Therapy for Relapsed/Refractory Multiple Myeloma

Michael Green, MD
The Permanente Medical Group
Who am I?
Who am I?
Disclosures for
Dr. Michael Green

<table>
<thead>
<tr>
<th>Category</th>
<th>Statement</th>
</tr>
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<tbody>
<tr>
<td>Research Support / P.I.</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Employee</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Consultant</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Major Stockholder</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
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<td>Speakers Bureau</td>
<td>No relevant conflicts of interest to declare</td>
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<tr>
<td>Honoraria</td>
<td>No relevant conflicts of interest to declare</td>
</tr>
<tr>
<td>Scientific Advisory Board</td>
<td>No relevant conflicts of interest to declare</td>
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</tbody>
</table>

Presentation does NOT include discussion of the off-label use of a drug or medical device
Treatment options in relapsed/refractory MM

- Proteasome inhibitors
  - Bortezomib
  - Carfilzomib
  - Ixazomib
- Immunomodulators
  - Lenalidomide
  - Pomalidomide
  - Thalidomide
- Monoclonal Antibodies
  - Daratumumab
  - Elotuzumab
- HDAC Inhibitors
  - Panobinostat
- Alkylating Agents
  - Cyclophosphamide
  - Bendamustine
  - Melphalan
- Cytotoxics
  - Vincristine
  - Doxorubicin
  - Cisplatin
  - Etoposide
- Steroids
- *** Selective Inhibitors of Nuclear Export
  - Sellinexor
# NCCN Guidelines Version 3.2019
## Multiple Myeloma

### Myeloma Therapy

<table>
<thead>
<tr>
<th>Preferred Regimens</th>
<th>Other Recommended Regimens</th>
<th>Useful In Certain Circumstances</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Bortezomib/lenalidomide/dexamethasone</td>
<td>• Daratumumab(^b)/bortezomib/dexamethasone (category 1)(^d)</td>
<td>• Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide (DT-PACE)(^i) ± bortezomib (VTD-PACE)(^x)</td>
</tr>
<tr>
<td>• Carfilzomib (twice weekly)(^h)/dexamethasone (category 1)(^l)</td>
<td>• Daratumumab(^b)/lenalidomide/dexamethasone (category 1)(^d)</td>
<td>• High-dose cyclophosphamide</td>
</tr>
<tr>
<td>• Carfilzomib (weekly)(^h)/dexamethasone</td>
<td>• Eloxatin(^b)/lenalidomide/dexamethasone (category 1)(^d)</td>
<td></td>
</tr>
<tr>
<td>• Carfilzomib(^h)/lenalidomide/dexamethasone (category 1)(^o)</td>
<td>• Ixazomib(^b)/lenalidomide/dexamethasone (category 1)(^o)</td>
<td></td>
</tr>
</tbody>
</table>

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\(^a\) Preferred regimens are those with the highest quality evidence.  
\(^b\) For patients who have had at least 1 prior regimen.  
\(^c\) Therapy recommendations are for patients who have received at least 1 prior line of therapy.  
\(^d\) For patients who have received prior therapy with lenalidomide or bortezomib.  
\(^e\) For patients who have received prior therapy with lenalidomide and bortezomib.  
\(^f\) For patients who have received prior therapy with lenalidomide and bortezomib and have received an active immunomodulator.  
\(^g\) For patients who have received prior therapy with lenalidomide.  
\(^h\) For patients who have received prior therapy with bortezomib.  
\(^i\) For patients who have received prior therapy with bortezomib and have received an active immunomodulator.  
\(^j\) For patients who have received prior therapy with bortezomib and have received immunomodulator and an immunomodulator.  
\(^k\) For patients who have received prior therapy with bortezomib, an active immunomodulator, and an immunomodulator.  
\(^l\) For patients who have received prior therapy with bortezomib and have received an active immunomodulator and an immunomodulator.  
\(^m\) For patients who have received prior therapy with bortezomib and have received an active immunomodulator and an immunomodulator.  
\(^n\) For patients who have received prior therapy with lenalidomide.  
\(^o\) For patients who have received prior therapy with lenalidomide and bortezomib.  
\(^p\) For patients who have received prior therapy with lenalidomide and bortezomib and have received an active immunomodulator.  
\(^q\) For patients who have received prior therapy with lenalidomide.  
\(^r\) For patients who have received prior therapy with lenalidomide and bortezomib.  
\(^s\) For patients who have received prior therapy with lenalidomide and bortezomib and have received an active immunomodulator.  
\(^t\) For patients who have received prior therapy with lenalidomide.  
\(^u\) For patients who have received prior therapy with lenalidomide and bortezomib.  
\(^v\) For patients who have received prior therapy with lenalidomide and bortezomib and have received an active immunomodulator.  
\(^w\) For patients who have received prior therapy with lenalidomide.  
\(^x\) For patients who have received prior therapy with lenalidomide and bortezomib.  
\(^y\) For patients who have received prior therapy with lenalidomide and bortezomib and have received an active immunomodulator.  
\(^z\) For patients who have received prior therapy with lenalidomide.  
\(^{1}\) For patients who have received prior therapy with lenalidomide and bortezomib.  
\(^{2}\) For patients who have received prior therapy with lenalidomide and bortezomib and have received an active immunomodulator.  
\(^{3}\) For patients who have received prior therapy with lenalidomide.  
\(^{4}\) For patients who have received prior therapy with lenalidomide and bortezomib.  
\(^{5}\) For patients who have received prior therapy with lenalidomide and bortezomib and have received an active immunomodulator.  

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This table provides a summary of therapy options for patients with multiple myeloma, categorized by preferred regimens, other recommended regimens, and useful in certain circumstances. The table includes specific combinations of drugs and dosages, as well as indications for use based on prior therapy. The guidelines are designed to help healthcare providers make informed decisions about treatment regimens for their patients.
Factors to consider for treatment selection

• Disease related factors
  – Nature of relapse: Indolent vs. aggressive
  – Risk stratification:
    Cytogenetic abnormalities
  – Disease burden

• Patient related factors
  – Renal insufficiency
  – Neuropathy
  – Heart Disease
  – Patient preference: convenience, travel, insurance, cost
Factors to consider for treatment selection

• Previous therapy
  – Progression
  – Intolerance
  – Maintenance dosing
  – Depth and duration of response

• Treatment toxicity
  – Performance Status
  – Neuropathy: bortezomib, thalidomide
  – Cardiac issues: carfilzomib
  – COPD: daratumumab
  – DVT/PE: IMIDs
  – Financial
Clinical Trial Review Cheat Sheet

- Phase of study
- Location of study
- Patient Population: Newly Diagnosed, Early Relapse, Late Relapse, and Heavily Pretreated
- End points: Surrogate Markers versus Patient Oriented
- Toxicities
So today I called for Progression Free Survival (PFS) to be renamed as Progression Free Duration (PFD) because “improved PFS” incorrectly sends out a signal to patients that survival is prolonged—when in reality it may or may not be prolonged & can even be worse.

@TheLancetOncol
Early Relapse
Triplet regimens vs. lenalidomide-dexamethasone

Carfilzomib, Lenalidomide, and Dexamethasone for Relapsed Multiple Myeloma

Prior lenalidomide exposure: 20%

Stewart et al. N Engl J Med 2017
Triplet regimens vs. lenalidomide-dexamethasone

Oral Ixazomib, Lenalidomide, and Dexamethasone for Multiple Myeloma

A Progression-free Survival in the Intention-to-Treat Population

- Hazard ratio: 0.74 (95% CI, 0.59–0.94)
- Median Progression-free Survival (mo):
  - Ixazomib Group: 20.6
  - Placebo Group: 14.7
- No. of Events of Progression or Death:
  - Ixazomib Group: 129
  - Placebo Group: 157

Prior lenalidomide exposure: 12%

Moreau et al.
Van de Donk, *Immunol Rev*
Triplet regimens vs. lenalidomide-dexamethasone

**Daratumumab, Lenalidomide, and Dexamethasone for Multiple Myeloma**

**Median PFS**
- RD 17.5 months
- Dara-RD Not reached

**Prior lenalidomide exposure:** 18%

Elotuzumab

• Binds SLAMF7/CS1 on MM, inducing ADCC
• Also binds same receptor on NK cells, stimulating activity

Hsi ED, Clin Can Res 2008
Triplet regimens vs. lenalidomide-dexamethasone

Elotuzumab Therapy for Relapsed or Refractory Multiple Myeloma

Median PFS
RD 14.9 months
Elo-RD 19.4 months

Prior lenalidomide exposure: 6%

Lonial et al.
Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study

Prior lenalidomide exposure: 38%

Triplet regimens vs. bortezomib-dexamethasone

Daratumumab, Bortezomib, and Dexamethasone for Multiple Myeloma


Prior lenalidomide exposure: 68%
Triplet regimens vs. bortezomib-dexamethasone

Randomized phase 2 study: elotuzumab plus bortezomib/dexamethasone vs bortezomib/dexamethasone for relapsed/refractory MM

CLINICAL TRIALS AND OBSERVATIONS

Prior lenalidomide exposure: 75%

## Selected toxicity of new combinations

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>ASPIRE (KRd)</th>
<th>TOURMALINE-MM1 (IRd)</th>
<th>ELOQUENT-2 (EloRd)</th>
<th>POLLUX (DRd)</th>
<th>ENDEAVOR (Kd)</th>
<th>CASTOR (DVD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral neuropathy</td>
<td>3%</td>
<td>2%</td>
<td>NA</td>
<td>NA</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>3%</td>
<td>3%</td>
<td>NA</td>
<td>NA</td>
<td>5%</td>
<td>NA</td>
</tr>
<tr>
<td>Cardiac toxicity</td>
<td>7%</td>
<td>6%</td>
<td>NA</td>
<td>NA</td>
<td>8%</td>
<td>NA</td>
</tr>
<tr>
<td>Pneumonia/infections</td>
<td>2%</td>
<td>1%</td>
<td>NA</td>
<td>10%</td>
<td>8%</td>
<td>11%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4%</td>
<td>6%</td>
<td>5%</td>
<td>5%</td>
<td>3%</td>
<td>4%</td>
</tr>
</tbody>
</table>
Phase III Studies: Early Relapse Disease

- >10 Randomized Trials
  - Many options – “dealer’s choice”

<table>
<thead>
<tr>
<th>Trial</th>
<th>Regimen</th>
<th>Prior Therapies</th>
<th>N</th>
<th>Median PFS, * mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASPIRE[a]</td>
<td>KRd vs Rd</td>
<td>1 to 3</td>
<td>792</td>
<td>26.3 vs 17.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HR = 0.69 (P = .0001)</td>
</tr>
<tr>
<td>ENDEAVOR[b]</td>
<td>Kd vs Vd</td>
<td>1 to 3</td>
<td>929</td>
<td>18.7 vs 9.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HR = 0.53 (P &lt; .0001)</td>
</tr>
<tr>
<td>TOURMALINE-MM1[c]</td>
<td>IRd vs Rd</td>
<td>1 to 3</td>
<td>722</td>
<td>20.6 vs 14.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HR = 0.74 (P = .01)</td>
</tr>
<tr>
<td>ELOQUENT-2[d]</td>
<td>ERd vs Rd</td>
<td>1 to 3, 10% prior len</td>
<td>646</td>
<td>19.4 vs 14.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HR = 0.70 (P &lt; .001)</td>
</tr>
<tr>
<td>POLLUX[e]</td>
<td>DRd vs Rd</td>
<td>≥ 1</td>
<td>569</td>
<td>&gt;32 vs 18.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HR = 0.37 (P &lt; .001)</td>
</tr>
<tr>
<td>CASTOR[f]</td>
<td>DVd vs VD</td>
<td>≥ 1</td>
<td>498</td>
<td>16.7 vs 7.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HR = 0.39 (P &lt; .001)</td>
</tr>
</tbody>
</table>

ASH 2018 Update:
- Pollux Study in RRMM
- PFS D-Rd 44.5 m vs Rd 17.5 m

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Late Relapse
Pomalidomide-based regimens

Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISMM): a randomised, open-label, phase 3 trial

Richardson et al. Lancet Oncol 2019
Pomalidomide-based regimens

Elotuzumab plus Pomalidomide and Dexamethasone for Multiple Myeloma

A Progression-free Survival

Hazard ratio for disease progression or death, 0.54 (95% CI, 0.34–0.86)  
\( P=0.008 \)

No. at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<th>17</th>
<th>18</th>
<th>19</th>
<th>20</th>
<th>21</th>
<th>22</th>
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<tr>
<td>Elotuzumab group</td>
<td>60</td>
<td>54</td>
<td>48</td>
<td>46</td>
<td>43</td>
<td>41</td>
<td>37</td>
<td>33</td>
<td>32</td>
<td>27</td>
<td>25</td>
<td>15</td>
<td>17</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Control group</td>
<td>57</td>
<td>51</td>
<td>42</td>
<td>33</td>
<td>31</td>
<td>24</td>
<td>22</td>
<td>20</td>
<td>16</td>
<td>14</td>
<td>10</td>
<td>8</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>1</td>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>

Dimopoulos et al.  
N Engl J Med 2018
Pomalidomide-based regimens

CLINICAL TRIALS AND OBSERVATIONS

Daratumumab plus pomalidomide and dexamethasone in relapsed and/or refractory multiple myeloma

ORR = 60%

17% CR or better
8% VGPR or better
9% VGPR or better
25% CR or better
18% sCR

98% previously exposed to len + bort
71% refractory to len + bort

Chari et al. Blood 2017
Pomalidomide-based regimens

Carfilzomib, Pomalidomide, Dexamethasone
Feasible in Patients With Relapsed/Refractory MM

- KPd demonstrated favorable outcomes in mostly lenalidomide-refractory and PI-naive/sensitive relapsed/refractory MM
- 84% of pts achieved PR or better
- Median PFS 12.9 months, with OS not yet reached

Rosenbaum et al. ASCO 2016: 8007
Heavily Pretreated/Multiply Relapsed
At present the playing field is not level. New drugs that are incremental improvements over existing drugs command high prices on par with truly innovative drugs that deliver landmark benefits. So why take risk innovating when incremental tinkering can deliver handsome rewards?
Panobinostat-based regimens

A phase 2 study of panobinostat with lenalidomide and weekly dexamethasone in myeloma

- n=27
- 81% refractory to lenalidomide
- 52% refractory to bortezomib
- ORR 41%
- CBR 74%
- Median PFS: 7.1 months

Chari et al. Blood Adv 2017
Panobinostat-based regimens

Panobinostat plus bortezomib and dexamethasone versus placebo plus bortezomib and dexamethasone in patients with relapsed or relapsed and refractory multiple myeloma: a multicentre, randomised, double-blind phase 3 trial

Median PFS
VD 8.1 months
Pano-VD 12 months
Prior lenalidomide exposure: 20%

San Miguel et al.
Lancet Oncol 2014
Oral Selinexor–Dexamethasone for Triple-Class Refractory Multiple Myeloma

N=122

100% refractory to ≥1 IMID, ≥1 PI and daratumumab

53% had high risk cytogenetics
- del17p
- t(4;14)
- t(14;16)
- gain1q

Grade ≥3 adverse events
- Thrombocytopenia (58%), anemia (44%), neutropenia (21%), Fatigue (25%), hyponatremia (21%), nausea (10%)

Chari et al.
N Engl J Med 2019
Pending
Overall Response\textsuperscript{a} and Confirmed MRD-negative Rates

- Median follow-up: 12.0 months
- Optional MRD testing in 11 patients with CR/sCR; 4 were MRD negative at 10\textsuperscript{-5}

Responses are anticipated to deepen over longer follow-up

Daratumumab + Carfilzomib + Dexamethasone MMY1001 Chari et al. ASCO 2018
Progression-free Survival Across Subgroups

- Median follow-up: 12.0 months

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Median PFS, mo</th>
<th>12-month PFS, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-treated</td>
<td>NE</td>
<td>71%</td>
</tr>
<tr>
<td>Len-exposed but not refractory</td>
<td>NE</td>
<td>87%</td>
</tr>
<tr>
<td>Len-refractory</td>
<td>14.1 (95% CI, 12.0-NE)</td>
<td>62%</td>
</tr>
<tr>
<td>PI/IMiD-refractory</td>
<td>NE (95% CI, 9.4-NE)</td>
<td>51%</td>
</tr>
</tbody>
</table>

Encouraging PFS observed in lenalidomide- and PI/IMiD-refractory patients
Global Phase III Pivotal Study of Isatuximab with Pd in RRMM

Richardson et al. ASCO 2018
Anti-BCMA CAR T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma

Refractory to:
- Bortezomib 61%
- Carfilzomib 58%
- Lenalidomide 73%
- Pomalidomide 79%
- Daratumumab 55%

Grade ≥3 adverse events:
- Neutropenia 85%
- Thrombocytopenia 45%
- Anemia 45%
- Cytokine release sx 6%

Targeting B-cell maturation antigen with GSK2857916 antibody-drug conjugate in relapsed or refractory multiple myeloma (BMA117159): a dose escalation and expansion phase 1 trial

Refractory to:
- Proteasome inhibitors 97%
- IMIDs 91%
- Daratumumab 37%

ORR 60%

Median PFS 8 months

Trudel et al. Lancet Oncol 2018
BCMA directed therapy

Anti-BCMA Bispecific T-cell engager (BiTE)

Hipp et al. Leukemia 2017
## Options for Relapsed/Refractory Multiple Myeloma

<table>
<thead>
<tr>
<th>IMids</th>
<th>Proteasome Inhibitors</th>
<th>Monoclonal Abs inhibitor</th>
<th>HDAC-inhibitor</th>
<th>BCL-2 inhibitor</th>
<th>XPO1 inhibitor</th>
<th>Anti-BCMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalidomide</td>
<td>Bortezomib</td>
<td>Daratumumab</td>
<td>Panobinostat</td>
<td>Venetoclax</td>
<td>Selinexor</td>
<td>AMG 4207</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anti-BCMA BiTE®</td>
<td></td>
<td>BCMA-ADC-GSK</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Bb2121/CARs</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>Carfilzomib</td>
<td>Elotuzumab</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Pomalidomide</td>
<td>Ixazomib</td>
<td>Isatuximab²</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Oprozomib¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>MOR202³</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Atezolizumab⁴</td>
<td></td>
<td></td>
<td></td>
<td>(Anti-PD-L 1 Ab)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ASH 2018</th>
<th>Oprozomib Hari # 803</th>
<th>Isatuximab Dimopoulos # 155</th>
<th>MOR202 Raab # 152</th>
<th>Atezolizumab Cho # 597</th>
<th>Venetoclax Costa # 303</th>
<th>Selinexor Chari # 598</th>
<th>AMG 420 Topp # 1010</th>
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</thead>
<tbody>
<tr>
<td>Mechanism</td>
<td>PI</td>
<td>Anti-CD38</td>
<td>Anti-CD38</td>
<td>Anti-PD-L1 Ab</td>
<td>BCL-2 Inhibitor</td>
<td>XPO-1 inhibitor</td>
<td>Anti-BCMA BITE</td>
</tr>
<tr>
<td></td>
<td>Oral (IR 200 mg/d)</td>
<td>IV 20 mg/kg</td>
<td>IV (30 min-2 hours)</td>
<td>IV 840 mg</td>
<td>Oral daily</td>
<td>Oral biWeekly</td>
<td>IV Continuous Infusion</td>
</tr>
<tr>
<td></td>
<td>(IR) or (GR) Day 1-2 QW</td>
<td>QWx1, then Q2W</td>
<td>QW</td>
<td>Cycle 1 Day 1.15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase/N</td>
<td>1b/N=47</td>
<td>2/N=164</td>
<td>1/N=56</td>
<td>1b/N=40</td>
<td>1-2/N=42</td>
<td>2/N=123</td>
<td>FIH 1/N=35</td>
</tr>
<tr>
<td>Combination</td>
<td>O+Dex O+Pom+Dex</td>
<td>Isa or Isa+Dex</td>
<td>-MOR+Dex MOR+Dex+Len MOR+Dex+Pom</td>
<td>Atezo+dara Atezo+dara+Len Atezo+dara+pom</td>
<td>Ven+Kyprolis+dex Selinexor+Dex Single agent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior Lines of Treatment</td>
<td>4 (1-17)</td>
<td>4 (2-11)</td>
<td>2-3</td>
<td>4 (1-10)</td>
<td>2 (1-3)</td>
<td>7 (3-18)</td>
<td>Penta-refractory</td>
</tr>
<tr>
<td>ORR</td>
<td>~67%</td>
<td>Isa:26% ≥VGPR 8% IsaD 44% ≥VGPR 18%</td>
<td>-28% -65% -48%</td>
<td>Atezo+dara 26% Atezo+dara+Len 57% Atezo+dara+pom70%</td>
<td>79%≥CR 38% +T11:14 100%</td>
<td>26.2%</td>
<td>2 sCR/MRD neg 6 CRs, 2 PR, 1 VGPR 400 mg ORR 83%</td>
</tr>
<tr>
<td>PFS</td>
<td>Isad:4.86 months Isad:9.26 months</td>
<td>1.5 month NR</td>
<td>15.9 months</td>
<td>PFS</td>
<td>PFS</td>
<td>3.7 months</td>
<td>PFS</td>
</tr>
<tr>
<td>Safety</td>
<td>GI NVD (1 GI bleeding), Anemia, Neutropenia, URI, Pneumonia</td>
<td>IR (40%) 4% d/c Back pain, URI, Pancytopenia</td>
<td>Pancytopenia, Hypertension, URI</td>
<td>G3 Rash G3 Elevated LFTs G3pancreatitis</td>
<td>GI, Pancytopenia, Pneumonia, CHF, AKI, TLS</td>
<td>GI, Pancytopenia, Fatigue, Weight loss, Hyponatremia</td>
<td>CRS, Polyneuropathy, Edema, Infections</td>
</tr>
</tbody>
</table>
CONCLUSIONS – Myeloma Therapies in Relapse

• There are a multitude of treatment options for relapsed Myeloma, it is important to think about optimal sequences individualizing management for patients (preference, comorbidities, disease/relapse characteristics)

• Early relapse
  – First line therapy if durable response
  – Monoclonal antibody based
  – Proteasome Inhibitor based – (High risk disease, PI sensitive)

• Later relapses
  – Pomalidomide based regimens
  – Clinical trial (CAR-T, BITE, Antibody drug conjugate)
  – Cytotoxic chemotherapy

• Need trials exploring the sequencing of drug combinations and optimal duration of treatment
THANK YOU!