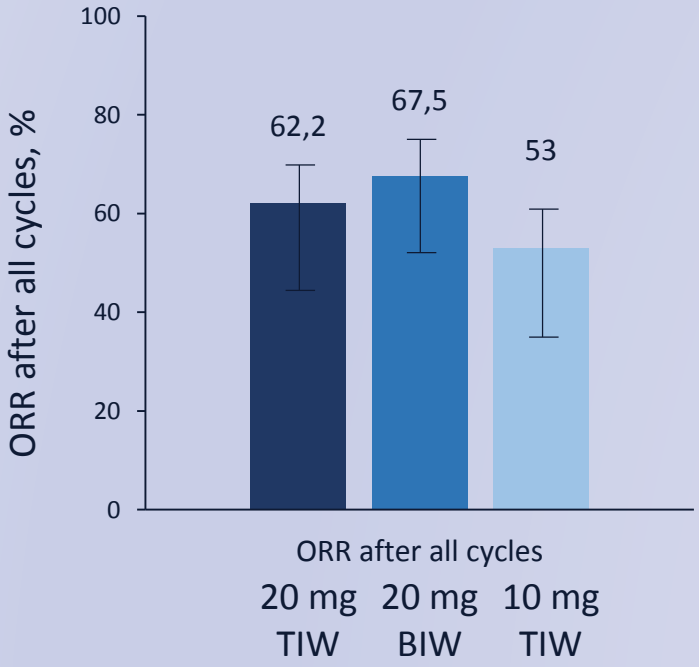
Patients aged ≤ 75 years from Cycle 5 onwards, and patients aged > 75 years for all cycles, received:
- s.c. bortezomib 1.3 mg/m^2 weekly
- oral dexamethasone 20 mg BIW

Patients were treated until PD, death, discontinuation due to toxicity, or consent withdrawal
- **Primary endpoint:** ORR[2] after up to 8 cycles of treatment
- **Secondary endpoints included:** ORR[2] after all treatment cycles, best response, DOR, TTR, PFS probability at 12 months, and safety

*Randomization was stratified by number of prior treatment lines (1; 2; 3 or 4) and age at screening (≤ 75 years; > 75 years). 1. San-Miguel JF, et al. *Lancet Oncol* 2014; 15:1195-206. 2. Rajkumar SV, et al. *Lancet Oncol* 2014;15:e538-e48. AE, adverse event; BIW, twice weekly; IMiD, immunomodulatory agent; DOR, duration of response; FVd, panobinostat, bortezomib and dexamethasone; IMWG, International Myeloma Working Group; PFS, progression-free survival; ORR, overall response rate; PD, progressive disease; QIW, four-times weekly; RRMM, relapsed or relapsed/refractory multiple myeloma; s.c., subcutaneous; TIW, three-times weekly; TTR, time to response; Vd, bortezomib and dexamethasone.

Overall Response, Time to Response, and Duration of Response with FVd

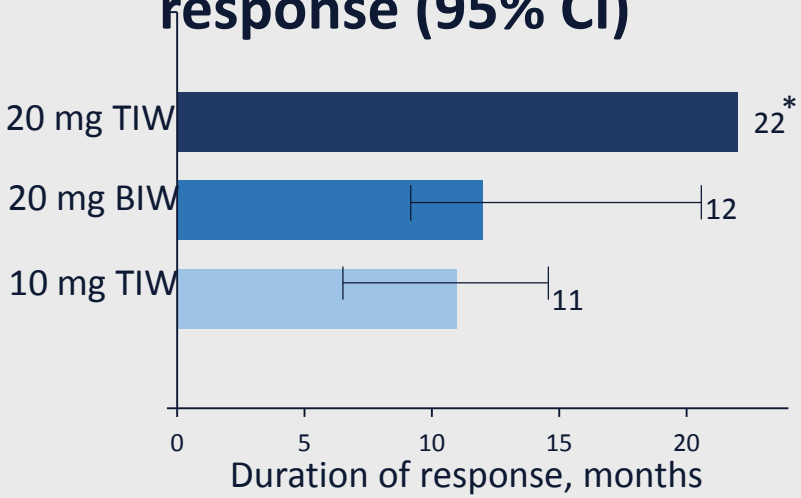
ORR after all cycles



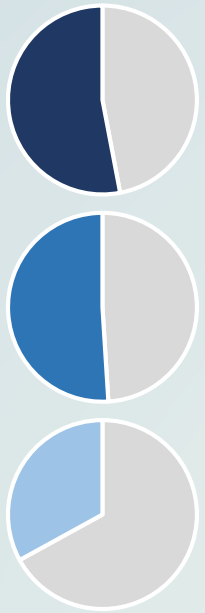
Median time to response:

- 20 mg TIW: 1 month
- 20 mg BIW: 2 months
- 10 mg TIW: 3 months

Median duration of response (95% CI)



PFS (95% CI) probability at 12 months



20 mg TIW: 53% (39; 64)

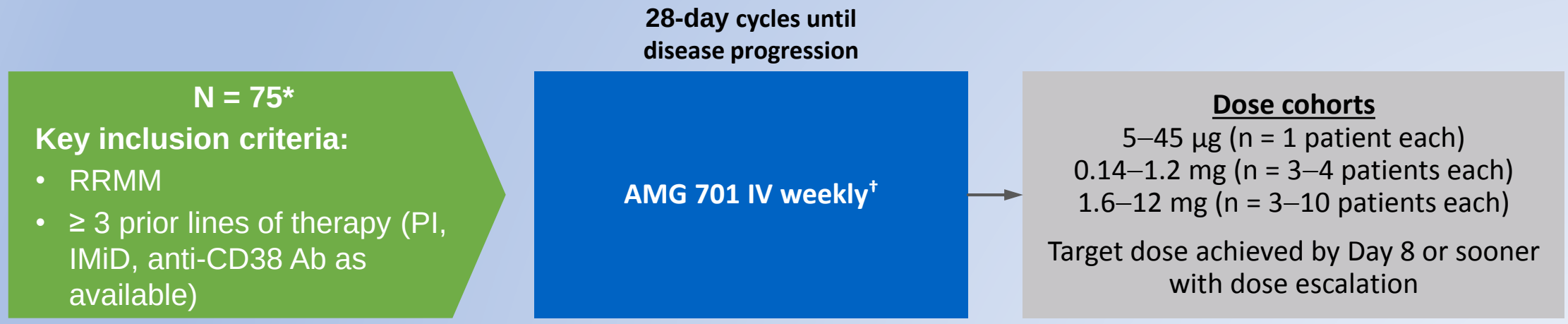
20 mg BIW: 51% (38; 63)

10 mg BIW: 33% (20; 45)

*22 (14, not estimable), months. BIW, twice weekly; FVd, panobinostat, bortezomib and dexamethasone; ORR, overall response rate; PFS, progression-free survival; TIW, three-times weekly.

Study Design[1,2]

- AMG 701 is a BiTE® molecule that binds BCMA on myeloma cells and CD3 on T cells
- This phase 1/2 FIH study (NCT03287908) sought to evaluate safety and tolerability and determine the optimal dose of AMG 701 in patients with RRMM;[1] this abstract presents results from phase 1[2]



Primary endpoint: safety, tolerability, biologically active dose
Select secondary endpoints: pharmacokinetics, anti-myeloma activity, response duration
Patient characteristics: median age 63 years, median time since diagnosis 5.9 years, median (range) of prior lines of therapy 6 (1–25), extramedullary disease 27%, prior SCT 83%, prior anti-CD38 antibody 93%, triple-refractory to a PI, IMiD, and anti-CD38 antibody 68%

*As of July 2, 2020. †A step-up dosing approach was added prior to certain target doses to prevent severe cytokine release syndrome.
Ab, antibody; BCMA, B-cell maturation antigen; BiTE, bispecific T-cell engager; FIH, first in human; IMiD, immunomodulatory drug; IV, intravenous; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma; SCT, stem cell transplant.
1. NCT03287908. Available at: https://www.clinicaltrials.gov/ct2/show/NCT03287908. Accessed November 9, 2020. 2. Harrison S, et al. Presented at 62nd ASH® Annual Meeting and Exposition; Dec 5–8, 2020; Virtual. Abstract 181.

Secondary Endpoints

Cohorts Assessed for Confirmed Responders ≥ PR

Target Dose, mg	Number of Responses/Evaluable*	Responses
0.14	0/3	
0.4	0/4	
0.8	1/4	1 MRD– sCR[†]
1.6[‡]	0/1	
1.2[‡]	0/4	
1.6	0/8	
3.0	3/11	2 PRs; 1 MRD– sCR
4.5	2/7	2 VGPRs
6.5	All: 4/10; Earlier escalation: 2/5	1 VGPR; 1 MRD– CR; 1 sCR; 1 MRD– sCR
9.0	All: 5/10; Earlier escalation: 5/6	3 PRs; 2 VGPRs
12.0	All: 2/7; cohort still enrolling	1 PR; 1 VGPR

- The most recent evaluable cohort reports an ORR of 83% (n = 5/6; 3 PRs, 2 VGPRs), with 4 of 5 responders being triple refractory[§]
- Response included 4 sCR, 1 MRD-negative CR, 6 VGPRs, and 6 PRs

Treatment Characteristics	N = 75
Median time to response (Q1, Q3), months	1 (1.0, 1.9)
Median time to best response (Q1, Q3), months	2.8 (1.0, 3.7)
Median duration of response (Q1, Q3), months	3.8 (1.9, 7.4)

- MRD was tested in 4 patients (3 sCR, 1 CR)
  - All were MRD-negative (3 by NGS, 1 by flow)
  - As of July 2, 2020, MRD negativity was ongoing at last observations, including up to 20 months later in 1 patient
- Responses were ongoing in 14/17 patients
- PK profile was favorable with AMG 701 exposures increasing in a dose-related manner

AMG 701 demonstrated a manageable safety profile, encouraging activity, and a favorable PK profile in patients with heavily pretreated RRMM

*Table does not include single-patient cohorts (5, 15, and 45 µg) nor 1 patient at 12 mg not yet assessed. [†]Dosing frequency reduced to Q2W in cycle 10 and q4W in cycle 18. [‡]Save for 1 patient at 1.6 mg with the DLT of CRS, all patients at doses of ≥1.2 mg received a step dose of 0.8 mg prior to target dose. [§]Data cut-off: July 2, 2020.

CR, complete response; FIH, first in human; Q1, Q3, quartile 1, quartile 3; MRD–, minimal residual disease negative; NGS, next-generation sequencing; ORR, overall response rate; PK, pharmacokinetic; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; VGPR, very good partial response.

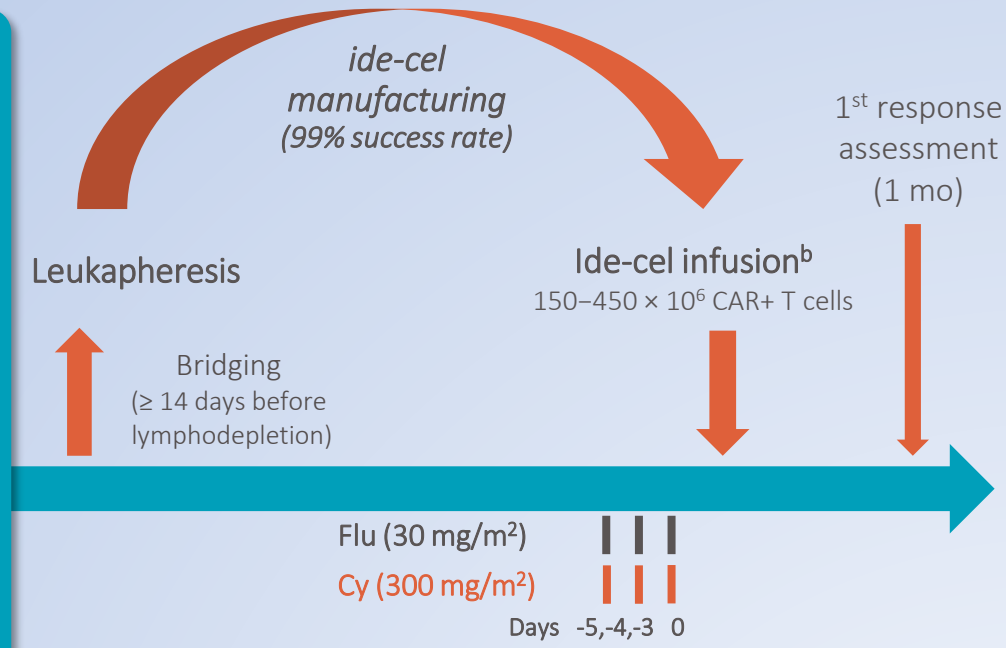
Harrison S, et al. Presented at 62nd ASH® Annual Meeting and Exposition; Dec 5–8, 2020; Virtual. Abstract 181.

Introduction and objective

- Multiple myeloma affects the older population more commonly than younger age groups; median age at diagnosis is 69 years in the US[1]
- Advanced age negatively impacts prognosis and limits treatment options for patients with hematologic malignancies, including multiple myeloma[2,3]
- Ide-cel, a BCMA-directed CAR T cell therapy, showed deep and durable responses across target dose levels of 150–450 × 10^6 CAR+ T cells in the pivotal phase II KarMMa study of patients with triple-class exposed RRMM[4]
- **Objective:** To examine the efficacy and safety of ide-cel in elderly patients in the KarMMa study

Pivotal phase II KarMMa study[4]

Patients with RRMM
- ≥ 3 prior regimens with ≥ 2 consecutive cycles each (or best response of PD)
- Previously exposed to
  - IMiD agent
  - Proteasome inhibitor
  - Anti-CD38 antibody
- Refractory to last prior therapy per IMWG criteria[a]



Primary endpoint: ORR (null hypothesis ≤ 50%)

EudraCT: 2017-002245-29
ClinicalTrials.gov: NCT03361748

BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; Cy, cyclophosphamide; Flu, fludarabine; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; ORR, overall response rate; PD, progressive disease; RRMM, relapsed and refractory multiple myeloma; US, United States.
[a]Defined as documented PD during or within 60 days from last dose of prior antimyeloma regimen; [b]Patients were required to be hospitalized for 14 days postinfusion. Ide-cel retreatment was allowed at PD for best response of at least stable disease.

1. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database. 2. Hassan M, et al. *Haematologica*. 2014;99:1124-1127.
3. Krok-Schoen JL, et al. *Cancer Med.* 2018;7:3425–3433. 4. Munshi NC, et al. *J Clin Oncol.* 2020;38[suppl, abstr]:8503.

CARTITUDE-1: Baseline Characteristics

Characteristic	N=97
Age, median (range) years	61.0 (43–78)
Male, n (%)	57 (58.8)
Extramedullary plasmacytomas ≥1, n (%)	13 (13.4)[a]
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	N=97
Prior lines of therapy, median (range)	6.0 (3–18)
Previous stem-cell transplantation, n (%)	
Autologous	87 (89.7)
Allogenic	8 (8.2)
Triple-class exposed,[c] n (%)	97 (100)
Penta-exposed,[d] n (%)	81 (83.5)
Triple-class refractory[c]	85 (87.6)
Penta-refractory[d]	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]Additional 6 patients had a soft-tissue component of a bone-based plasmacytoma (total plasmacytomas, 19.6%). [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.

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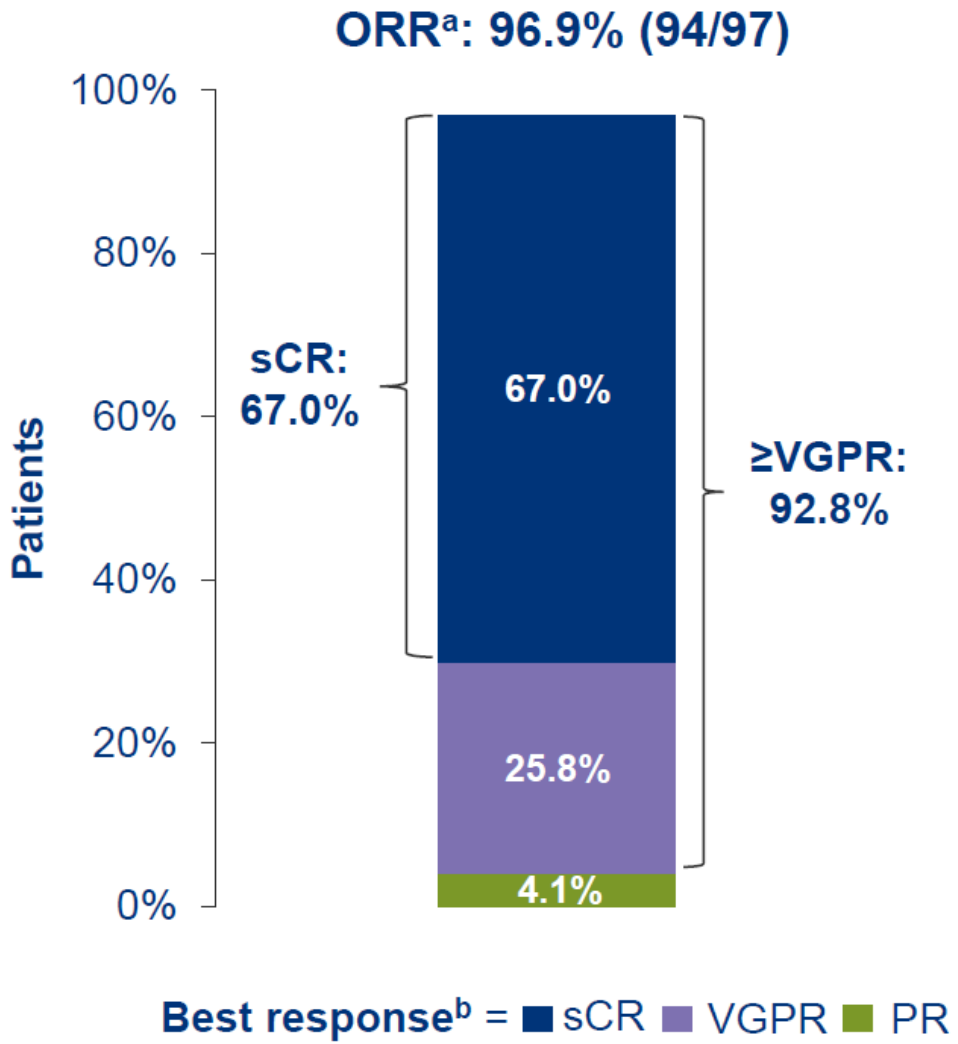
CARTITUDE-1: ORR and MRD Assessment



	N	Frequency in evaluable patients n=57[c]	Frequency in all treated n=97[d]
Overall MRD-	53	93.0%	54.6%
MRD- and sCR	33	57.9%	34.0%
MRD- and ≥VGPR	49	86.0%	50.5%

- Median time to first response: 1 month (0.9–8.5)
- Responses ongoing in 70 (72.2%) patients
- Of evaluable patients, 93.0% achieved MRD 10^{-5} negativity
  - Median time to MRD 10^{-5} negativity: 1 month (0.8–7.7)
- Among patients with 6 months individual follow-up, most had cilta-cel CAR+ T cells below the level of quantification (2 cells/μL) in peripheral blood

CAR, chimeric antigen receptor; CR, complete response; MRD, minimal residual disease; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
[a]PR or better, Independent Review Committee assessed. [b]No patient had CR or stable disease as best response. [c]MRD was assessed in evaluable samples at 10^{-5} threshold by next-generation sequencing (clonoSEQ, Adaptive Biotechnologies) in all treated patients at Day 28, and at 6, 12, 18, and 24 months regardless of the status of disease measured in blood or urine; patients were not evaluable primarily due to lack of an identifiable clone in the baseline bone marrow sample. [d]All treated patients.

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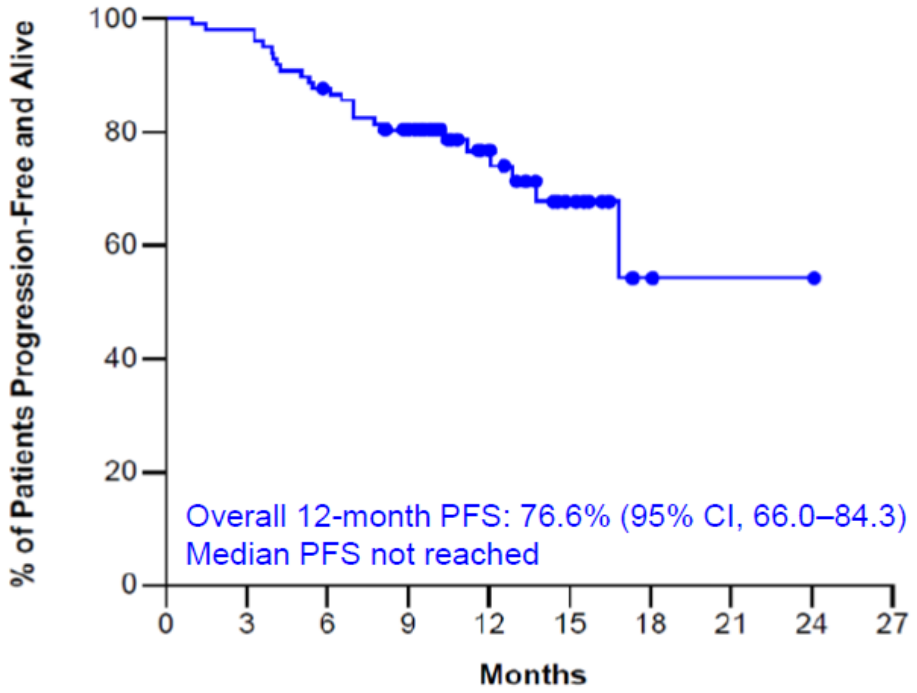
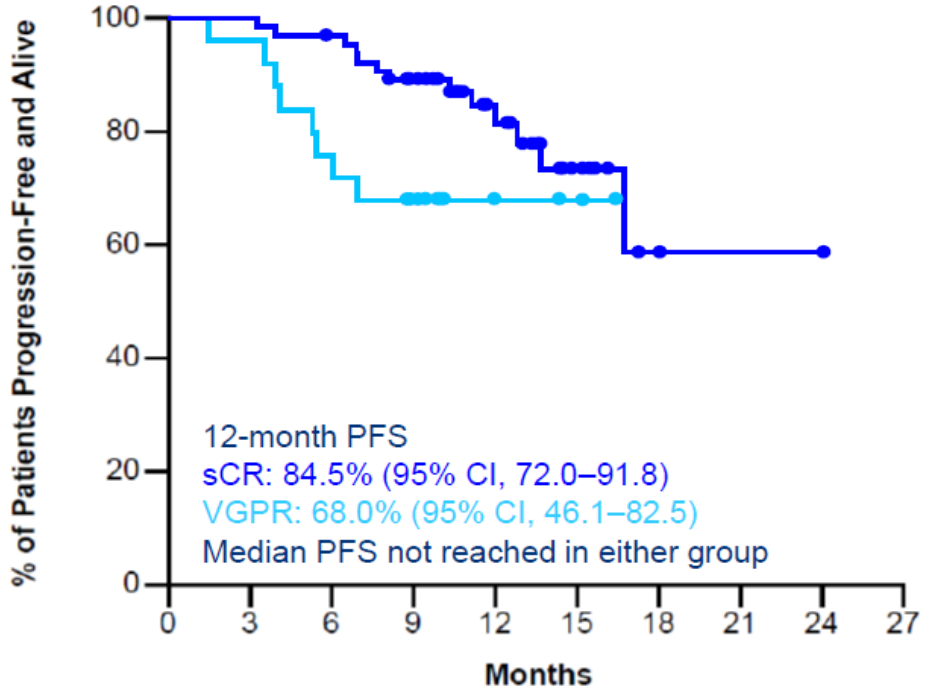
CARTITUDE-1: PFS

Overall PFS



No. at risk	97	95	84	71	30	14	2	1	1	0

PFS by sCR and VGPR



No. at risk										
sCR	65	65	62	53	27	12	2	1	1	0
VGPR	25	24	19	15	3	2	0	0	0	0

At median duration of follow-up of 12.4 months (range, 1.5–24.9), median PFS has not been reached
12-month PFS rate: 76.6% (95% CI, 66.0–84.3)
12-month OS rate: 88.5% (95% CI, 80.2–93.5)

OS, overall survival; PFS, progression-free survival; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

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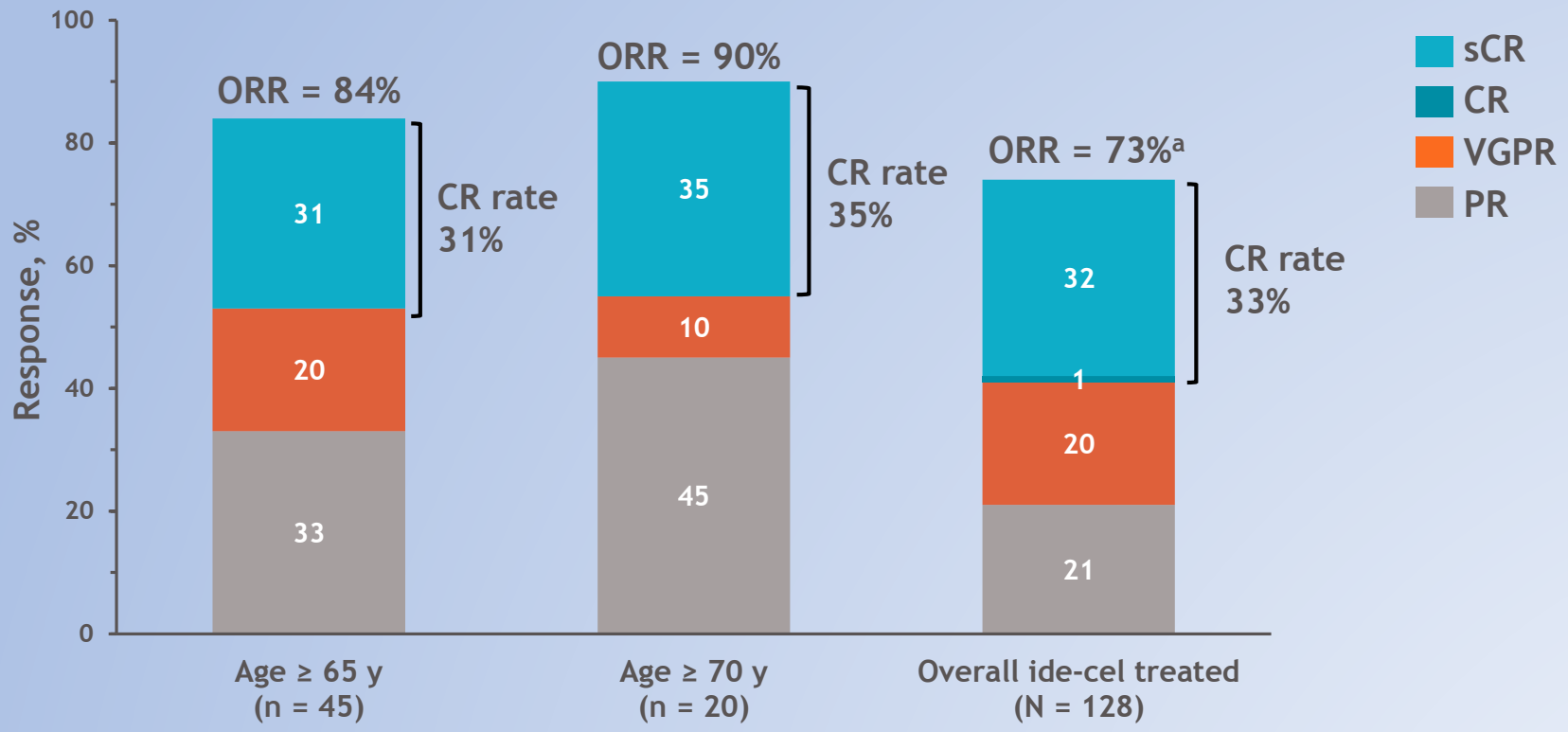
Overall response

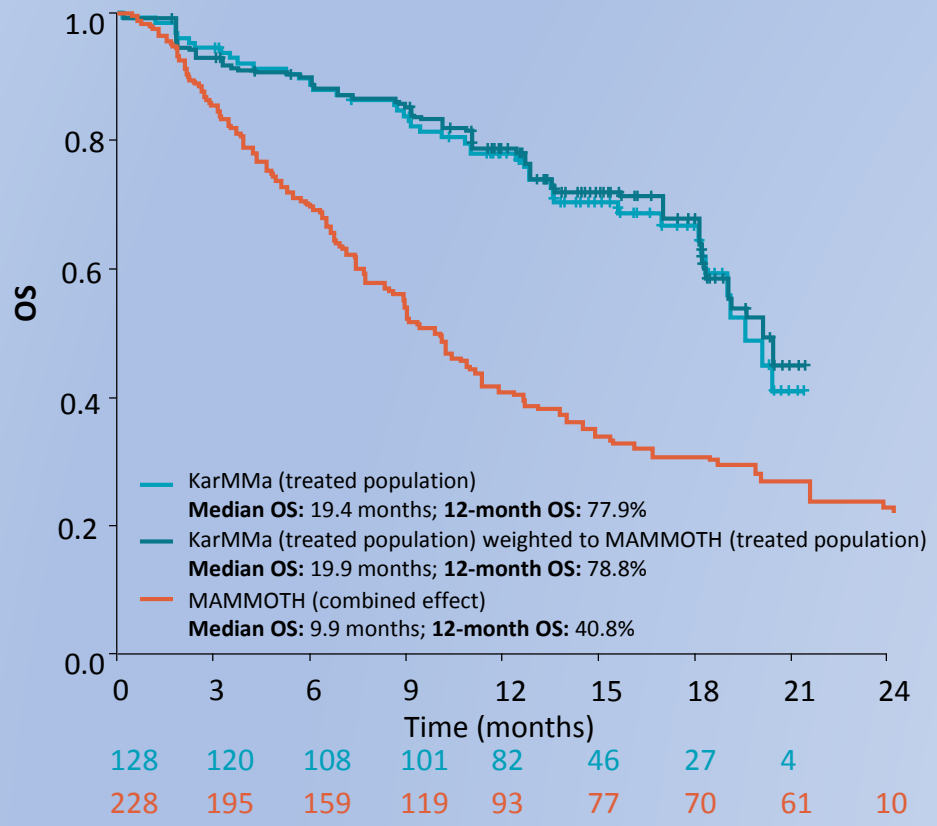


- ORR and CR rates in the elderly groups were comparable with those observed in the overall ide-cel treated population
- Median time to first response was 1.0 month in both elderly groups and in the overall treated population[b]
- Median duration of response was consistent across age groups, ranging from 10.7 to 11.0 months[b]

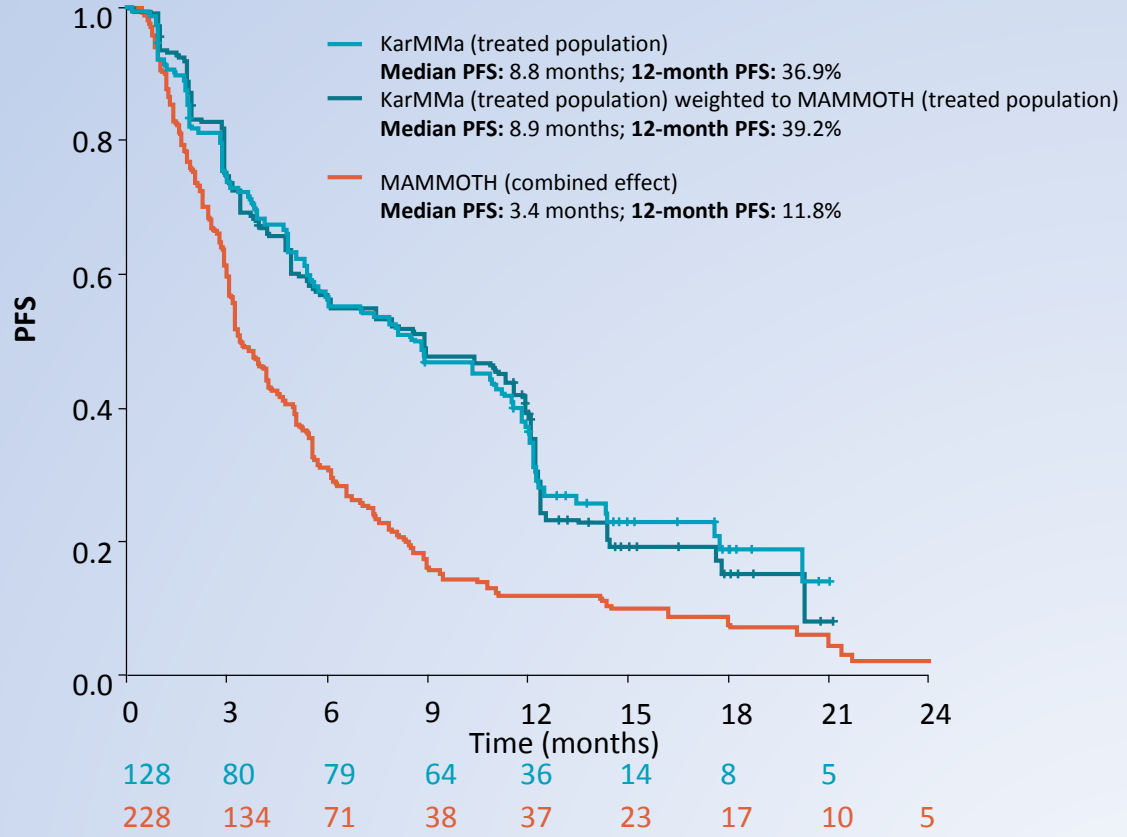
- Data cutoff date: 14 Jan 2020.
- CR, complete response; ORR, overall response rate (≥ PR); PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
- [a]Values may not add up to total due to rounding; [b]Time to first response and duration of response were assessed in responders: n = 38 for ≥ 65 years group, n = 18 for ≥ 70 years group, and n = 94 for overall ide-cel treated population.

OS and PFS: ide-cel versus conventional care

OS: Ide-cel (KarMMa treated population) versus conventional care (MAMMOTH treated population)



PFS: Ide-cel (KarMMa treated population) versus conventional care (MAMMOTH treated population)



- Median OS and median PFS were significantly longer for the ide-cel-treated population (weight-matched) compared with the conventional care population in MAMMOTH in the base case

OS, overall survival; PFS, progression-free survival.