BEATING CANCER IS IN OUR BLOOD.

LIVING WITH MULTIPLE MYELOMA

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Hackensack Meridian Health
Hackensack, NJ

DISCLOSURES

Living with Multiple Myeloma

Noa Biran, MD:

Grant/Research: Merck, Karyopharm, BMS, & Janssen
Consultant: Janssen, Karyopharm, BMS, Sanofi, & Oncopeptides
Speaker Bureau: Janssen, Karyopharm, BMS, Sanofi, & Oncopeptides
What is Multiple Myeloma?

- Blood cancer that develops in bone marrow, where blood cells are produced
- Plasma cells, a type of white blood cell, become malignant
  - Plasma cells, produce infection fighting antibodies called immunoglobulins
- Malignant plasma cells (myeloma cells)
  - Produce large quantities of abnormal antibodies: monoclonal or M proteins, light chains (Bence-Jones)
  - Crowd out and inhibit production of normal blood cells and antibodies

Progression to Multiple Myeloma

- Premalignant
  - Primary initiating events: IGH translocations, Hyperdiploidy
- Undetermined Significance (MGUS)
- Smoldering Myeloma
- Multiple Myeloma
  - Secondary genetic events: Acquired mutations, Copy number alterations
Survival Continues to Improve for Patients with Multiple Myeloma

Jordan Nunnelee, BA, Qiu Hong Zhao, MS, Don M. Benson, Jr., MD, PhD, Ashley E. Rosko, MD, Maria Chaudhry, MD, Naresh Bumma, MD, Abdullah Mohammad Khan, MBBS, MSc, Srinivas Devakonda, MD, Yvonne A. Efebera, MD MPH, Nidhi Sharma, PhD, Improvement in Survival of Multiple Myeloma Patients: A Long-Term Institutional Experience, Blood, 2019.

Triple Class Refractory Multiple Myeloma

- Disease progression while on or within 60 days of a

**Proteasome inhibitor**
- Bortezomib
- Carfilzomib
- Ixazomib

**Immunomodulator**
- Thalidomide
- Lenalidomide
- Pomalidomide

**Anti-CD38 Monoclonal Antibody**
- Daratumumab
- Isatuximab
### Triple-Class Refractory: When All Else Fails

**FDA Approved**

<table>
<thead>
<tr>
<th>Chemotherapy</th>
<th>BCMA-Directed</th>
<th>XPO1-inhibitor</th>
<th>Mono-Abs</th>
<th>HDAC-inhibitor</th>
<th>Peptide drug conjugate</th>
</tr>
</thead>
<tbody>
<tr>
<td>KD-PACE/VDP-PACE/VDR-PACE</td>
<td>Belantamab mafodotin</td>
<td>Selinexor</td>
<td>Isatuximab</td>
<td>Panobinostat</td>
<td>Melflufen</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Ide-cel</td>
<td>Elotuzumab</td>
<td>Vorinostat*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melphalan</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bendamustine*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Not FDA approved for MM

### Ongoing Clinical Trials

<table>
<thead>
<tr>
<th>Monoclonal Antibodies and ADCs</th>
<th>CELMoDs/small molecule inhibitors</th>
<th>BiSpecifics</th>
<th>Cellular Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAK-079 (high-affinity CD38)</td>
<td>Iberdomide (cereblon E3 ligase)</td>
<td>BCMA x CD3:</td>
<td>Cilta-cel</td>
</tr>
<tr>
<td>TAK-169 (CD38 fused with shiga-like toxin payload)</td>
<td>CCC-92480 (cereblon E3 ligase) Venetoclax (bcl-2)</td>
<td>AMG-701 Teclistimab CC-93269 REGN5458 Elranatamab</td>
<td>Orva-cel</td>
</tr>
<tr>
<td>TAK-573 (CD38 fused with IFHNa2b)</td>
<td></td>
<td></td>
<td>LCAR-B38M</td>
</tr>
</tbody>
</table>

| | | | Lummicar-2 |
| | | | ALLO-715 |
| | | | Descartes-011 and -018 |

| | | | |
| | | | | |

<table>
<thead>
<tr>
<th>BiSpecifics</th>
<th>Cellular Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPRC5D x CD3 Talquetamab</td>
<td>Cilta-cel Orva-cel LCAR-B38M Lummicar-2 ALLO-715 Descartes-011 and -018</td>
</tr>
</tbody>
</table>
**Proposed Treatment Algorithm**

- **Multiple Relapse**
  - **Triple Class Refractory**
    - Refractory to IMiD, PI, Anti-CD38
    - Combinations with Cyclophosphamide that do not have IMID, PI, Anti CD38
    - Anti BCMA strategy
      - BCMA ADC (eg., Belantamab)
      - Bispecific Anti BCMA
      - BCMA CAR-Ts
  - **Penta-class Refractory**
    - Refractory to IMID, PI, Anti CD38, Alkylators, and Anti BCMA
    - Existing drugs:
      - Elotuzumab
      - Selinexor
      - Venetoclax
      - Panobinostat
      - Bendamustine
      - VDT PACE
    - New Drugs:
      - New Monoclonals
      - Iberdomide, CC-94480
      - New ADCs
      - New bi-specifics
      - New CAR-Ts

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**IKEMA – Isatuximab/car/dex vs car/dex**

- Patients had 1-3 prior therapies
- Median 2 prior lines, 93% prior PI, 76% prior len, 20% refractory to IMId and PI.
- Median PFS NR v 19.15 months, HR = 0.53, median f/u 20.7

OCEAN Study – Melphalan flufenamide +dex versus pom/dex

- 2-4 prior therapies, planned 495 patients, ongoing
- 16% v 12% triple class refractory, 51% and 48% previous ASCT

Median PFS
6.8 vs 4.9 months HR 0.79, p=0.03
No prior ASCT, 9.3 v 4.6 months HR 0.59, p<0.001.
In PRIOR ASCT, no difference in median PFS

Schjesvold, et al. IMW 2021, Abstract OA850

BOSTON Study – Selinexor/bortezomib/dex vs bortezomib/dex

- 1-3 prior therapies, N=402, 13 triple-class exposed, 6 triple-class refractory
- Median PFS 13.9 vs 9.5 months, HR 0.70

Groscki et al, Lancet 2020
Antibody Drug Conjugates

BCMA – B-cell Maturation Antigen

- Receptor for BAFF and APRIL
- Expressed on mature B cell subsets, plasma cells and plasmacytoid DCs
- Maintains plasma cell homeostasis.

Hengeveld et al Bl Cancer J 2015; Maus, June, Clin Can Res 2013
Belantamab Mafodotin

**Figure 1. Mechanisms of action of GSK2857916**

- **ADC**, antibody-dependent cytotoxicity; **ADCC**, antibody-dependent cell-mediated cytotoxicity; **BCMA**, B cell maturation antigen; **MMAF**, monomethyl auristatin F.

**Mechanisms of action**

1. **BCMA receptor signaling inhibition**
2. **ADC mechanism**
   - Targets dividing cells
3. **ADCC mechanism**
   - Targets dividing and non-dividing cells
4. **Immunogenic cell death**

**Belantamab + bortezomib + dex DREAMM-6**

*In patients with ≥1 prior line of therapy, B-Vd treatment had an ORR of 78% (95% CI 52.4-93.6)*

*CBR was 83% (95% CI 58.6-96.4)*

*All patients had an evaluable response*

*50% of patients experienced VGPR*

*DoR is not yet reached*

*In patients with ≥1 prior line of therapy, Vd treatment demonstrated an ORR of 50%-63%*
DREAMM-5 Belantamab in combination with 5 different novel agents


CELMoDS and Small Molecule Inhibitors
Iberdomide

- Oral, potent novel CRBN E3 ligase modulator compound that co-opts Cereblon to enable enhanced degradation of target proteins including Ikaros and Aiolos
- In preclinical models, induces potent direct antmyeloma and immune-stimulatory activity
- Active in len- and pom-resistant myeloma cell lines and enhances cell mediated killing through immune stimulation.


Iberdomide in combination with daratumumab, bortezomib and carfilzomib

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>IberDd (N=43)</th>
<th>IberVd (N=25)</th>
<th>IberKd (N=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>45.9%</td>
<td>56%</td>
<td>50%</td>
</tr>
<tr>
<td>Median DOR</td>
<td>NR</td>
<td>35.7 weeks</td>
<td>NR</td>
</tr>
</tbody>
</table>

RP2D 1.6 mg in IberDd cohort
Dose evaluation continues in IberVd and IberKd cohorts.

CAR-T Cell Therapy

In myeloma-CAR-T cells target myeloma-specific antigens, i.e. BCMA

Timeline of CAR-T cell Development in Multiple Myeloma

- 1990: First-generation CAR (CD3ξ)
- 1993: First-generation CAR (CD3ξ)
- 2000: 2nd generation CAR (CD28-CD3ξ)
- 2004: 2nd generation CAR (4-1BB-CD3ξ)
- 2007: 4th generation CAR (TRUCKs)
- 2011: FDA approval of CD19 CAR T therapy (Kymriah) for ALL
- 2017: FDA approval of CD19 CAR T therapy (Breyana) for NHL
- 2019: cilta-cel (JNJ-5613) granted Breakthrough therapy designation award by FDA
- 2020: FDA approval of cilta-cel (JNJ-5613) for myeloma?
- 2021: FDA approval of Idec-cel (bb2121) for myeloma?
Primary Objectives:
Phase 1b: Safety and RP2D
Phase 2: Efficacy

Key Eligibility:
- Progressive MM per IMWG criteria
- 3 or more prior lines of therapy OR double refractory
- Prior PI, IMiD, and anti-CD38
- ECOG PS 1 or better

Usmani S et al, ASCO 2021
CARTITUDE-1: Overall Response Rate

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 sCR: 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 risk²³⁴)

Presented By: Saad Usmani

Usmani S et al, ASCO 2021

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Ide-Cel versus Cilta-Cel

<table>
<thead>
<tr>
<th>CART</th>
<th>Ide-Cel</th>
<th>Cilta-Cel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design</td>
<td>KarMM-A-2 (phase 2)</td>
<td>CARTITUDE-1 (phase 1b/2)</td>
</tr>
<tr>
<td>Target</td>
<td>BCMA</td>
<td>BCMA</td>
</tr>
<tr>
<td>Patients, median age</td>
<td>n= 128, 61</td>
<td>n= 97, 61</td>
</tr>
<tr>
<td>Median prior lines</td>
<td>6 (3-6)</td>
<td>6 (3-3)</td>
</tr>
<tr>
<td>Triple-class/penta refractory</td>
<td>84%/26%</td>
<td>87%/42.3%</td>
</tr>
<tr>
<td>Tumor BCMA expression (&gt;50%)</td>
<td>85%</td>
<td>91.9%</td>
</tr>
<tr>
<td>CART target dose</td>
<td>150 – 450 x 10⁶ CAR T-cells</td>
<td>0.75 x 10⁶ CAR T-cells/kg</td>
</tr>
<tr>
<td>ORR at therapeutic dose</td>
<td>81% (450 x 10⁶)</td>
<td>97.9% (0.75 x 10⁶)</td>
</tr>
<tr>
<td>sVGPR/sCR/IRM/CRD rates</td>
<td>65%/39%/28%</td>
<td>94.8%/80.4%/57.7%</td>
</tr>
<tr>
<td>PFS/DOR</td>
<td>12.1(8.8–12.3)/11.3 (10.3–11.4)</td>
<td>18-month PFS - 66%/DOR - 21.8 m</td>
</tr>
<tr>
<td>OS</td>
<td>19.4 mo (95% CI, 18.2–NE)</td>
<td>18-month OS - 80.9%</td>
</tr>
<tr>
<td>CRS (any Grade&gt;Grade 3)</td>
<td>96%/6%</td>
<td>94.8%/5.4%</td>
</tr>
<tr>
<td>Median time to onset/duration of CRS</td>
<td>1 day (1-12)/5 days (1-63)</td>
<td>7 days (1-12)/4 days (1-97)</td>
</tr>
<tr>
<td>Neurotoxicity (any Grade&gt;Grade 3)</td>
<td>18%/3%</td>
<td>20%/0.3%</td>
</tr>
<tr>
<td>Neutropenia (any Grade&gt;Grade 3)</td>
<td>91%/89%</td>
<td>95.9%/94.8%</td>
</tr>
<tr>
<td>Anemia (any Grade&gt;Grade 3)</td>
<td>70%/60%</td>
<td>81.4%/68%</td>
</tr>
<tr>
<td>Thrombocytopenia (any Grade&gt;Grade 3)</td>
<td>63%/52%</td>
<td>79.4%/59.8%</td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>27%/8%</td>
<td>32%/3.1%</td>
</tr>
<tr>
<td>Hypophosphatemia (any Grade&gt;Grade 3)</td>
<td>30%/16%</td>
<td>30.9%/7.2%</td>
</tr>
</tbody>
</table>

Novel CAR-T Cell Approaches

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Sponsor</th>
<th>Phase</th>
<th>Antigen</th>
<th>Co-Signaling Domain</th>
<th>Transfer Method</th>
<th>Cell Source</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT03455972</td>
<td>Soochow University</td>
<td>1-2</td>
<td>CD19+ BCMA</td>
<td>OX40/CD28+ EGFRt</td>
<td>Lentiviral</td>
<td>autologous</td>
<td>ORR 100%</td>
</tr>
<tr>
<td>NCT04613557</td>
<td>Celyad</td>
<td>1</td>
<td>BCMA</td>
<td>NA</td>
<td>NA</td>
<td>Allogeneic - shRNA based elimination of TCR</td>
<td>NA</td>
</tr>
<tr>
<td>NCT04093596</td>
<td>Allogene</td>
<td>1</td>
<td>BCMA</td>
<td>NA</td>
<td>N/A</td>
<td>Allogeneic</td>
<td>ORR 60% at Dose-level 3</td>
</tr>
</tbody>
</table>

Incremental Cost-effectiveness Thresholds for Coverage

**Key Findings: Incremental cost-effectiveness**

- Between $50,000 and $150,000 per QALY is generally considered to be cost-effective in the US
- Societal willingness to pay (~1-3x per capita GDP)
- Individual WTP (~2x annual salary)

UK: ~$30,000/QALY
Sweden: ~$50,000/QALY

**Ide-Cel Cost Effective Analysis**

- Ide-cel
  - List Price: $419,500 per infusion
  - Total cost: $646,000
- Life years gained: 1.5
- Incremental cost-effectiveness ratio: $319,000/QALY

**Probabilistic sensitivity analysis**
- < $50,000 / QALY: <1%
- < $100,000 / QALY: <1%
- < $150,000 / QALY: 3%

**Conclusions:**
- Ide-cel provides net clinical benefit over historical treatment, though uncertainty is large
- The therapy is NOT cost effective at current prices
- Cost/QALY >> $150,000
- Discounts from the list price of at least 37% are needed to approach reasonable willingness to pay thresholds in the US

Tice JA, ASCO 2021.
Bi-Specifics/T-cell Engagers

BiTEs have potential advantages over CAR-T

- Off the shelf v time consuming production
- Precise dosing vs drug variability
- Broad range of specifies
- Improved tolerability with diminished rate sof CRS/ICANS/hematotoxicity.
- Retreatment has been successful
- Deepest remission after 1- 3months (CAR –T >2 months for optimal response)
Bispecific Antibodies Summary

<table>
<thead>
<tr>
<th>Bispecific</th>
<th>Tecristamab</th>
<th>Elranatamab</th>
<th>Talquetamab</th>
<th>AMG-701</th>
<th>CC-93269</th>
<th>REGN5458</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target</td>
<td>BCMA</td>
<td>BCMA</td>
<td>GPRCS D</td>
<td>BCMA</td>
<td>BCMA</td>
<td>BCMA</td>
</tr>
<tr>
<td>Treatment</td>
<td>Weekly SC</td>
<td>Weekly SC</td>
<td>Weekly SC</td>
<td>Weekly IV</td>
<td>Weekly IV</td>
<td>Weekly IV</td>
</tr>
<tr>
<td>Patients (N)</td>
<td>73</td>
<td>30</td>
<td>82</td>
<td>85</td>
<td>30</td>
<td>49</td>
</tr>
<tr>
<td>Prior lines</td>
<td>5</td>
<td>8</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Triple-class refractory</td>
<td>79%</td>
<td>87%</td>
<td>99%</td>
<td>62%</td>
<td>90%</td>
<td>100%</td>
</tr>
<tr>
<td>ORR at therapeutic dose</td>
<td>65% (≥VGPR 58%)</td>
<td>83.3% (≥VGPR 66.7%)</td>
<td>70% (≥VGPR 60%)</td>
<td>83% (≥VGPR 50%)</td>
<td>88.9%</td>
<td>62.5%</td>
</tr>
<tr>
<td>Duration of Response</td>
<td>Median follow-up 9 months – 80% continuing treatment</td>
<td>Not reached at 13 months</td>
<td>Not reached at 7.2 months</td>
<td>NR (6.5 months)</td>
<td>NR</td>
<td>6 months</td>
</tr>
<tr>
<td>CRS (Grade 1/2)</td>
<td>60% / 15%</td>
<td>83.3% / 16.7%</td>
<td>67%</td>
<td>27/28/9</td>
<td>76.7</td>
<td>39</td>
</tr>
<tr>
<td>ADA (immunogenicity)</td>
<td>1%</td>
<td>10.7%</td>
<td>12%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Promising Responses in Triple-Class Exposed Disease
Talquetemab: GPRC5D x CD3 Bispecific

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SC Total n=82</th>
<th>RP2D (405 μg/kg SC QW) n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior lines of therapy, n, median (range)</td>
<td>6.0 (2–17)</td>
<td>6.0 (2–14)</td>
</tr>
<tr>
<td>Exposure status, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior BCMA therapy*</td>
<td>20 (24)</td>
<td>8 (27)</td>
</tr>
<tr>
<td>Triple-class*</td>
<td>81 (99)</td>
<td>30 (100)</td>
</tr>
<tr>
<td>Penta-drug*</td>
<td>64 (78)</td>
<td>24 (80)</td>
</tr>
<tr>
<td>Refractory status, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PV*</td>
<td>69 (84)</td>
<td>26 (83)</td>
</tr>
<tr>
<td>Carfilzomib</td>
<td>54 (66)</td>
<td>19 (63)</td>
</tr>
<tr>
<td>IMiD*</td>
<td>76 (93)</td>
<td>28 (93)</td>
</tr>
<tr>
<td>Pomalidomide</td>
<td>67 (82)</td>
<td>26 (87)</td>
</tr>
<tr>
<td>Anti-CD38 mAb</td>
<td>77 (94)</td>
<td>30 (100)</td>
</tr>
<tr>
<td>BCMA*</td>
<td>14 (17)</td>
<td>5 (16)</td>
</tr>
<tr>
<td><strong>Triple-class</strong></td>
<td>62 (76)</td>
<td>23 (77)</td>
</tr>
<tr>
<td><strong>Penta-drug</strong></td>
<td>23 (28)</td>
<td>6 (20)</td>
</tr>
<tr>
<td>To last line of therapy</td>
<td>69 (84)</td>
<td>26 (87)</td>
</tr>
</tbody>
</table>


BiTes versus CAR-T

Einsele H, IMW 2021.
BiTes versus CAR-T

**Goals for Treatment for Triple Refractory Myeloma**

- Improve symptoms
- Obtain a deep response
- Use your best therapy rather than reserve for later
- Consider Clinical Trials

---

**Efficacy/Toxicity**

<table>
<thead>
<tr>
<th></th>
<th>CAR T</th>
<th>Bispecifics</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>80 - 100%</td>
<td>&gt;60 - 83%</td>
</tr>
<tr>
<td>CR</td>
<td>40 - 85%</td>
<td>13 - 50%</td>
</tr>
<tr>
<td>PFS</td>
<td>&gt;1 - 1.5 yrs</td>
<td>&gt;6 mo.</td>
</tr>
<tr>
<td>CRS Gr. 3</td>
<td>3 - 6%</td>
<td>0 - 3%</td>
</tr>
<tr>
<td>ICANS Gr. 3</td>
<td>3 - 10%</td>
<td>0 - 1%</td>
</tr>
</tbody>
</table>

Following CAR T Cell Therapy grade 3 cyopenia can last for of 2-3 months !!

⇒ Hematotoxicity clearly less frequent/less severe/shorter after BiTEs vs CART cells

Munshi N et al. NEJM 2012; Madduri D et al. ASH 2020 #177; Garfall AL et al. ASH 2020 #180; Lesokhin AM et al. ASH 2020 #3206; Madduri D et al. ASH 2020 #291; Rodriguez et al. ASH 2020 #295; Chari A et al. ASH 2020 #290; Cohen AD et al. ASH 2020 #292; Harrison S et al. ASH 2020 #181; Costello C et al. ASH 2020 #134; Kumar et al. ASH 2020 #133; Piasecki et al. ASH 2020 #2350; Colonna et al. ASH 2020 #2358.
COVID19 and MM Vaccination

The present study shows that patients with MM seem to mount a less effective immune response to vaccination against COVID-19.

Older Patients With Myeloma May Have Suboptimal Response to COVID-19 Vaccination


COVID 19 Vaccination in Patients with Multiple Myeloma

Should I get the COVID-19 vaccine?
The IMF strongly recommends that patients with multiple myeloma (MM), smoldering multiple myeloma (SMM), or monoclonal gammopathy of undetermined significance (MGUS) receive a COVID-19 vaccination with the Pfizer or MODERNA vaccines, whichever is available. These vaccines offer excellent benefits, and in general, have very limited and brief side effects or toxicities. As of now, the efficacy of these vaccines far outweighs any toxicity concerns.

*The IMF is very pleased to note the full approval of the Pfizer-BioNTech COVID-19 vaccine. This reflects what has been both remarkable efficacy plus and an excellent safety profile. This full approval versus the prior Emergency Use Authorization (EUA) will encourage those with vaccine hesitancy to proceed with vaccination. In addition, doctors now have flexibility to prescribe booster shots as appropriate. In the workplace, many more vaccine mandates are now anticipated which can definitely improve safety overall.

How should I make a decision about getting the vaccine?
The decision to take the COVID-19 vaccine is best made with your doctor. PLEASE discuss the planning for vaccination with your doctor. It is possible your doctor may have additional questions or concerns depending upon your exact situation.

Do I have to get the same vaccine for both shots?
Generally speaking, most people will indeed receive the planned two-step dosing for their vaccination with the Pfizer or MODERNA vaccines. If it is feasible to take the same brand of vaccine for both doses, then do so. If not, a slight delay to wait for the same brand of vaccine for your second dose is acceptable. Finally, the use of alternate brand of vaccine can be considered if availability is an issue, but please discuss this with your doctor.

International Myeloma Society COVID-19 and MM Data

• Patients with multiple myeloma are at increased risk of severe infection and higher mortality.

• All patients with myeloma or precursor disease (MGUS and smoldering myeloma) and AL amyloid should be candidates for COVID-19 vaccine and booster.

• Vaccine induced immune response may decrease infection rate and decrease severity of illness.

Timing of Vaccine

• If patient’s myeloma is stable, and holding therapy is not a concern, then the vaccine should be administered between the courses of therapy.

• An ideal situation would be to hold treatment 7 days before 1st dose to 7 days after 2nd dose. This would mean holding MM therapy for around 5-6 weeks, depending upon type of vaccine and the interval between doses.

• Keeping importance of maintaining MM therapy in mind, when such long pause is not possible, consider giving 1st dose of the vaccine 2-7 days after the last dose of MM therapy and up to 10 days before restarting MM therapy, with 2nd vaccination given at the appropriate interval.

• Wait 3 months after auto-SCT.

• Ideal antibody testing is 7-21 days after 2nd vaccination.
Supportive Care/Quality of Life

Bisphosphonates for Myeloma Bone Disease

How they work
- Prevent bone disease from getting worse

Benefits
- Decreases pain and reduces skeletal related fractures

Dosing
- IV infusion in doctor’s office every 3–4 weeks
- Kidney function can alter dosing or choice of drug

Medication types
- Zometa (zoledronic acid): 15-minute infusion
- Aredia (pamidronate): 2-hour infusion

Side effects
- Reduced kidney function
- Fracture of the femur
- Osteonecrosis of the jaw (ONJ)
- Low calcium levels (hypocalcemia)
Newly Approved Xgeva (denosumab) for Bone Loss

- Newly diagnosed MM patients
- 859 patients
- Xgeva (denosumab)
- Zometa
- Both equally effective in delaying a skeletal-related event
- Fewer side effects related to kidney toxicity with Xgeva
- Risk of ONJ is similar in both medications (1.2% higher risk with Xgeva)

Reducing the Risk of ONJ: Oral Health Recommendations

- Complete major dental work before beginning bisphosphonate therapy
- Practice good oral hygiene
- Schedule regular dental visits
- Let your dentist know that you are receiving bisphosphonates
- Keep your doctor informed of dental issues/need for dental work
- Be attentive! ONJ seems to be related to the length of time patients are on bisphosphonates
Orthopedic Procedures to Stabilize the Spine

- Minimally invasive procedures
- Can be performed without hospitalization
- Small incision
- Cement filler stabilizes bone
- Potential for relatively rapid symptom relief (approximately 1 month with kyphoplasty)

Effects of Myeloma: Decreased Kidney Function

- Detection
  - Decreased amount of urine
  - Increase in creatinine and other proteins
- Other causes beside myeloma
  - Hypertension
  - Diabetes
  - Some medications
  - Dehydration
- Treatment
  - Fluids
  - Avoid nonsteroidal anti-inflammatory drugs such as Aleve, Advil/Motrin
  - Plasmapheresis
  - Treat other causes
  - Dialysis (severe)
**Side Effects of Commonly Used Treatments: Velcade**

**Peripheral Neuropathy**

**Potential causes**
- Monoclonal protein deposits on nerves
- Previous use of: Velcade, Thalidomide, Vincristine, melphalan
- Vitamin deficiency

**Signs/Symptoms**
- Weakness
- Numbness/tingling
- Burning
- Muscle cramping

**Treatment**
- Proper foot care/support
- Treat underlying cause
- Medications: oral and topical
- Physical therapy
- Potential neurology consult for further evaluation and treatment
- Dose schedule modifications!

*Don’t forget to discuss side effects with your provider!*

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**Side Effects of Commonly Used Treatments: Lenalidomide (Revlimid)**

**Fatigue**
- Stay active: exercise, exercise, exercise!
- Healthy, well-balanced diet
- Stay hydrated
- Healthy sleep habits

**Diarrhea**
- Increase fluids
- Fiber-binding agents: Metamucil
- Anti-diarrheal medications: Imodium, Cholestyramine
- Diet management

**Muscle cramps**
- Tonic water
- Increase hydration
- Stretching/massage
- Assess for other causes (electrolytes, low calcium)
- Decrease dose

**Rash**
- Antihistamines: loratadine, cetirizine, Benadryl
- Over-the-counter anti-itch creams – hydrocortisone or Benadryl
- Potential referral to dermatology

*Don’t forget to discuss side effects with your provider!*
Side Effects of Commonly Used Treatments: Carfilzomib (Kyprolis)

**Common side effects**
- Fatigue
- In minority of patients: trouble breathing or shortness of breath, drop in blood counts

**Infrequently observed but potentially serious side effects**
- Concerns: heart and lung toxicities
- Side effects: reversible and manageable

**Signs to watch for**
- Shortness of breath, difficulty breathing
- Chest pain
- Elevated blood pressure
- Headache

**Treatment**
- Manage blood pressure: low sodium diet, BP control
- Heart evaluation: EKG and echocardiogram
- Lung evaluation: Pulmonary function testing
- Dose changes

Don’t forget to discuss side effects with your provider!

Side Effects of Commonly Used Treatments: Daratumumab (Darzalex)

- Infusion-related reactions
- Fatigue
- Nausea
- Back pain
- Fever
- Changes in blood counts (anemia, thrombocytopenia, neutropenia)
Side Effects of Commonly Used Treatments: Steroids (Dexamethasone)

- Insomnia
- Fluid retention
- Mood changes
- Dyspepsia—heartburn
- Elevation in glucose

- Healthy sleep habits
- Timing
- Medication to assist with sleeping as needed
- Monitor for swelling of extremities and “puffy” face
- Monitor weight changes/gain
- Reduce dose
- Irritable, anxiety, difficulty concentrating
- Severe cases → depression, euphoria
- Dietary modifications (spicy, acidic foods)
- Avoid NSAIDs
- Acid-blocking medications
- Take steroid with food; use enteric-coated aspirin with food
- Monitor glucose and refer/treat as needed

Lifestyle Enhancements

- Eat a well-balanced diet
- Get more exercise
- Regular sleep/rest periods
- Decrease alcohol consumption
- Give up tobacco
- Minimize or eliminate stress
- Take care of your emotional/mental well-being as well as your physical health!

OPTIMISTIC OUTLOOK!
QUESTION & ANSWER
Living with Multiple Myeloma

• Ask a question by phone:
  – Press star (*) then the number 1 on your keypad.

• Ask a question by web:
  – Type your question
  – Click Enter

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.

**CLINICAL TRIAL SUPPORT CENTER**
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

**NUTRITION CONSULTATIONS**
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email. www.LLS.org/Consult.

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**LLS EDUCATION & SUPPORT RESOURCES**

**Online Chats**
Online Chats are free, live sessions, moderated by oncology social workers.

*Banding Together Fridays Online Chat* is specifically addressing questions and concerns about living with a blood cancer during COVID-19. Register now at 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 cancer: www.LLS.org/Finances

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

We have one goal: A world without blood cancers