נוגדנים ביספציפים או בלנטמב אחרי CAR-T

RABIN MEDICAL CENTER
BEILINSON • HASHARON

ד"ר יוליה וקסמן

CLINICAL TRIALS AND OBSERVATIONS

Efficacy and safety of teclistamab in patients with relapsed/refractory multiple myeloma after BCMA-targeting therapies

Cyrille Touzeau,[1] Amrita Y. Krishnan,[2] Philippe Moreau,[1] Aurore Perrot,[3] Saad Z. Usmani,[4] Salomon Manier,[5] Michele Cavo,[6] Carmen Martinez Chamorro,[7] Ajay K. Nooka,[8] Thomas G. Martin,[9] Lionel Karlin,[10] Xavier Leleu,[11] Nizar J. Bahlis,[12] Britta Besemer,[13] Lixia Pei,[14] Sarah Stein,[15] Shun Xin Wang Lin,[15] Danielle Trancucci,[14] Raluca I. Verona,[15] Suzette Girgis,[15] Xin Miao,[15] Clarissa M. Uhlar,[15] Katherine Chastain,[14] and Alfred L. Garfall[16]

- Teclistamab was studied in patients previously exposed to BCMA-targeted treatment in the **cohort C of MajesTEC 1** trial
- At a median follow-up of 28 months, **40** patients with prior BCMA-targeted therapy had received subcutaneous 1.5 mg/kg weekly teclistamab
- Prior anti-BCMA therapy included ADC (n=29), CAR-T (n=15), or both (n=4)
- **The ORR was 53%,** 48% of patients achieved VGPR or better, and 30% achieved CR or better
- The mPFS was 4.5 months and the mOS 15.5 months

Touzeau, Blood 2024

8008 Oral Abstract Session

Efficacy and safety of elranatamab in patients with relapsed/refractory multiple myeloma (RRMM) and prior B-cell maturation antigen (BCMA)-directed therapies: A pooled analysis from MagnetisMM studies.

- The MagnetisMM program (MM-1, MM-3, MM-9) enrolled patients treated with prior BCMA-directed therapies
- Pooled analysis of **86** patients. Patients received a median of 7 prior lines of therapy, including BCMA-directed ADC (67%), CAR T-cells (42%), 9% received both
- ORR for pts with prior BCMA-directed ADC and **CAR-T cells** was 41% and **53%,** respectively
- DOR rate for pts with prior BCMA-directed ADC and CAR-T cells were 67% and 79% at 9 mo, respectively
- The mPFS in the whole population was 4.8 months, and the median OS was not reached by 10 months, with a rate of 60% at 9 mo

Nooka, ASCO 2023

P915

Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma

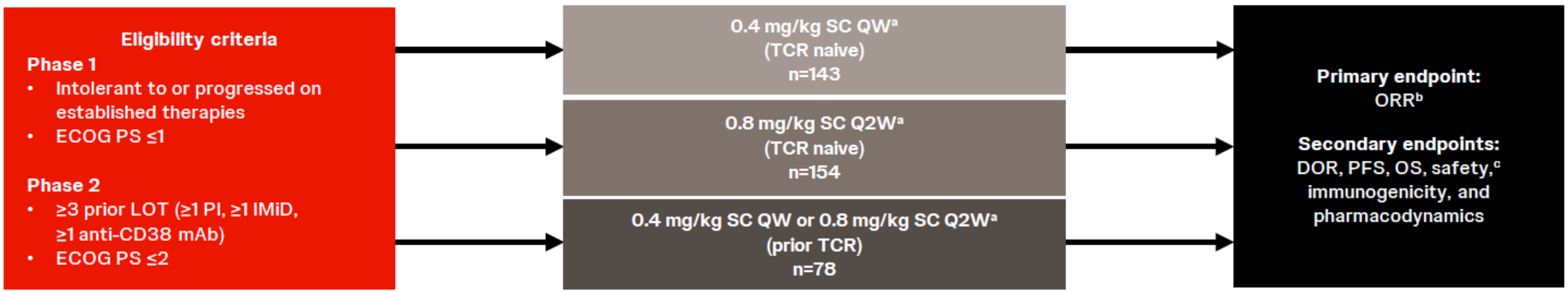
Leo Rasche[1], Carolina Schinke[2], Cyrille Touzeau[3], Monique C Minnema[4], Niels WCJ van de Donk[5], Paula Rodríguez-Otero[6], María-Victoria Mateos[7], Jing Christine Ye[8], Deeksha Vishwamitra[9], Indrajeet Singh[9], Xiang Qin[9], Michela Campagna[10], Tara Masterson[9], Brandi W Hilder[9], Jazzianne Tolbert[9], Thomas Renaud[11], Christoph Heuck[9], Colleen Kane[9], Ajai Chari[12]

[1]University Hospital of Würzburg, Würzburg, Germany; [2]Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [3]Centre Hospitalier Universitaire de Nantes, Nantes, France; [4]University Medical Center Utrecht, Utrecht, Netherlands; [5]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [6]Clínica Universidad de Navarra, CIMA, CIBERONC, IDISNA, Pamplona, Spain; [7]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [8]MD Anderson Cancer Center, University of Texas, Houston, TX, USA; [9]Janssen Research & Development, Spring House, PA, USA; [10]Janssen Research & Development, Madrid, Spain; [11]Janssen Research & Development, Raritan, NJ, USA; [12]Mount Sinai School of Medicine, New York, NY, USA, at the time that the work was performed.

Methods

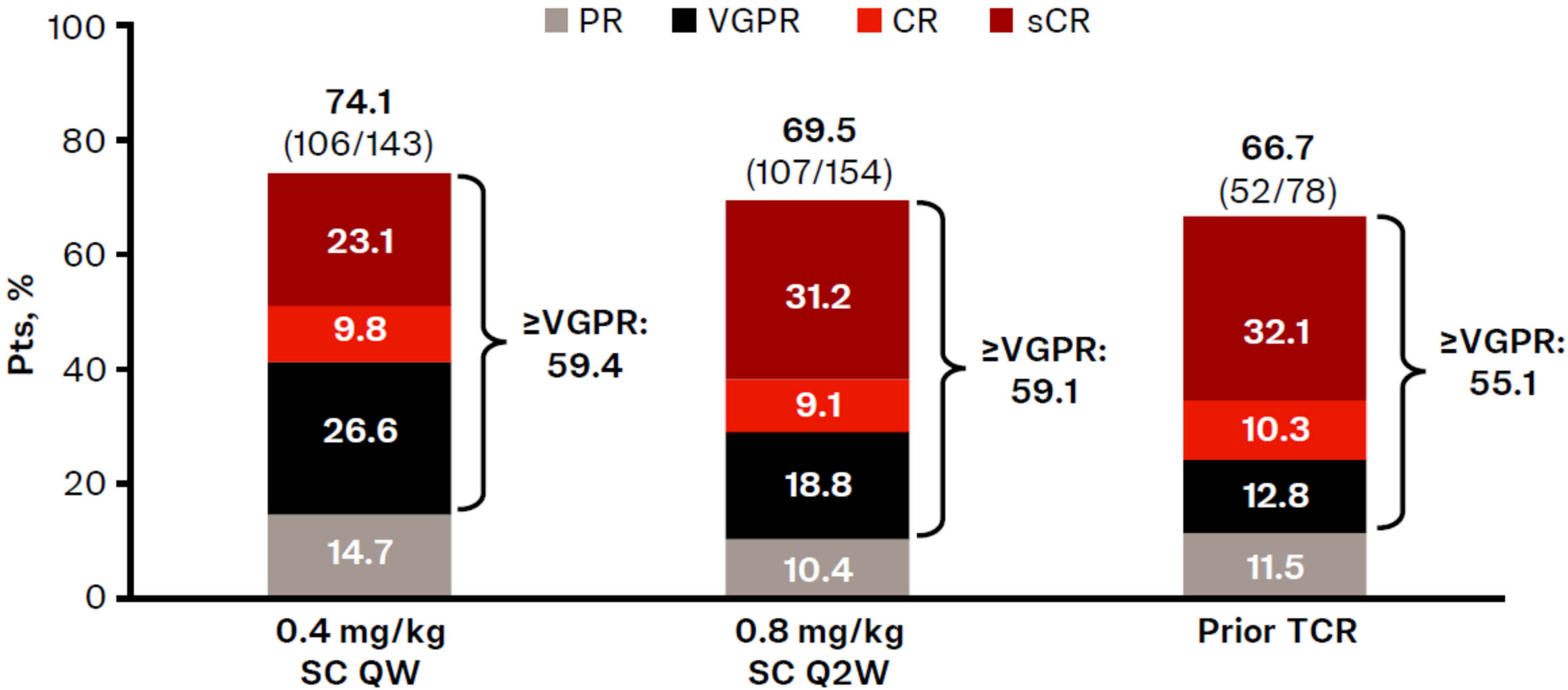
- MonumenTAL-1 (NCT03399799/NCT04634552) enrolled pts with RRMM who were naive or exposed to prior TCR (**Figure 1**)

Figure 1: MonumenTAL-1 phase 1/2 study design



[a]With 2–3 step-up doses. [b]Assessed by IRC using International Myeloma Working Group criteria.[7,8] [c]CRS and ICANS were graded by ASTCT criteria[9]; all other AEs were graded by CTCAE v4.03. ASTCT, American Society of Transplantation and Cellular Therapy; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ICANS, immune effector cell–associated neurotoxicity syndrome; IMiD, immunomodulatory drug; IRC, independent review committee; LOT, line of therapy; mAb, monoclonal antibody; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor.

Figure 2: ORR[a]



[a]Due to rounding, individual response rates may not sum to the ORR.
PR, partial response; sCR, stringent complete response.

Table 1: Efficacy outcomes

Outcome	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
mFU, mo	29.8	23.4	20.5
mDOR (95% CI),[a] mo	9.5 (6.7–13.4)	17.5 (12.5–NE)	N/A[b]
mDOR in pts with ≥CR (95% CI), mo	28.6 (19.4–NE)	NR (21.2–NE)	N/A[b]
mPFS (95% CI), mo	7.5 (5.7–9.4)	11.2 (8.4–14.6)	7.7 (4.1–14.5)
24-mo OS rate (95% CI), %	60.6 (51.7–68.4)	67.1 (58.3–74.4)	57.3 (43.5–68.9)

[a]n=106 (QW), n=107 (Q2W), and n=52 (prior TCR). [b]NR due to heavy censoring from 12 to 20 mo; the estimate may not be reliable at this time point. See **Supplemental Table 2** for efficacy outcomes in the USPI population (≥4 prior LOT). mDOR, median duration of response; mFU, median follow-up; N/A, not available; NE, not estimable; NR, not reported; USPI, United States prescribing information.

P915

Long-Term Efficacy and Safety Results From the Phase 1/2 MonumenTAL-1 Study of Talquetamab, a GPRC5D×CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma

Leo Rasche[1], Carolina Schinke[2], Cyrille Touzeau[3], Monique C Minnema[4], Niels WCJ van de Donk[5], Paula Rodríguez-Otero[6], María-Victoria Mateos[7], Jing Christine Ye[8], Deeksha Vishwamitra[9], Indrajeet Singh[9], Xiang Qin[9], Michela Campagna[10], Tara Masterson[9], Brandi W Hilder[9], Jaszianne Tolbert[9], Thomas Renaud[11], Christoph Heuck[9], Colleen Kane[9], Ajai Chari[12]

[1]University Hospital of Würzburg, Würzburg, Germany; [2]Myeloma Center, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [3]Centre Hospitalier Universitaire de Nantes, Nantes, France; [4]University Medical Center Utrecht, Utrecht, Netherlands; [5]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [6]Clínica Universidad de Navarra, CIMA, CIBERONC, IDISNA, Pamplona, Spain; [7]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [8]MD Anderson Cancer Center, University of Texas, Houston, TX, USA; [9]Janssen Research & Development, Spring House, PA, USA; [10]Janssen Research & Development, Madrid, Spain; [11]Janssen Research & Development, Raritan, NJ, USA; [12]Mount Sinai School of Medicine, New York, NY, USA, at the time that the work was performed.

- The **MonumelTAL-1** trial showed good efficacy of Tal in patients previously exposed to anti-BCMA CAR-T, validating the principle of changing the target
- Particularly, in the subgroup of patients previously exposed to **CART**, an **ORR of 71%** and a **mPFS of 12 months** were noticed
- Furthermore, the ORR was comparable in patients who received CAR-T as immediate prior line vs any prior line of therapy before Tal (75.9% vs 71.4%, respectively)

CEVOSTAMAB IN PATIENTS WITH RRMM WHO ARE TRIPLE-CLASS REFRACTORY AND HAVE RECEIVED A PRIOR BCMA-TARGETED ADC OR CAR T-CELL: INITIAL RESULTS FROM THE PHASE I/II CAMMA 2 STUDY

Shaji Kumar

Author(s): Shaji Kumar, Jesus Berdeja, Douglas Sborov, Paolo Corradini, Yael Cohen, Alexander Lesokhin, Moshe Gatt, Laura Paris, Laura Rosiñol, Hang Quach, Joshua Richter, Ameet Mishra, Oliver Catalani, Katerina Chineneyze, Paresh Sewpaul, Elisabeth Wassner Fritsch, Michel Delforge

(Abstract release date: 05/14/24) EHA Library. Kumar S. 06/13/2024; 422314; S210

- The CAMMA 2 study included the cohort A1 where cevostamab was given to patients exposed to a prior anti BCMA targeting ADC or CAR
- Phase I/II study, 21 patients (10 ADC and 11 CART), median prior lines of treatment 6, median time on treatment 73 days
- ORR of 67% (38% VGPR+)- 60% ADC, and 73% in the group with prior CAR T

EHA 2024

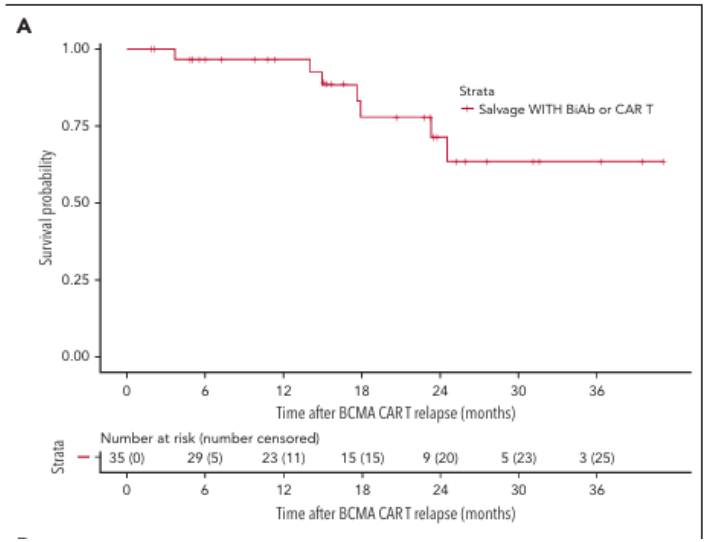
blood
Regular Article

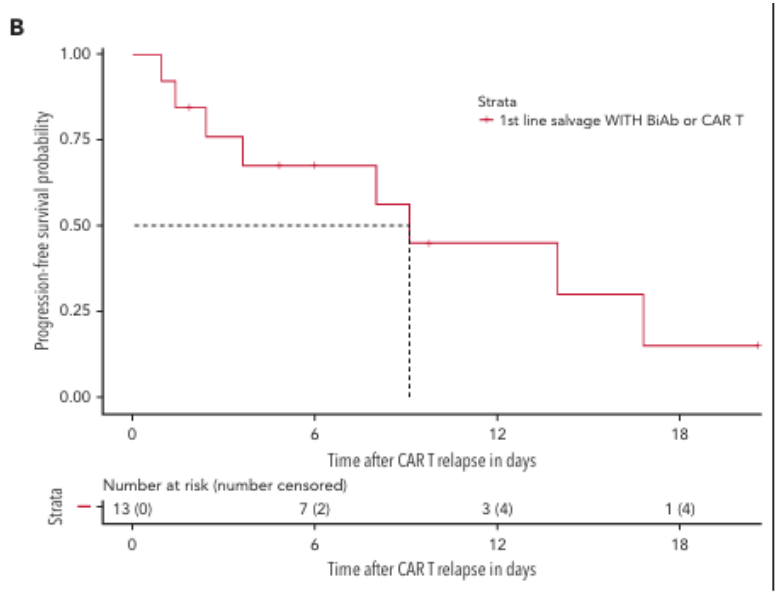
LYMPHOID NEOPLASIA

Interventions and outcomes of patients with multiple myeloma receiving salvage therapy after BCMA-directed CAR T therapy

Oliver Van Oekelen,[1,2,*] Karthik Nath,[3,*] Tarek H. Mouhieddine,[1,4] Tasmin Farzana,[3] Adolfo Aleman,[1] David T. Melnekoff,[1] Yogita Ghodke-Puranik,[1] Gunjan L. Shah,[3,5] Alexander Lesokhin,[3,6] Sergio Giralt,[3,5] Santiago Thibaud,[1,4] Adriana Rossi,[1,4] Cesar Rodriguez,[1,4] Larysa Sanchez,[1,4] Joshua Richter,[1,4] Shambavi Richard,[1,4] Hearn J. Cho,[1,4,7] Ajai Chari,[1,4] Saad Z. Usmani,[3,5,6] Sundar Jagannath,[1,4] Urvi A. Shah,[6] Sham Mailankody,[3,6,**] and Samir Parekh[1,4,8,9,**]

- In a retrospective US cohort of 79 CART-cells-treated patients, 35 received a TCR agent (bispecific antibody or subsequent CAR T) at any given time point after CAR T-cells
- The ORR was 91%, mPFS of salvaged patients was 9 mos and OS was not reached at 21 months of follow-up





REGULAR ARTICLE

blood advances

Salvage therapies including retreatment with BCMA-directed approaches after BCMA CAR-T relapses for multiple myeloma

Kevin R. Reyes,[1] Yen-Chun Liu,[2] Chiung-Yu Huang,[3] Rahul Banerjee,[4,5] Thomas Martin,[4] Sandy W. Wong,[4] Jeffrey L. Wolf,[4] Shagun Arora,[4] Nina Shah,[4] Ajai Chari,[4] and Alfred Chung[4]

[1]School of Medicine, University of California San Francisco, San Francisco, CA; [2]Department of Statistical Science, Duke University, Durham, NC; [3]Department of Epidemiology and Biostatistics and [4]Division of Hematology/Oncology, University of California San Francisco, San Francisco, CA; and [5]Division of Medical Oncology, Department of Medicine, University of Washington, Seattle, WA

- A retrospective analysis of 68 patients with relapsed disease after BCMA-directed CAR-T
- With a median follow-up of 13.5 months, median OS from time of relapse until death was 18 months
- Fifty-eight patients received subsequent myeloma-directed therapies, with a total of 265 lines of therapy (LOTs).
- The ORR for first-line salvage therapy was 41%
- Among all LOTs, high response rates were observed among those receiving another BCMA-directed CAR-T (89%), BCMA-directed BsAbs (60%), CD38-directed combinations (80% when combined with BsAb; 50% when combined with immunomodulatory drugs and/or proteasome inhibitors), and alkylator-combinations (50% overall; 69% with high-dose alkylators).
- Thirty-four patients received at least 1 line of salvage BCMA-directed therapy; median progression-free survival was 8.3 months (95% CI, 7.9 to NR), 3.6 months (95% CI, 1.4 to NR), and 1 month (95% CI, 0.9 to NR) with median duration of response (DOR) of 8 months, 4.4 months, and 2.8 months for subsequent BCMA-directed CAR-T, BsAb, and belantamab mafadotin, respectively.
- Retreatment with BCMA-directed CAR-T and BsAbs can be effective salvage options after BCMA-directed CAR-T relapse; however, DORs appear limited, and further studies with new combinations and alternative targets are warranted

Leukemia www.nature.com/leu

ARTICLE OPEN

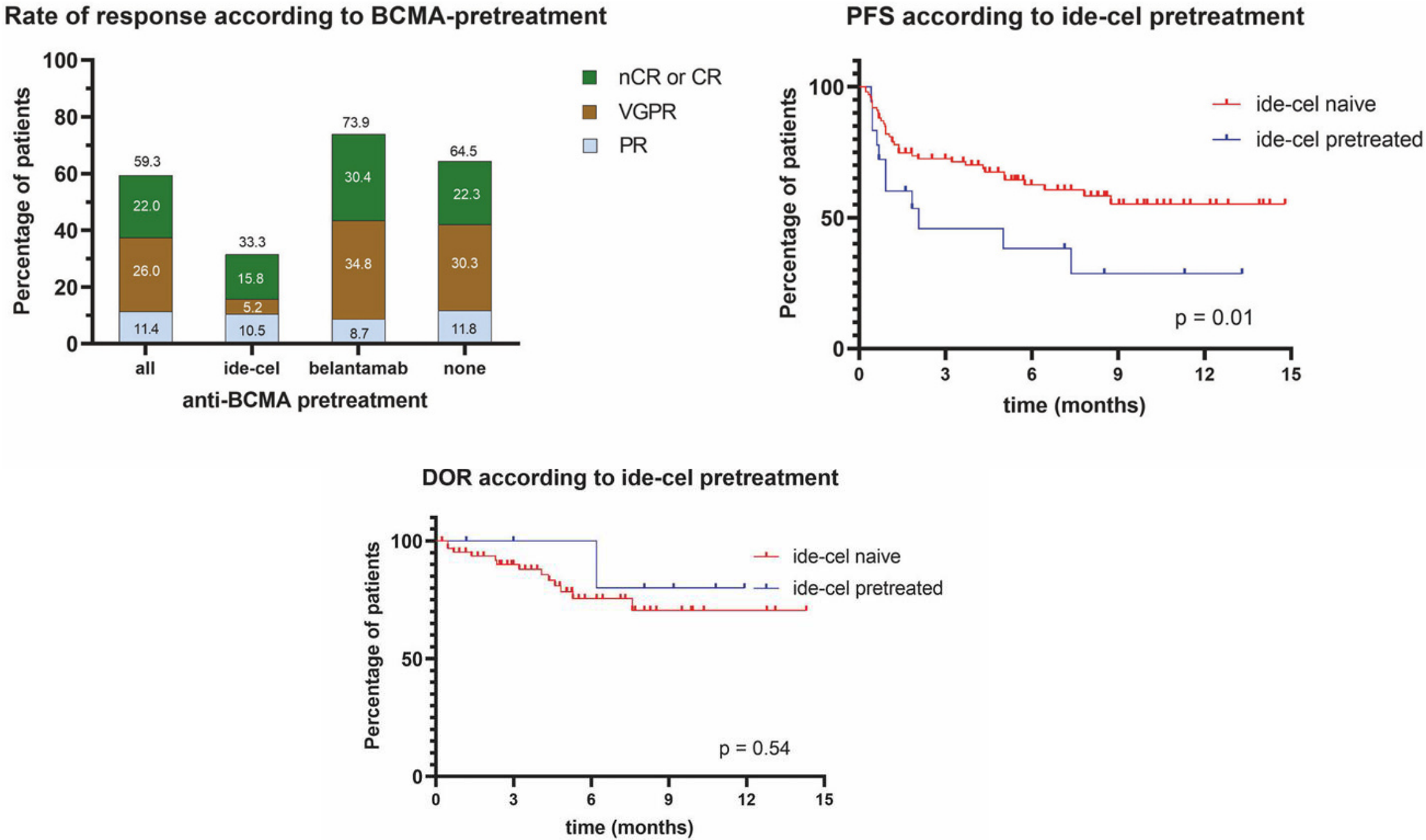
Check for updates

MULTIPLE MYELOMA, GAMMOPATHIES

Real-world analysis of teclistamab in 123 RRMM patients from Germany

C. Riedhammer[1], F. Bassermann[2], B. Besemer[3], M. Bewarder[4], F. Brunner[5], A. Carpinteiro[6], H. Einsele[1], J. Faltin[7], J. Frenking[8], D. Gezer[9,10], S. Goldman-Mazur[11], M. Hänel[12], M. Hoegner[2], K. M. Kortuem[1], J. Krönke[13], M. Kull[14], T. Leitner[15], C. Mann[16], R. Mecklenbrauck[17], M. Merz[11], A. Morgner[12], A. Nogai[13], M. S. Raab[8], R. Teipel[18], R. Wäsch[19] and L. Rasche[1]✉

- 123 patients, 37% of patients had received BCMA directed pretreatment including ide-cel (21/123, 17.1%)
- Significantly lower ORR and mPFS in patients with extramedullary disease (37%/2.1 months), and/or an ISS of 3 (37%/1.3 months), and **ide-cel pretreated patients (33%/1.8 months).**
- The DOR in ide-cel pretreated patients was **comparable** to that of anti-BCMA naive patients


Rate of response according to BCMA-pretreatment
Percentage of patients
100
80
60
40
20
0
59.3
22.0
26.0
11.4
33.3
15.8
5.2
10.5
73.9
30.4
34.8
8.7
64.5
22.3
30.3
11.8
all
ide-cel
belantamab
none
anti-BCMA pretreatment
nCR or CR
VGPR
PR
PFS according to ide-cel pretreatment
Percentage of patients
100
50
0
0
3
6
9
12
15
time (months)
ide-cel naive
ide-cel pretreated
p = 0.01
DOR according to ide-cel pretreatment
Percentage of patients
100
50
0
0
3
6
9
12
15
time (months)
ide-cel naive
ide-cel pretreated
p = 0.54

Data arising from real-life experience of patients treated with Tec or Elra or Tal confirmed the evidence derived from clinical trial

- It is not clear whether the time elapsing between CAR-T cell infusion and the subsequent therapy with an anti-BCMA BsAb may affect ORR and PFS
- The few real-life experiences available when Tal was used after an anti-BCMA CAR T-cell therapy confirmed the good rate of response (with ORR of 72-78%) obtained in the MonumelTAL-1 trial

Overall, data arising from selected cohorts of pivotal trials and from real life experiences show good efficacy of BsAbs in patients relapsed after an anti-BCMA CAR T-cell therapy

	Prior TCR	Subsequesnt TCR	ORR %	mDOR m	mPFS m	mOS m
MajesTEC 1 cohort C	CART	Tec	53	14.4	4.5	15.5
MagnetisMM pulled analysis	CART	Elra	53	79% @ 9 m	4.8	60% @ 9 m
MonomenTAL Priot TCR	CART	Tal	67	NA	7.7	57% @24 m
CAMMA cohort A1	CART	Cevo	67	NA	NA	NA