ADVANCES IN MULTIPLE MYELOMA

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Slide credits to Dr. Rahma Warsame

WELCOMING REMARKS
ADVANCES IN MULTIPLE MYELOMA

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The Leukemia & Lymphoma Society
Rye Brook, NY
WELCOMING REMARKS
ADVANCES IN MULTIPLE MYELOMA

This program is supported by

Angela Dispenzieri, MD
Professor of Medicine
Research Chair, Division of Hematology
Mayo Clinic
Rochester, MN
DISCLOSURES

<table>
<thead>
<tr>
<th>Companies</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Janssen</td>
<td>Advisory board and independent review committee</td>
</tr>
<tr>
<td>Oncopeptides, Sorrento</td>
<td>Data monitoring safety committee</td>
</tr>
<tr>
<td>Alynlam, Pfizer, Takeda, BMS</td>
<td>Research dollars</td>
</tr>
</tbody>
</table>

The presentation includes off-label information on treatment regimens

KEY POINTS

- Understand diagnosis and staging of multiple myeloma
- Review treatment paradigm
- Immunotherapy for multiple myeloma
  - Naked antibodies
  - Antibody drug conjugates
  - Bispecific antibodies
  - Chimeric antigen receptor T-cell therapy (CART)
- Future directions
1. WHAT IS MULTIPLE MYELOMA?

- Sixty percent plasma cells
- Light chains I/U > 100
- MRI with > 1 focal lesion
- Calcium high
- Renal impairment
- Anemia
- Bone damage

![Diagram of normal plasma cells and multiple myeloma cells](image)

Rajkumar SV. Lancet Oncol. 2014

2. MULTIPLE MYELOMA – EPIDEMIOLOGY

- Cancer of plasma cells in the bone marrow that produce monoclonal immunoglobulins/proteins
- Approximately 1-2% of all cancers
- Cancer of older adults
  - Median age at diagnosis 65-74
  - 10% are <50
- More common in African American individuals

![Diagram of normal plasma cells and multiple myeloma cells](image)

Siegel RL. Cancer Statistics. 2021
Waxman AJ. Blood. 2010
3. PLASMA CELL – BASICS

Plasma cell: terminally differentiated B-cell that secretes Immunoglobulins (Ig factory)

- Immunoglobulins
  - Heavy chain
    - IgM, IgG, IgA, IgD, IgE
  - Light chain
    - Kappa and lambda

*Handy-dandy tumor maker that can be followed in blood and/or urine*

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MYELOMA BONE MARROW MILIEU

Bone marrow microenvironment of MM patients differs in cellular and non-cellular composition from healthy individuals

4. MULTIPLE MYELOMA – RISK STRATIFICATION

**Overall Survival International Staging System (R-ISS) in Multiple Myeloma**

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
</tr>
</thead>
<tbody>
<tr>
<td>All of the following:</td>
<td>Neither Stage I or III</td>
<td>• B2M ≥5.5 mg/L and elevated LDH -and/or- del(17p), t(4;14), or t(14;16) by FISH</td>
</tr>
<tr>
<td>• B2M &lt;3.5 mg/L</td>
<td>• B2M ≥5.5 mg/L</td>
<td>• B2M ≥5.5 mg/L and elevated LDH -and/or- del(17p), t(4;14), or t(14;16) by FISH</td>
</tr>
<tr>
<td>• Serum albumin ≥3.5 g/dL</td>
<td>• Normal LDH</td>
<td></td>
</tr>
<tr>
<td>• No del(17p), t(4;14), or t(14;16) by FISH</td>
<td>• No del(17p), t(4;14), or t(14;16) by FISH</td>
<td></td>
</tr>
</tbody>
</table>

**MM RISK STRATIFICATION - FISH**

- High Risk genetic abnormalities
  - t(4;14)
  - t(14;16)
  - t(14;20)
  - Del 17p or p53 mutation
  - Gain 1q (amplification or duplication)
- R-ISS stage 3
- High risk plasma cell S-phase

- Standard Risk
  - All others including:
    - Trisomies
    - t(11;14)
    - t(6;14)

[https://www.msmart.org/](https://www.msmart.org/)
5. MYELOMA TREATMENT PARADIGM

**Induction**
- Induction followed by continuous therapy

**Consolidation**
- SCT Eligible
- SCT Ineligible
- Induction followed by continuous therapy

**Maintenance**
- Relapse 1
- Relapse 2
- Relapse 3
- Relapse 4

**Refractory Disease**
- VRD, DRd, D-VRD

**Diagnosis & Risk Stratification**
- Tumor Burden

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**Diagnosis & Risk Stratification**
- t(11;14), t(6;14), Trisomies
- Del 17p, Gain 1q
- Double or Triple Hit Myeloma

**Transplant eligible**
- 4 cycles of VRd
- Collect Stem Cells
- VRd x 4-6 cycles
- Len until progression; delayed ASCT
- ASCT; Consider tandem ASCT
- Bortezomib-based maintenance till progression

**Transplant ineligible**
- DRd Or VRd for ~9 cycles → by Len maintenance
- Del 17p, Gain 1q
- Double or Triple Hit Myeloma
- VRd for ~9 cycles → by bortezomib-based maintenance

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Vrd, Bortezomib, lenalidomide, dexamethasone; Dara, daratumumab

Considerations for Treatment Selection for Relapsed MM

**Patient Factors**
- Age: second ASCT? Frail?
- Comorbidities:
  - Cardiac/Renal impairment?
  - Neuropathy?

**Disease Biology**
- Biochemical recurrence only or clinical relapse?
- Maintained or unmaintained?
- High risk?

**Treatment Factors**
- Choice of 1st line of therapy; prior ASCT?
- Duration/depth of prior response
- Trial availability?

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**Pillars of Myeloma therapy**

**Alkylators/Cytotoxics**
- Melphalan
- Cyclophosphamide
- Bendamustine
- Anthracyclines

**Proteasome Inhibitors**
- Bortezomib
- Carfilzomib
- Ixazomib

**IMiDs**
- Lenalidomide
- Pomalidomide
- Thalidomide
- Iberdomide

**Antibodies**
- Daratumumab
- Isatuximab
- Elotuzumab
- Belantamab mafodotin

**Targeted therapies/ Novel MOAs**
- Venetoclax
- Panobinostat
- Selinexor

**Immune Cell Therapy**

**Steroids (Dexamethasone, Prednisone)**

Therapy upon relapse will be impacted by changes in frontline therapy:
6. RETRAIN THE IMMUNE SYSTEM TO **KILL** MM

EMERGING IMMUNOTHERAPIES IN MULTIPLE MYELOMA

Shah A, Mailankody S. BMJ 2020; 370
NAKED ANTIBODIES

Monoclonal antibody

Cancer cell

EMERGING IMMUNOTHERAPIES IN MULTIPLE MYELOMA

Shah A, Mailankody S. BMJ 2020; 370
CD38 T-MABS ARE EVERYWHERE!

<table>
<thead>
<tr>
<th>T-mAb</th>
<th>Newly diagnosed MM</th>
<th>RRMM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daratumumab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D-VTd</td>
<td>D-Pd</td>
<td></td>
</tr>
<tr>
<td>D-VMP</td>
<td>D-Kd</td>
<td></td>
</tr>
<tr>
<td>D-Rd</td>
<td>D-Vd</td>
<td></td>
</tr>
<tr>
<td>Master: KRd ± Dara</td>
<td></td>
<td>D-Rd</td>
</tr>
<tr>
<td>Perseus: VRd ± Dara</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isatuximab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isa-Kia</td>
<td>Isa-Pd</td>
<td></td>
</tr>
<tr>
<td>(KRD ± Isa)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(VRd ± Isa)</td>
<td></td>
<td>Isa-Kd</td>
</tr>
<tr>
<td>(VCd ± Isa)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Randomized trials on-going in MM maintenance, MGUS, and SMM spaces

EMERGING IMMUNOTHERAPIES IN MULTIPLE MYELOMA

Shah A, Mailankody S. BMJ 2020; 370
ANTIBODY DRUG CONJUGATE

Benefits
- Targeted release of chemotherapy/immunotoxin/immunotherapy
- Attracts immune cells that clear cancer even if the treatment does not
- Dead cancer cells attract even more immune effector cells enhancing its potential response

Risk
- Still not 100% specific for myeloma cells and can cause tissue specific toxicity
BELANTAMAB

- BCMA ADC
  - Humanized IgG1 anti-BCMA monoclonal antibody & monomethyl auristatin F (toxin)
  - IV infusion over 3 minutes every 3 weeks
- Progression free survival 2.8 months
- Continued response can be seen in patients with ADC on hold

Time to Best Response

2.5 mg/kg dose cohort – FDA approved dose
- ORR 32% (31/97)
- >=VGPR 19% (18/97)


BELANTAMAB

OCULAR TOXICITY

In patients with keratopathy (MECs) events Grade ≥2 per KVA, 48% (29/60) had >1 event

Of these patients, 76% (13/17) had 1 event and 24% (4/17) had 2 events (no patients had >2 events)

1 patient discontinued due to keratopathy (MECs), 1 due to blurred vision, and 1 due to reduced BCVA
**BELANTAMAB + POM/DEX**  
(Algonquin Study, NCT03715478)

### Table 1: Summary of corneal events, ocular symptoms and efficacy data by cohort

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Median number for treatment cycles (range)</th>
<th>≥G3 Keratopathy (%)</th>
<th>≥G3 blurred vision n (%)</th>
<th>AEs leading to dose holds</th>
<th>AEs leading to dose reductions</th>
<th>≥VGPR n/N (%)</th>
<th>ORR n/N (%)</th>
<th>6-month PFS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.92 SINGLE n=12</td>
<td>13.5 (2-23)</td>
<td>5 (41.7%)</td>
<td>4 (33.3%)</td>
<td>7 (58.3%)</td>
<td>0 (0%)</td>
<td>7/11 (63.6%)</td>
<td>9/11</td>
<td>80%</td>
</tr>
<tr>
<td>2.5 SINGLE n=7</td>
<td>27 (13-29)</td>
<td>7 (100%)</td>
<td>4 (57.1%)</td>
<td>7 (100%)</td>
<td>7 (100%)</td>
<td>7/7 (100%)</td>
<td>7/7</td>
<td>100%</td>
</tr>
<tr>
<td>2.5 LOADING N=5</td>
<td>9 (5-17)</td>
<td>4 (80%)</td>
<td>0 (0%)</td>
<td>5 (100%)</td>
<td>5 (100%)</td>
<td>4/5 (80%)</td>
<td>5/5</td>
<td>80%</td>
</tr>
<tr>
<td>2.5 BIMONTHLY (N=12)</td>
<td>6 (4-10)</td>
<td>10 (83.3%)</td>
<td>2 (16.7%)</td>
<td>7 (58.3%)</td>
<td>5 (41.7%)</td>
<td>9/12 (75%)</td>
<td>11/12</td>
<td>100%</td>
</tr>
<tr>
<td>2.5 TRIMONTHLY N=11</td>
<td>6 (1-10)</td>
<td>8 (72.7%)</td>
<td>2 (18.2%)</td>
<td>4 (36.4%)</td>
<td>5 (45.5%)</td>
<td>4/7 (57.1%)</td>
<td>5/7</td>
<td>71.4%</td>
</tr>
<tr>
<td>2.5 SPLIT N=7</td>
<td>12.5 (3-22)</td>
<td>7 (87.5%)</td>
<td>4 (50%)</td>
<td>8 (100%)</td>
<td>6 (75%)</td>
<td>6/8 (75%)</td>
<td>7/8</td>
<td>87.5%</td>
</tr>
<tr>
<td>3.4 SPLIT N=5</td>
<td>7.5 (1-21)</td>
<td>3 (60%)</td>
<td>2 (40%)</td>
<td>3 (60%)</td>
<td>1 (20%)</td>
<td>3/4 (75%)</td>
<td>4/5</td>
<td>100%</td>
</tr>
<tr>
<td>All cohorts N=60</td>
<td>8 (1-29)</td>
<td>44 (73.3%)</td>
<td>18 (30%)</td>
<td>41 (68.3%)</td>
<td>29 (48.3%)</td>
<td>40/54 (74.1%)</td>
<td>48/54</td>
<td>86.5%</td>
</tr>
</tbody>
</table>

**Eligibility criteria**
- ≥1 prior line, Len refractory, Pi exposed or refractory, Mild/moderate renal impairment allowed

**Most frequent AE's**
- Keratopathy 99.5%, blurred vision 97.5%, fatigue 93.4%, neuropenia (62.5%), thrombocytopenia (50%), fever (46.9%), diarrhea (34.4%), constipation (34.4%), and dry eye (28.1%)

**MODAKAFUSP ALFA IS A NOVEL, FIRST-IN-CLASS IMMUNOCYTOKINE DESIGNED TO DELIVER IFNA2B TO CD38+ CELLS**

**Modakafusp alfa**
- Binds with high affinity to unique epitope of CD38
- Signals through IFNAR2 to:
  - activate innate and adaptive immune cells
  - direct anti-proliferative/ apoptotic signals to tumor cells
- CD38 is widely expressed on multiple myeloma cells, and subsets of tumor cells of other hematologic malignancies
- Modakafusp alfa binds with high affinity to unique epitope of CD38
- CD38-targeted attenuated IFNα fusion protein displays a 10,000-fold greater specificity than native IFNα for CD38+ vs CD38− cells
- The CD38-targeted attenuated IFNα fusion protein displays a 10,000-fold greater specificity than native IFNα for CD38+ vs CD38− cells
- Modakafusp alfa is a novel, first-in-class immunocytokine designed to deliver IFNA2B to CD38+ cells

**Innate immune cell activation**
- NK cell
- Macrophage
- MDSC
- Dendritic cell

**Adaptive immune cell activation**
- T cell
- B cell
- Multiple myeloma cell binding
- Multiple myeloma cell death

**References**
5. Calabretta E, Conti-Staso C. Cells. 2020;9:802
TAK-573: NOVEL ANTI-CD38 AND IFNα (modakafusp-alfa)

- Humanized CD38 that recognize different epitope from daratumumab and isatuximab
- IgG4 with no Fc function
- Attenuated IFNα molecules
  - Induce innate immune response
  - Induce adaptive immune response
- Key eligibility criteria
  - RRMM, ≥3 prior lines of therapy
  - Refractory to at least 1 PI an 1 IMiD
  - Daratumumab washout of 90 days for patients > 5 months of therapy in escalation
  - No daratumumab washout for expansion phase

**ORR with 1.5 mg/kg Q4W modakafusp alfa**

- 0%
- 10.3%
- 20.7%
- 23.1%
- 20.6%
- 38%
- 31%
- 28%
- 20%

**Patients, %**

**All patients (N=29)**

**Anti-CD38 mAb-refractory patients (n=26)**

**Anti-BCMA exposed patients (n=15)**

**Key eligibility criteria**

- RRMM, ≥3 prior lines of therapy
- Refractory to at least 1 PI an 1 IMiD
- Daratumumab washout of 90 days for patients > 5 months of therapy in escalation
- No daratumumab washout for expansion phase

EMERGING IMMUNOTHERAPIES IN MULTIPLE MYELOMA

Shah A, Mallankody S. *BMJ* 2020; 370
BISPECIFIC ANTIBODY

- Cytokine release
- T cell activation
- Perforin/Granzymes

BISPECIFIC ANTIBODIES

- Novel immune therapy approach designed to bind antigens on MM cells and cytotoxic T cells
- Early phase clinical trials targeting BCMA, GPRC5D, and FcRH5 have shown favorable safety profiles
- Most are IV or subcutaneous injections weekly or every other week
- Therapy is ongoing until progression
- Unknown sequence of therapy if benefit after CAR T
### Therapeutic Bispecific T-Cell Engagers for MM

<table>
<thead>
<tr>
<th>Drug</th>
<th>Prior lines</th>
<th>ORR (%) @ therapeutic dose</th>
<th>≥ VGPR (%)</th>
<th>G3+ CRS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMG-701</td>
<td>6</td>
<td>83</td>
<td>50</td>
<td>9</td>
</tr>
<tr>
<td>TNB-33B</td>
<td>6</td>
<td>80</td>
<td>73</td>
<td>0</td>
</tr>
<tr>
<td>REGN5458</td>
<td>5</td>
<td>62</td>
<td>NR</td>
<td>0</td>
</tr>
<tr>
<td>Teclistamab (JNJ-64007957)</td>
<td>5</td>
<td>65</td>
<td>58</td>
<td>0</td>
</tr>
<tr>
<td>Elranatamab (PF-06863135)</td>
<td>8</td>
<td>83</td>
<td>66</td>
<td>0</td>
</tr>
<tr>
<td>CC-93269</td>
<td>5</td>
<td>89</td>
<td>33</td>
<td>3</td>
</tr>
<tr>
<td>Talquetamab (GPRC5D/CD3)</td>
<td>6</td>
<td>70</td>
<td>60</td>
<td>2</td>
</tr>
<tr>
<td>Cevostamab (FcRH5/CD3)</td>
<td>6</td>
<td>53</td>
<td>32</td>
<td>2</td>
</tr>
</tbody>
</table>

Harison ASH 2020, abs 181; Rodriguez ASH 2020, abs 293; Madduri ASH 2020, abs 291; Krishnan ASCO 2021; Bahlis ASCO 2021; Costa ASH 2019, abs 142; Berdeja ASCO 2021, abs 8008; Cohen ASH 2020

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### Cevostamab: FcRH5 Bispecific Antibody Phase I Study

- FcRH5: Fc receptor homolog 5
- 100% expression on MM cells
- Humanized IgG
- Prior CART, bispecific ab, and ADC allowed
- IV q3 weeks, for 17 cycles
- Cycle 1 step wise dosing

<table>
<thead>
<tr>
<th>N (%) unless stated</th>
<th>N=53</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any CRS event*</td>
<td>40 (76)</td>
</tr>
<tr>
<td>Grade 1</td>
<td>18 (34)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>21 (40)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>1 (2)%</td>
</tr>
<tr>
<td>Median time to onset, hours (range)</td>
<td>6–12 (0–6, &gt;48)</td>
</tr>
<tr>
<td>Any neurological event</td>
<td>15 (28)</td>
</tr>
<tr>
<td>Grade 1</td>
<td>10 (19)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>5 (9)</td>
</tr>
<tr>
<td>Median time to onset, hours (range)</td>
<td>12–24 (0–6, &gt;48)</td>
</tr>
</tbody>
</table>

All CRS events resolved with standard of care, tocilizumab (13 pts, 25%) or steroids (9 pts, 17%)
CEVOSTAMAB: FCRH5 BISPECIFIC ANTIBODY PHASE I STUDY

- 51/53 pts efficacy evaluable; no response in ≤3.6/10.8mg cohorts
- ORR* in ≥3.6mg/20mg cohorts
  - 53% (18/34) in all pts
  - 41% (7/17) in penta-drug refractory pts
  - 63% (5/8) in pts with prior anti-BCMA
- Median time to first response/best response: 29.5 days (range: 21–105)/57.5 days (range: 21–272)
- Response irrespective of target expression level in patients assessed to date
- MRD negativity by NGS (<10^{-5}) detected in 6/7 evaluable pts with ≥VGPR

Response Rate (%) in ≥3.6/20 mg cohorts

TALQUETAMAB: G PROTEIN-COUPLED RECEPTOR CLASS C GROUP 5 MEMBER D (GPRC5D) BISPECIFIC ANTIBODY PHASE I STUDY

- Eligible patient’s intolerant to standard therapies, prior BCMA directed treatments allowed
- Data as of July 2021 – 95 patients received SC talquetamab
- Two doses studied 405 µg/kg weekly, and 800 µg/kg biweekly
- No discontinuations due to AE’s at either dose
- GPRC5D – function unknown
- High expression in MM cells and limited expression in normal human tissue
- Expr in MM cells associated with poor prognosis
- Given subcutaneously
- Common AE’s at 405 µg/kg weekly
  - CRS 73%, neutropenia 67%, Dysgeusia 60%, skin changes 77% and infections in 37%
- Common AE’s at 800 µg/kg biweekly
  - CRS 78%, dry mouth 44%, neutropenia 44%, skin changes 65% and 17% infections

Redrawn from: Krishnan A et.al. ASH 2021 abstract 158
TALQUETAMAB

• 30 evaluable patients at 405 mg/kg weekly dose ORR was 70% (≥VGPR 57%)
• 17 evaluable patients at 800mg/kg biweekly, ORR 71% (≥VGPR 53%)

OVERVIEW OF BISPECIFIC ANTIBODIES

• Several targeting BCMA in clinical trials
• Non-BCMA directed antibodies are encouraging
• CRS and neurotoxicity less grade 3, than CAR T cells
• Maximum response and duration of response yet to be determined
• More likely to be an option to combine with other agents
CAR-T CELLS

BCMA

Chimeric antigen receptor

CAR T-CELL THERAPY

Benefits

• High response rates (~75% of patients)
• No maintenance
• No steroids
• Effective even in heavily pretreated or previously refractory patients

Remove blood from patient to get T cells

Make CAR T cells in the lab

Insert gene for CAR

Chimeric antigen receptor (CAR)

Grow millions of CAR T cells

CAR T cells bind to cancer cells and kill them

Lymphodepleting chemotherapy
CAR T CELLS – RISKS

- Cytokine release syndrome (CRS)
  - Fevers, chills
  - Low blood pressure
  - Low oxygen levels
  - Multi-system organ damage

- Neurotoxicity
  - Delirium
  - Loss of ability to speak
  - Inability to write
  - Decreased alertness (obtundation)
  - Seizures

- Prolonged cytopenias

May occur within minutes or hours but generally appears within days or weeks. Coincides with maximal T-cell expansion. May need hospital/ICU care.

IDE-CEL REGISTRATION STUDY (KARMMA-1) RESULTS

CR/sCR: 20.2 (12.3-NE)
VGPR: 11.3 (6.1-12.2)
PR: 5.4 (3.8-8.2)
Nonresponders: 1.8 (1.2-1.9)

- Single dose CAR-T with no maintenance therapy
- ORR of 73% and CRR of 33%
- mOS 19.4 mo (95% CI 18.2 – NE)

Time from Dx to CART screen: 6 yr (1-17)
6 prior lines of therapy
84% triple refractory
KARMMA-1 STUDY (IDE-CEL) LONG TERM FOLLOW UP

- Overall survival (OS) is not decreased with age, extramedullary disease or triple refractory disease
- OS is decreased by R-ISS stage

FDA approved
March 26, 2021

CILTA-CEL (Ciltacabtagene autoleucel; Carvykti)
REGISTRATION STUDY CERTITUDE-1

- 3 or more prior lines of therapy
- Triple class exposed
- Median # lines of therapy 6 (4-8)
- Median Follow up 12.4 months
- ORR: 97%; sCR: 67%, MRD sCR: 34%
- 18-month PFS 66%
- 18-month OS 81%


Berdeja, JG. Lancet. July 2021
CILTA-CEL (Ciltacabtagene autoleucel; Carvykti)
REGISTRATION STUDY CERTITUDE-1

- 3 or more prior lines of therapy
- Triple class exposed
- Median # lines of therapy 6 (4-8)
- Median Follow up 12.4 months
- ORR: 97%; sCR: 67%, MRD sCR: 34%
- 18-month PFS 66%
- 18-month OS 81%

FDA Approved Feb. 28, 2022


CAR T-CELL THERAPY DATA

<table>
<thead>
<tr>
<th>T-cell therapy</th>
<th>Ide-cel KarMMa-1</th>
<th>Cilta-cel CARTITUDE</th>
<th>P-BCMA-101 PRIME</th>
<th>Bb21217 CRB-402</th>
<th>CT053 LUMMICAR</th>
<th>Allo-715 UNIVERSA L</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>(N = 128)</td>
<td>(N = 97)</td>
<td>(N = 55)</td>
<td>(N = 69)</td>
<td>(N = 20)</td>
<td>(N = 31)</td>
</tr>
<tr>
<td>ORR</td>
<td>73%</td>
<td>97%</td>
<td>67%</td>
<td>73%</td>
<td>94%</td>
<td>60-67%</td>
</tr>
<tr>
<td>CR/sCR</td>
<td>33%</td>
<td>67%</td>
<td>NA</td>
<td>29%</td>
<td>29%</td>
<td>NA</td>
</tr>
<tr>
<td>Durability</td>
<td>mPFS 8.8 mo</td>
<td>12 mo PFS 76%</td>
<td>NA</td>
<td>mDOR 17 mo</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

18-month PFS rates
66.0% (95% CI, 54.9-75.0)
75.9% (95% CI, 63.8-84.5)

Follow-up: 18 months (range, 1.5-30.5)

Berdje, JG. Lancet. July 2021
WHY DOES CAR T NOT ALWAYS WORK?

- MM is too aggressive (progresses before infusion)
- Patient T cells are less effective
- Do not persist long enough
- Loss of target by MM cell

FUTURE OF CAR T-CELL THERAPY

- Obtaining T cells earlier in the disease
- Obtain T cells from healthy donors
- Use other targets other than BCMA
- Manufacturing differences, optimize to expedite manufacturing
### CAR-T INVESTIGATIONS IN EARLIER LINES OF THERAPY

<table>
<thead>
<tr>
<th>Line</th>
<th>Study</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td></td>
<td>Induction, Consolidation, Maintenance</td>
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<tr>
<td>2nd</td>
<td>KarMMa-2: Ide-cel in high-risk MM, early relapse after 1L/ASCT.</td>
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<tr>
<td>3rd</td>
<td>KarMMa-4: Ide-cel in high-risk newly diagnosed MM</td>
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<tr>
<td>4th</td>
<td>KarMMa-3: Randomized, controlled study for Ide-cel vs SOC triplet regimens.</td>
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<td>CARTITUDE-2: Cilta-cel in multiple exploratory cohorts</td>
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<td></td>
<td>CARTITUDE-5: Cilta-cel in NDMM, transplant not considered</td>
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</tr>
<tr>
<td></td>
<td>CARTITUDE-4: Cilta-cel vs SOC triplet regimens in randomized, controlled study</td>
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</tr>
</tbody>
</table>

### 7. FUTURE IS BRIGHT

As of today, the FDA has approved for MM 3 naked t-mAb, 1 cargo loaded t-mAb, and 2 CAR-T

Within next year or two, more coming including bi-specific T-cell engagers

Many more novel therapies on the horizon

https://www.dreamstime.com/stock-photos-golden-path-bright-future-eps-image5580023
With each passing year, the difference between age and gender based expected survival and survival for patients with multiple myeloma SHRINKS.

Fonseca et al. Leukemia (2017) 1915 – 1921

Landmark therapeutic innovations. ASCT, autologous stem cell transplant; VAD, vincristine, doxorubicin, and dexamethasone; VBMCP, vincristine
ACKNOWLEDGEMENTS

Patients

Multiple Myeloma Awareness®

The Leukemia & Lymphoma Society®

warsame.rahma@mayo.edu  dispenzieri.angela@mayo.edu
@RahmaWarsameMD
ASK A QUESTION
ADVANCES IN MULTIPLE MYELOMA

Ask a question by phone:
Press star (*) zero (0) on your keypad to ask a question
To remove your question press star (*) 2 on your keypad

Ask a question by web:
Click “Ask a question”
Type your question
Click “Submit”

Due to time constraints, we can only take one question per person.
Once you’ve asked your question, the operator will transfer you back into the audience line.

LLS EDUCATION & SUPPORT RESOURCES

HOW TO CONTACT US:
To contact an Information Specialist about disease, treatment and support information, resources and clinical trials:

Call: (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET
Chat live online: www.LLS.org/InformationSpecialists
Monday to Friday, 10 a.m. to 7 p.m. ET
Email: www.LLS.org/ContactUs
All email messages are answered within one business day.

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Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.
www.LLS.org/Navigation

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Online Chats
Online Chats are free, live sessions, moderated by oncology social workers. To register for one of the chats below, or for more information, please visit www.LLS.org/Chat.

Education Videos
View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit www.LLS.org/EducationVideos.

Patient Podcast
The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit www.TheBloodline.org.

The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancers:
www.LLS.org/Finances

To order free materials: www.LLS.org/Booklets
THANK YOU

This program is supported by

We have one goal: A world without blood cancers