CAR T-Cell Therapy for Relapsed/Refractory Multiple Myeloma

Nina Shah, MD
Professor of Clinical Medicine
Multiple Myeloma Translational Initiative
Division of Hematology-Oncology
University of California San Francisco
BCMA: B-cell maturation antigen

- Member of TNFR (TNFRS17)
- Regulate B-cell proliferation and survival, maturation to plasma cells
- Expression/activation associated with myeloma cell growth/survival
- Exclusively expressed on the surface of plasmablasts and differentiated PCs

Cho et al, Frontiers in Immunol, 2018
Tobon et al, Autoimm Dis, 2013
Idecabtagene vicleucel (ide-cel, bb2121), a BCMA-targeted CAR T cell therapy, in patients with relapsed and refractory multiple myeloma (RRMM): initial KarMMA results

Nikhil C. Munshi, MD¹; Larry D. Anderson, Jr, MD, PhD²; Nina Shah, MD³; Sundar Jagannath, MD⁴; Jesus Berdeja, MD⁵; Sagar Lonial, MD⁶; Noopur Raje, MD⁷; David S. Siegel, MD, PhD⁸; Yi Lin, MD, PhD⁹; Albert Oriol, MD¹⁰; Philippe Moreau, MD¹¹; Ibrahim Yakoub-Agha, MD, PhD¹²; Michel Delforge, MD¹³; Fabio Petrocca, MD¹⁴; Jamie N. Connarn, PhD¹⁵; Payal Patel¹⁵; Liping Huang, PhD¹⁵; Timothy B. Campbell, MD, PhD¹⁵; Kristen Hege, MD¹⁵; and Jesus San Miguel, MD, PhD¹⁶ on behalf of the KarMMA study investigators

¹The LeBow Institute for Myeloma Therapeutics and Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; ²Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX, USA; ³University of California San Francisco, San Francisco, CA, USA; ⁴Mount Sinai Hospital, New York, NY, USA; ⁵Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN, USA; ⁶Emory School of Medicine, Atlanta, GA, USA; ⁷Massachusetts General Hospital, Boston, MA, USA; ⁸Hackensack University Medical Center, Hackensack, NJ, USA; ⁹Mayo Clinic, Rochester, MN, USA; ¹⁰Institut Josep Carreras and Institut Catala d’Oncologia, Hospital Germans Trias i Pujol, Badalona, Spain; ¹¹Centre Hospitalier Universitaire de Nantes, Nantes, France; ¹²Centre Hospitalier Regional Universitaire de Lille, Lille, France; ¹³University Hospital Leuven, Leuven, Belgium; ¹⁴bluebird bio, Cambridge, MA, USA; ¹⁵Bristol Myers Squibb, Princeton, NJ, USA; and ¹⁶Clinical Universidad de Navarra, Navarra, Spain

Presentation Number 8503

Presented By Nikhil Munshi at ASCO 2020
Phase II Pivotal KarMMa Study

- 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

Endpoints

- **Primary**: ORR (null hypothesis ≤50%)
- **Secondary**: CRR (key secondary; null hypothesis ≤10%), Safety, DOR, PFS, OS, PK, MRD, QOL, HEOR
- **Exploratory**: Immunogenicity, BCMA expression/loss, cytokines, T cell immunophenotype, GEP in BM

**Study Status as of Jan 14, 2020**

- Screened N=158
- Leukapheresed N=140
- Treated N=128 (Target Dose CAR+ T cells)
  - 150 × 10^6 n=4
  - 300 × 10^6 n=70
  - 450 × 10^6 n=54

**Median Follow-up (mo)**

- 150 × 10^6 18.0
- 300 × 10^6 15.8
- 450 × 10^6 12.4
- Total 13.3

CRR, complete response rate; Cy, cyclophosphamide; DOR, duration of response; Flu, fludarabine; GEP in BM, gene expression profile in bone marrow; HEOR, health economics and outcomes research; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetics; QOL, quality of life.

*Defined as documented disease progression during or within 60 d from last dose of prior antmyeloma regimen. Patients were required to be hospitalized for 14 d post-infusion. ide-cel retreatment was allowed at disease progression for best response of at least stable disease. By next-generation sequencing.

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

Presented By Nikhil Munshi at TBD
Best Overall Response

CRS: 84%
Neurotox: 18%
Median # prior regimens: 6

- Primary (ORR >50%) and key secondary (CRR >10%) endpoints met in the ide-cel treated population
  - ORR of 73% (95% CI, 65.8–81.1; P<0.0001*)
  - CRR (CR/sCR) of 33% (95% CI, 24.7–40.9; P<0.0001)
- Median time to first response of 1.0 mo (range, 0.5–8.8); median time to CR of 2.8 mo (range, 1.0–11.8)
- Median follow-up of 13.3 mo across target dose levels

Data cutoff: 14 Jan 2020. MRD-negative defined as <10^5 nucleated cells by next generation sequencing. Only MRD values within 3 mo of achieving CR/sCR until progression/death (exclusive) were considered.
Values may not add up due to rounding.
CR/sCR, complete response/stringent CR; CRR, CR rate; MRD, minimal residual disease; ORR, overall response rate (≥PR); PR, partial response; VGPR, very good PR. *P value at the primary data cutoff with same ORR and 95% CI.
Progression-Free Survival

Median (95% CI): 8.8 mo (5.6–11.6)

At risk, N: 128, 102, 83, 70, 64, 56, 35, 19, 13, 8, 4, 0

Data cutoff: 14 Jan 2020. PFS, progression-free survival.

Munshi et al, ASCO 2020
Progression-Free Survival

**PFS by Target Dose**

- **Median (95% CI), mo**
  - 150 x 10^6: 2.8 (1.0–NE)
  - 300 x 10^6: 5.8 (4.2–8.9)
  - 450 x 10^6: 12.1 (8.8–12.3)

**PFS by Best Response**

- **Median (95% CI), mo**
  - CR/sCR: 20.2 (12.3–NE)
  - VGPR: 11.3 (6.1–12.2)
  - PR: 5.4 (3.8–6.2)
  - Nonresponders: 1.8 (1.2–1.9)

**At risk, N**
- 150 x 10^6: 4, 2, 2, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 0
- 300 x 10^6: 70, 56, 42, 33, 29, 24, 17, 14, 11, 7, 2, 0
- 450 x 10^6: 54, 44, 40, 36, 34, 31, 17, 4, 1, 0, 0

- PFS increased with higher target dose; median PFS was 12 mo at 450 x 10^6 CAR+ T cells
- PFS increased by depth of response; median PFS was 20 mo in patients with CR/sCR

Data cutoff: 14 Jan 2020, NE, not estimable; PFS, progression-free survival.

Munshi et al, ASCO 2020
KarMMA: Updated OS¹

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.

Shah N, et al. ASH 2020 [abstract #1653]
Figure 3. Mean change from baseline in EORTC QLQ-C30 subscale scores

A. Fatigue

B. Pain

D, day; M, month; MID, Minimal Important Difference.
Baseline defined as last non-missing assessment on/prior to day of lymphodepleting chemotherapy.
Error bars represent 95% confidence intervals.
Figure 3. Mean change from baseline in EORTC QLQ-C30 subscale scores (Cont.)

C. Physical Functioning

D. Global Health/QoL

D, day; M, month; MID, Minimal Important Difference.
Baseline defined as last non-missing assessment on/prior to day of lymphodepleting chemotherapy.
Error bars represent 95% confidence intervals.
KarMMa: Clinically meaningful improvements were observed on all functioning EORTC QLQ-C30 secondary subscales. These improvements were statistically significant for the Role Functioning and Social Functioning subscales at multiple time points.

Day 1 is day of infusion. Error bars denote 95% confidence intervals. D1, Day 1; M, month; MID, minimal important difference.

Shah N, et al. ASH 2020 [abstract #437]
Ide-cel total package

- Safety ✅
- Efficacy ✅
- PFS ✓
- Likely improvement of PFS over conventional care ✓
- QOL improvement ✓

*FDA NEWS RELEASE*

FDA Approves First Cell-Based Gene Therapy for Adult Patients with Multiple Myeloma
CILTACABTAGENE AUTOLEUCEL, A B-CELL MATURATION ANTIGEN–DIRECTED CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY, IN RELAPSED/REFRACTORY MULTIPLE MYELOMA: UPDATED RESULTS FROM CARTITUDE-1

Saad Z Usmani1, Jesus G Berdeja2, Deepu Madduri3, Andrzej Jakubowiak4, Mounzer Agha5, Adam D Cohen6, Parameswaran Hari7, Tzu-Min Yeh8, Yunsı Olyslager9, Arnob Banerjee10, Carolyn C Jackson5, Alicia Allred10, Enrique Zudaire10, William Deraedt9, Xiaoling Wu11, Marlene J Carrasco-Alfonso11, Muhammad Akram11, Yi Lin12, Thomas Martin13, Sundar Jagannath9

1Levine Cancer Institute-Atrium Health, Charlotte, NC, USA; 2Sarah Cannon Research Institute, Nashville, TN, USA; 3Mount Sinai Medical Center, New York, NY, USA; 4University of Chicago, Chicago, IL, USA; 5UPMC Hillman Cancer Center, Pittsburgh, PA, USA; 6Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; 7Medical College of Wisconsin, Milwaukee, WI, USA; 8Janssen R&D, Raritan, NJ, USA; 9Janssen R&D, Beerse, Belgium; 10Janssen R&D, Spring House, PA, USA; 11Legend Biotech USA, Inc, Piscataway, NJ, USA; 12Mayo Clinic, Rochester, MN, USA; 13UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA

June 8, 2021
CARTITUDE-1: Introduction

- CARTITUDE-1 (NCT03548207) is a phase 1b/2 study evaluating cilta-cel, a CAR T-cell therapy with two BCMA–targeting single-domain antibodies, in patients with R/R MM who have been heavily pretreated\(^1\)

  - At a median follow-up of 12.4 months after cilta-cel treatment, the overall response rate was 97% with an sCR rate of 67%; overall 12-month PFS and OS rates were 77% and 89%, respectively

- Here, we present updated results from CARTITUDE-1 in patients with a longer follow-up (median: 18 months)

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BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; OS, overall survival; PFS, progression-free survival; R/R MM, relapsed refractory multiple myeloma; sCR, stringent complete response; VHH, variable heavy chain.

# CARTITUDE-1: Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range) years</td>
<td>61.0 (43–78)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>57 (58.8)</td>
</tr>
<tr>
<td>Black/African American, n (%)</td>
<td>17 (17.5)</td>
</tr>
<tr>
<td>All plasmacytomas, n (%)</td>
<td>19 (19.6)</td>
</tr>
<tr>
<td>Extramedullary plasmacytomas, n (%)</td>
<td>13 (13.4)</td>
</tr>
<tr>
<td>Bone-based plasmacytomas, n (%)</td>
<td>6 (6.2)</td>
</tr>
<tr>
<td>Bone-marrow plasma cells ≥60%, n (%)</td>
<td>21 (21.9)</td>
</tr>
<tr>
<td>Years since diagnosis, median (range)</td>
<td>5.9 (1.6–18.2)</td>
</tr>
<tr>
<td>High-risk cytogenetic profile, n (%)</td>
<td>23 (23.7)</td>
</tr>
<tr>
<td>del17p</td>
<td>19 (19.6)</td>
</tr>
<tr>
<td>t(14;16)</td>
<td>2 (2.1)</td>
</tr>
<tr>
<td>t(4;14)</td>
<td>3 (3.1)</td>
</tr>
<tr>
<td>Tumor BCMA expression ≥50%, n (%)</td>
<td>57 (91.9)</td>
</tr>
<tr>
<td>Prior lines of therapy, median (range)</td>
<td>6.0 (3–18)</td>
</tr>
<tr>
<td>Prior lines of therapy, n (%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>17 (17.5)</td>
</tr>
<tr>
<td>4</td>
<td>16 (16.5)</td>
</tr>
<tr>
<td>≥5</td>
<td>64 (66.0)</td>
</tr>
<tr>
<td>Previous stem-cell transplantation, n (%)</td>
<td></td>
</tr>
<tr>
<td>Autologous</td>
<td>87 (89.7)</td>
</tr>
<tr>
<td>Allogeneic</td>
<td>8 (8.2)</td>
</tr>
<tr>
<td>Triple-class exposed, n (%)</td>
<td>97 (100)</td>
</tr>
<tr>
<td>Penta-drug exposed, n (%)</td>
<td>81 (83.5)</td>
</tr>
<tr>
<td>Triple-class refractory</td>
<td>85 (87.6)</td>
</tr>
<tr>
<td>Penta-drug refractory</td>
<td>41 (42.3)</td>
</tr>
<tr>
<td>Refractory status, n (%)</td>
<td></td>
</tr>
<tr>
<td>Carfilzomib</td>
<td>63 (64.9)</td>
</tr>
<tr>
<td>Pomalidomide</td>
<td>81 (83.5)</td>
</tr>
<tr>
<td>Anti-CD38 antibody</td>
<td>96 (99.0)</td>
</tr>
<tr>
<td>Refractory to last line of therapy, n (%)</td>
<td>96 (99.0)</td>
</tr>
</tbody>
</table>

BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; PI, proteasome inhibitor.

*a* All plasmacytomas include extramedullary and bone-based plasmacytomas. *Denominator n=62, the number of evaluable samples; BCMA expression detected in all evaluable samples. *At least 1 PI, at least 1 IMiD, and 1 anti-CD38 antibody. *At least 2 PIs, at least 2 IMiDs, and 1 anti-CD38 antibody.

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CARTITUDE-1: Overall Response Rate

ORR: 97.9%

Best response
- **PR**
- **VGPR**
- **sCR**

CR, complete response; ORR, overall response rate; sCR, stringent complete response; VGPR, very good partial response. ORR assessed by independent review committee. *Subgroups by number of prior lines of therapy (≤4, >4), refractoriness (triple-class, pentadrug), cytogenetic risk (high risk, standard risk), baseline bone marrow plasma cells (≤30%, >30 to <60%, ≥60%), baseline tumor BCMA expression (≥median, <median), and baseline plasmacytomas (including extramedullary and bone-based).

With longer follow-up, responses deepened with increasing rate of sCR

- Median time to first response: 1 month (range, 0.9–10.7)
- Median time to best response: 2.6 months (range, 0.9–15.2)
- Median time to ≥CR: 2.6 months (range, 0.9–15.2)
- Median duration of response: 21.8 months (95% CI, 21.8–NE)
  - Estimated 73% of responders have not progressed or died at 12 months
  - Median duration of response not reached in patients with sCR
- Response rates were comparable (range, 95–100%) across different subgroups (eg, number of prior lines of therapy, refractoriness, extramedullary plasmacytomas, and cytogenetic risk)

N=97

80.4% sCR
80.4%
94.8% ≥VGPR
14.4%
3.1%

Patients, %
0 20 40 60 80 100

Saad Z Usmani

Presented By: Saad Z Usmani

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CARTITUDE-1: Progression-Free Survival

- **18-month PFS**
  - All Patients: 66.0% (95% CI, 54.9–75.0)
  - sCR: 75.9% (95% CI, 63.6–84.5)

- **18-month OS**
  - All patients: 80.9% (95% CI, 71.4–87.6)

**Median duration of follow-up:** 18 months (range, 1.5–30.5)

Median: 22.8 months (95% CI, 22.8–NE)

Median: not reached

**Number at Risk**

- **All Patients**
  - Months: 0, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30
  - Patients at Risk: 97, 95, 85, 77, 73, 55, 26, 9, 1, 1, 0

- **Responders With sCR**
  - Months: 0, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30
  - Patients at Risk: 78, 78, 76, 71, 68, 51, 26, 9, 1, 1, 0

**Medians**

- **All Patients**
  - Progression-Free Survival: Median: 22.8 months (95% CI, 22.8–NE)

- **sCR**
  - Progression-Free Survival: Median: not reached

**Notes:**

- NE, not estimable; PFS, progression-free survival; OS, overall survival; sCR, stringent complete response.

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CARTITUDE-1: Safety

No new safety signals with longer follow-up

<table>
<thead>
<tr>
<th>Hematologic AEs ≥25%, n (%)</th>
<th>Any grade</th>
<th>Grade 3/4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>93 (95.9)</td>
<td>92 (94.8)</td>
</tr>
<tr>
<td>Anemia</td>
<td>79 (81.4)</td>
<td>66 (68.0)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>77 (79.4)</td>
<td>58 (59.8)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>60 (61.9)</td>
<td>59 (60.8)</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>51 (52.6)</td>
<td>48 (49.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nonhematologic AEs ≥25%, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolism and nutrition disorders</td>
</tr>
<tr>
<td>Hypocalcemia</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
</tr>
<tr>
<td>Decreased appetite</td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
</tr>
<tr>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Fatigue</td>
</tr>
<tr>
<td>Cough</td>
</tr>
<tr>
<td>AST increased</td>
</tr>
<tr>
<td>ALT increased</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRS N=97</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with a CRS event, a n (%)</td>
</tr>
<tr>
<td>Time to onset, median (range) days</td>
</tr>
<tr>
<td>Duration, median (range) days</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Total CAR T-cell neurotoxicities, n (%)</th>
<th>N=97</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Grade</td>
<td>20 (20.6)</td>
</tr>
<tr>
<td>Grade ≥3</td>
<td>10 (10.3)</td>
</tr>
<tr>
<td>ICANS, n (%)</td>
<td></td>
</tr>
<tr>
<td>Any Grade</td>
<td>16 (16.5)</td>
</tr>
<tr>
<td>Grade ≥3</td>
<td>2 (2.1)</td>
</tr>
<tr>
<td>Other neurotoxicities, c n (%)</td>
<td></td>
</tr>
<tr>
<td>Any Grade</td>
<td>12 (12.4)</td>
</tr>
<tr>
<td>Grade ≥3</td>
<td>9 (9.3)</td>
</tr>
</tbody>
</table>


aCRS 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.

bThe patient with 97-day duration died due to CRS/HLH.

cEvents not reported as ICANS (ie, onset after a period of recovery from CRS and/or ICANS).
Efficacy and Safety of the BCMA-Directed CAR T-Cell Therapy, Ciltacabtagene Autoleucel, in Patients with Progressive Multiple Myeloma after 1–3 Prior Lines of Therapy: Initial Results from CARTITUDE-2

Mounzer Agha1*, Adam Cohen2, Deepu Madduri3, Yael C Cohen4, Michel Delforge5, Jens Hillengass6, Hartmut Goldschmidt7, Katja Weisel8, Marc-Steffen Raab9,10, Christoph Scheid11, Jordan M Schecter12, Kevin C De Braganca12, Helen Varsos12, Liwei Wang12, Martin Vogel13, Marlene J Carrasco-Alfonso14, Muhammad Akram14, Xiaoling Wu14, Tonia Nesheiwat14, Hermann Einsele15

1UPMC Hillman Cancer Center, Pittsburgh, PA, USA; 2Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; 3Mount Sinai Medical Center, New York, NY, USA; 4Tel-Aviv Sourasky (Ichilov) Medical Center, and Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel; 5Universitaire Ziekenhuizen Leuven, Leuven, Belgium; 6Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; 7University Hospital Heidelberg, Internal Medicine V and National Center for Tumor Diseases (NCT), Heidelberg, Germany; 8University Medical Center Hamburg Eppendorf, Hamburg, Germany; 9University Hospital Heidelberg, Heidelberg, Germany; 10Clinical Cooperation Unit Molecular Hematology/Oncology, German Cancer Research Center, Heidelberg, Germany; 11University of Cologne, Cologne, Germany; 12Janssen R&D, Raritan, NJ, USA; 13Janssen Global Services, LLC, Raritan, NJ, USA; 14Legend Biotech USA, Inc, Piscataway, NJ, USA; 15Universitätsklinikum Würzburg, Medizinische Klinik und Poliklinik II, Würzburg, Germany
<table>
<thead>
<tr>
<th>Trial</th>
<th>CAR T product</th>
<th>Med prior lines</th>
<th>Special Sauce</th>
<th>ORR</th>
<th>CRS %</th>
<th>Neurotox %</th>
<th>Survival data</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>KarMMa-1 (phase II, n=128)</td>
<td>bb2121 (Ide-cel)</td>
<td>6</td>
<td></td>
<td>73% (82% @450 dose)</td>
<td>84%</td>
<td>18%</td>
<td>mPFS 8.8mo, 12.1 mo @450 dose OS 24.8</td>
<td>CAR-T Par-T in 2021!!</td>
</tr>
<tr>
<td>CARTITUDE-1 (phase Ib/II, n=97)</td>
<td>JNJ-4528 (Cilta-cel)</td>
<td>6</td>
<td>Bi-epitope binding to BCMA</td>
<td>97%</td>
<td>92%</td>
<td>20.1% (16.5% ICANS)</td>
<td>@ 18 mo: 66% prog-free; DOR 21.8 m</td>
<td>Google to the yahoo?</td>
</tr>
<tr>
<td>LUMMICAR-2 (phase Ib/II, n=18-20)</td>
<td>CT053</td>
<td>5</td>
<td>Fully human</td>
<td>94% (n=18)</td>
<td>77-83%</td>
<td>15-17%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>PRIME (phase I/II, n=55)</td>
<td>P-BCMA-101</td>
<td>8</td>
<td>Piggy-bac system, centyrin technology</td>
<td>67% w/ nanoplasmid (n=6); 44-75% w/OG mfg (n=30)</td>
<td>17%</td>
<td>3.8%</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>CRB-402 (phase I, n-69)</td>
<td>bb21217</td>
<td>6</td>
<td>PI3Ki culture to increase Tscm cells</td>
<td>68% (73% at 450 dose, 84% w/OG mfg)</td>
<td>70%</td>
<td>16%</td>
<td>mDOR 17 mo (all doses) Memory cell phenotype in DP may correlate w/ response</td>
<td></td>
</tr>
<tr>
<td>UNIVERSAL (phase I, n=26-31)</td>
<td>Allo-715</td>
<td>5</td>
<td>Allo CART</td>
<td>60-67% at 320 dose</td>
<td>45%</td>
<td>0</td>
<td>NA</td>
<td>Variability in LD, tx within 5 days of enrollment!! No GVH</td>
</tr>
<tr>
<td>FasT CART</td>
<td>GCO12F</td>
<td>5</td>
<td>CD19 BCMA dual CAR T, ON manfact</td>
<td>95%</td>
<td>95%</td>
<td>0</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>
CARTITUDE-2: Phase 2 Multi-Cohort Study in Various MM Settings

**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

**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
- Apheresis
- Lymphodepletion Cy/Flu (Day -5 to -3)
- Cilta-cell infusion (Target: 0.75×10^6 CAR T cells/kg)
- Follow-up

**T-cell transduction and expansion to manufacture cilta-cell**

Bridging therapy as needed

**Consolidation**
- Cohort D + Len (2 years)
- Cohort E + Len + Dara (2 years)

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*Excluding prior BCMA-targeting cellular therapy.

ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cell, cilta-cabtagon e autoicusa; CR, complete response; Cy, cyclophosphamide; Dara, daratumumab; D-VIRd, daratumumab, bortezomib, lenalidomide, and dexamethasone; Flu, thalidomide; 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.
CARTITUDE-2: Overall Response Rate and MRD Negativity

- Median time to first response: 1.0 month (range, 0.7–3.3)
- Median time to CR or better: 1.9 months (range, 0.9–5.1)
- All patients (n=4) with MRD-gradable samples at the $10^{-5}$ threshold were MRD negative at data cut-off

Data cut-off date: Jan 2021. *Number who did not respond had stable disease. †MRD was assessed in evaluable samples (i.e., patients with identifiable clone at baseline and sufficient cells for testing at $10^{-6}$ threshold in post-treatment samples) by next-generation sequencing (Chemevick, Adaptive Biotechnologies) in all treated patients.

CR, complete response; MRD, minimal residual disease; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
Ide-cel has arrived…now what??

- Label: 4 lines of treatment
- Our patients
  1. VRD $\rightarrow$ ASCT $\rightarrow$ len maintenance
  2. DPD
  3. KCD
  4. ???

- But what about the #myelennial patients??
- KRD, D-VRD may make this a little more challenging
- $\rightarrow$ but no one ever said single agent dex couldn’t be a line…
- How will we decide between CAR and T-cell engager?
Case 2: 68 y/o F receives BCMA CAR T cells for RRMM

- 24 h after infusion of T cells she has fever to 38.5, BP 106/66
- Feels fatigued
- CRP = 3.6 → 72.8
- Receives acetaminophen → fever recurs, BP now 89/56
- Received tocilizumab → defervesces, BP better
- 2 days later fever recurs but with newly elevated ferritin, decreasing fibrinogen
- Receives anakinra → afebrile after 24 hours