ASH 2022 UPDATE - MULTIPLE MYELOMA

FAITH DAVIES
Professor of Medicine, NYU Grossman School of Medicine.
DISCLOSURES

Advisory boards

• Amgen
• AbbVie
• BMS/Celgene
• GSK
• Janssen
• Meridian Therapeutics
• Oncopptide
• Regeneron
• Sanofi
• Takeda

Off label drug use – bispecific antibodies and ADCs
Areas with new important data

- Data concerning population screening for plasma cell dyscrasia (iSTOP study)
- Treatment of high risk smoldering
- Upfront therapy – frail, high risk
- Maintenance
- Relapse therapy
- Disease monitoring (MRD analysis, mass spec)

- Single cell analysis of tumor and microenvironment
Newly diagnosed – Elderly frail patients

- Fitness and ability to tolerate MM treatment varies among older patients
  - Frailty is associated with increased risk of death, disease progression, higher rates of non-hematologic AEs, and treatment discontinuation in patients with MM

- DRd is a standard regimen for newly diagnosed transplant-ineligible patients with MM, but rates of pneumonia are higher with DRd vs Rd, particularly in frail patients

- IFM 2017-03 is a phase III trial evaluating whether a dexamethasone-sparing regimen of daratumumab + lenalidomide would be effective and limit toxicity in frail patients compared with lenalidomide + dexamethasone
  - Current interim analysis at 12 months of therapy reported on response and safety

IFM 2017-03

- Randomized, open-label, multicenter phase III trial

  *Stratification by ISS (I vs II vs III) and age (<80 vs ≥80 yr)*

  Patients aged ≥65 yr with newly diagnosed MM; IFM frailty score ≥2*
  
  (N = 293)

  *IFM frailty score: 0-1 = fit; ≥2 = frail.
  
  Based on age, CCI and ECOG

Randomization 2:1

DR† (n = 199)

- **Daratumumab** SC 1800 mg Q1W for 8 wk;
  then Q2W for 16 wk; then Q4W thereafter
- **Lenalidomide** 25 mg D1-21 Q28D

Rd (n = 94)

- **Lenalidomide** 25 mg D1-21 Q28D
- **Dexamethasone** 20 mg D1, 8, 15, 22 Q28D

Treatment
Continued
until PD or unacceptable AE

†DR included low-dose dexamethasone 20 mg/wk during cycles 1,2, along with SC daratumumab dosing.

- Primary endpoint: PFS (not yet reported)
- Interim analysis at 12 mo of therapy: ORR, ≥ VGPR, MRD rate, grade ≥3 AEs

## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DR (n = 199)</th>
<th>Rd (n = 94)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, yr (range)</td>
<td>81 (68-92)</td>
<td>81 (68-90)</td>
</tr>
<tr>
<td>Age category, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65 to &lt;70 yr</td>
<td>2 (1)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>70 to &lt;75 yr</td>
<td>30 (15)</td>
<td>13 (14)</td>
</tr>
<tr>
<td>75 to &lt;80 yr</td>
<td>49 (25)</td>
<td>19 (20)</td>
</tr>
<tr>
<td>≥80 yr</td>
<td>118 (59)</td>
<td>61 (65)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>101 (51)</td>
<td>48 (51)</td>
</tr>
<tr>
<td>ECOG PS 0/1/2, %</td>
<td>10/46/44</td>
<td>10/50/40</td>
</tr>
<tr>
<td>Charlson ≤1, n (%)</td>
<td>113 (58)</td>
<td>57 (61)</td>
</tr>
<tr>
<td>IFM frailty score, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>57 (29)</td>
<td>35 (37)</td>
</tr>
<tr>
<td>3</td>
<td>81 (41)</td>
<td>26 (28)</td>
</tr>
<tr>
<td>4</td>
<td>44 (22)</td>
<td>24 (26)</td>
</tr>
<tr>
<td>5</td>
<td>17 (9)</td>
<td>9 (10)</td>
</tr>
<tr>
<td>ISS disease stage I/II/III, %</td>
<td>17/51/32</td>
<td>19/53/28</td>
</tr>
<tr>
<td>Measurable disease type, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>113 (57)</td>
<td>49 (52)</td>
</tr>
<tr>
<td>IgA</td>
<td>38 (19)</td>
<td>20 (21)</td>
</tr>
<tr>
<td>PBJ only</td>
<td>21 (11)</td>
<td>10 (11)</td>
</tr>
<tr>
<td>SFLC only</td>
<td>27 (14)</td>
<td>15 (16)</td>
</tr>
<tr>
<td>Cytogenetics profile,* n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard risk</td>
<td>148 (83)</td>
<td>60 (78)</td>
</tr>
<tr>
<td>High risk</td>
<td>31 (17)</td>
<td>17 (22)</td>
</tr>
<tr>
<td>del17p</td>
<td>16 (9)</td>
<td>11 (14)</td>
</tr>
<tr>
<td>t(4;14)</td>
<td>9 (5)</td>
<td>5 (6)</td>
</tr>
<tr>
<td>t(14;16)</td>
<td>6 (3)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Creatinine clearance, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 mL/min</td>
<td>1 (1)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>30 to &lt;60 mL/min</td>
<td>119 (60)</td>
<td>50 (53)</td>
</tr>
<tr>
<td>≥60 mL/min</td>
<td>79 (40)</td>
<td>41 (44)</td>
</tr>
</tbody>
</table>

### Response Rates

<table>
<thead>
<tr>
<th>Response</th>
<th>DR (n = 199)</th>
<th>Rd (n = 94)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR, %</td>
<td>96</td>
<td>85</td>
<td>.001</td>
</tr>
<tr>
<td>▪ CR</td>
<td>17</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>▪ VGPR</td>
<td>47</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>▪ PR</td>
<td>32</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>≥ VGPR</td>
<td>64</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>MRD at 10^{-5} by NGS,* %</td>
<td>10</td>
<td>3</td>
<td>.012</td>
</tr>
</tbody>
</table>

- Similar improvement in rate of ≥ VGPR with DR across all subgroups analyzed, including IFM frailty score (P = .87) and cytogenetic risk (P = .29)
- Fewer discontinuations in DR arm vs Rd arm (32% vs 45%)

*Patients with missing data were considered MRD positive.
# Safety

<table>
<thead>
<tr>
<th>Most Common Grade ≥3 AEs</th>
<th>DR (n = 199)</th>
<th>Rd (n = 94)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any grade ≥3 AE, n (%)</td>
<td>164 (82)</td>
<td>64 (68)</td>
<td>.010</td>
</tr>
<tr>
<td>SAE, n (%)</td>
<td>109 (55)</td>
<td>59 (63)</td>
<td>.21</td>
</tr>
<tr>
<td>Grade ≥3 hematologic AEs, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Anemia</td>
<td>21 (11)</td>
<td>2 (2)</td>
<td>.010</td>
</tr>
<tr>
<td>▪ Neutropenia</td>
<td>91 (46)</td>
<td>17 (18)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>▪ Thrombocytopenia</td>
<td>18 (9)</td>
<td>3 (3)</td>
<td>.089</td>
</tr>
<tr>
<td>Grade ≥3 infection, n (%)</td>
<td>26 (13)</td>
<td>17 (18)</td>
<td>.29</td>
</tr>
<tr>
<td>▪ Non‒COVID-19 infections</td>
<td>17 (9)</td>
<td>13 (14)</td>
<td>.21</td>
</tr>
<tr>
<td>▪ Pneumonia</td>
<td>5 (3)</td>
<td>7 (7)</td>
<td>.060</td>
</tr>
<tr>
<td>▪ COVID-19</td>
<td>9 (5)</td>
<td>4 (4)</td>
<td>1</td>
</tr>
<tr>
<td>Treatment discontinuation for AE, n (%)</td>
<td></td>
<td></td>
<td>.65</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Most Common Grade ≥3 AEs</th>
<th>IFM Frailty Score 2 + 3 (n = 199)</th>
<th>IFM Frailty Score 4 + 5 (n = 94)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DR (n = 138)</td>
<td>Rd (n = 61)</td>
</tr>
<tr>
<td>SAE, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Non‒COVID-19 infections</td>
<td>13 (9)</td>
<td>8 (13)</td>
</tr>
<tr>
<td>▪ Pneumonia</td>
<td>10 (7)</td>
<td>6 (10)</td>
</tr>
<tr>
<td>▪ COVID-19</td>
<td>2 (1)</td>
<td>3 (5)</td>
</tr>
<tr>
<td></td>
<td>3 (2)</td>
<td>2 (3)</td>
</tr>
</tbody>
</table>

Conclusions

• In phase III IFM 2017-03 trial assessing frail patients with newly diagnosed MM, DR was associated with higher response rates vs Rd
  – ORR: 96% with DR vs 85% with Rd
  – Higher MRD negativity rates (10% vs 3%, respectively) and rapid responses
• DR associated with favorable safety profile and no increased risk of infection or pneumonia compared to Rd
  – Treatment discontinuation rates were similar between arms
• Encouraging potential for dexamethasone-sparing strategy in frail patients, but longer follow-up is needed, with PFS

Extended intensified post-ASCT consolidation with Daratumumab, Bortezomib, Lenalidomide and Dexamethasone (Dara-VRd) for Ultra-High Risk (UHiR) Newly Diagnosed Myeloma (NDMM) and Primary Plasma Cell Leukemia (pPCL): the UK OPTIMUM/MUKnine Trial.


The Institute for Cancer Research, London, United Kingdom; Clinical Trials Research Unit, Leeds Institute of Clinical Trials Research, University of Leeds, Leeds, United Kingdom; HMDS Laboratory, St James’ Institute of Oncology, Leeds, United Kingdom; Norfolk and Norwich University Hospitals NHS Trust, Norwich, United Kingdom; Haematology, Leicester Royal Infirmary/University Hospitals of Leicester NHS Trust, Leicester, United Kingdom; Birmingham Heartlands Hospital, Birmingham, United Kingdom; Royal Marsden Hospital and Institute of Cancer Research, London, United Kingdom; Department of Haematology, University of Newcastle, Newcastle-upon-Tyne, United Kingdom; University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; University of Leeds, Leeds, United Kingdom; Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, United Kingdom; CTRU, University of Leeds, Leeds, United Kingdom; University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom
High-Risk MM - the unmet need

Current status

~ 20-25%

Relapse <24m
(<18m post ASCT)

Post-hoc modifications:
• Difficult to rescue at relapse

Aim/Hypothesis

Use improved biological risk prediction:
• Improve outcome upfront

Currently no uniform treatment standard

ASCT = autologous stem cell transplantation
UK multi-centre phase 2 trial for UHiR MM and PCL - Screening protocol

39 NHS hospitals
Mostly community (DGH)
Sep 2017 – Jul 2019

Suspected or confirmed NDMM/PCL
Recruited to OPTIMUM Screening (n=472)

Did not have a symptomatic Multiple Myeloma or PCL diagnosis (n=60)
• Asymptomatic Myeloma (n=22)
• MGUS (n=14)
• Other (n=16)
• No confirmed diagnosis (n=8)

Enrollment

Central sample

Genetic & GEP Risk screening

Multiple Myeloma or PCL diagnosis (n=412)

Risk screening result (n=412)
• Ultra High risk (n=138)
• Non-high risk (n=221)
• Partial result (n=24)
• Missing risk result (n=29)

87% complete screening result

Remained in OPTIMUM Screening (n=305; including 30 high risk patients)
• Standard of Care therapy – Data collection

Registered and eligible for OPTIMUM Treatment Trial (n=107)

Recruitment 10 months ahead of projection
Trial screening for UHiR MM, inclusive for PCL

**Tumour genetics**
- **2+ HRCA (Double hit)**
  - ~15% patients
- **Genome instability**

**Gene expression**
- **GEP risk signature (SKY92)**
  - ~20% patients
- **Combined profiling**
  - ~25% patients
  - Double hit: ~5%
  - SKY92 and Double hit: ~10%
  - SKY92: ~10%

**PB Phenotype**
- **Primary Plasma Cell Leukemia (PCL; ≥20%)**
  - Proliferation
  - Niche independence

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Clinical UHiR context – digital comparator trial

OPTIMUM design (appraisal framework for external comparator trials (Thorlund et al., 2020)):
- Currently no treatment standard for UHiR group – UK standard at design: VTD, single ASCT, observation
- Mirrored molecular UHiR criteria (Double hit and/or SKY92 risk signature)
- Contemporaneous external dataset: most recent UK phase 3 Myeloma XI trial for NDMM
  - KCRd (carfilzomib, cyclophosphamide, lenalidomide, dexamethasone) or CRd induction
    At time of design randomisation result not yet available
- Recruitment in same healthcare system
  - Same NHS hospitals/geography, virtually identical trial entry criteria

OPTIMUM

‘Digital comparator’

KCRd/CRd HD +ASCT R/Obs

The Prior (n=120 UHiR MM)

18 months PFS comparison
Bayesian framework
PFS and OS follow-up

V-HD +ASCT Dara-CVRd Dara-VRd Dara-VR Dara-R
**Trial objectives**

Evaluate efficacy of Dara-(C)VRd before and after ASCT in Ultra High-Risk MM and PCL

- Progression free survival at 18 months compared against The Prior
- **Progression free and overall survival end of Consolidation 2**
- MRD at key timepoints

- Determine safety and toxicity of Dara-CVRd induction and Dara-VRd consolidation

**Trial therapy**

### Bridging
- Max 2 cycles

### Induction
- Max 6 cycles (incl bridging)

#### Dara-CVRd
- Daratumumab iv 16 mg/kg
  - Cycle 1&2: Days 1, 8, 15
  - Cycle 3+: Day 1
- Cyclophosphamide po 500 mg
  - Days 1, 8
- Bortezomib sc 1.3 mg/m²
  - Days 1, 4, 8, 11
- Lenalidomide po 25 mg
  - Days 1-14
- Dexamethasone po 40 mg
  - Days 1, 4, 8, 11

#### V-HD-MEL +ASCT
- Melphalan iv 200 mg/m²
  - Day -1
- Autologous Stem Cell Transplantation
  - Day 0
- Bortezomib 1.3 mg/m²
  - Days -1, +5, +14,* Weekly after haematopoietic recovery
- Days 1, 4, 8, 11

#### Stem Cell Mobilisation
- 21d cycles

*Permissive bortezomib dose reduction schedule
†20mg for elderly/frailer

### Consolidation 1
- 6 Cycles
- Start 100-120d post ASCT

#### Dara-VRd
- Daratumumab sc 1800 mg Day 1
- Bortezomib sc 1.3 mg/m²
  - Days 1, 8, 15, 22*
- Lenalidomide po 25 mg
  - Days 1-21
- Dexamethasone po 40 mg
  - Day 1, 8, 15, 22

#### Consolidation 2
- 12 Cycles

#### Maintenance
- Until progression

#### Dara-VR
- Daratumumab sc 1800 mg Day 1
- Bortezomib sc 1.3 mg/m²
  - Days 1, 8, 15*
- Lenalidomide po 25 mg
  - Days 1-21

#### Dara-R
- Daratumumab sc 1800 mg Day 1
- Lenalidomide po 25 mg Day 1-21

#### MRD time points

- 28d cycles

*Brown S, et al., BMJ Open 2021*
# UHiR populations: OPTIMUM and Myeloma XI

## Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>OPTIMUM (n=107)</th>
<th>Myeloma XI (n=120)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median age, yrs (range)</strong></td>
<td>60 (35-78)</td>
<td>62 (33-69)</td>
</tr>
<tr>
<td><strong>Male, n (%)</strong></td>
<td>64 (60%)</td>
<td>69 (58%)</td>
</tr>
<tr>
<td><strong>ISS Stage 1, n (%)</strong></td>
<td>29 (27%)</td>
<td>23 (19%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ISS Stage 2, n (%)</strong></td>
<td>43 (40%)</td>
<td>53 (44%)</td>
</tr>
<tr>
<td><strong>ISS Stage 3, n (%)</strong></td>
<td>34 (32%)</td>
<td>38 (32%)</td>
</tr>
<tr>
<td><strong>ISS missing, n (%)</strong></td>
<td>1 (1%)</td>
<td>6 (5%)</td>
</tr>
<tr>
<td><strong>ECOG Performance Status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>0, n (%)</strong></td>
<td>51 (48%)</td>
<td>47 (39%)</td>
</tr>
<tr>
<td><strong>1, n (%)</strong></td>
<td>42 (39%)</td>
<td>46 (38%)</td>
</tr>
<tr>
<td><strong>≥2, n (%)</strong></td>
<td>10 (9%)</td>
<td>22 (18%)</td>
</tr>
<tr>
<td><strong>missing, n (%)</strong></td>
<td>4 (4%)</td>
<td>5 (4%)</td>
</tr>
<tr>
<td><strong>Molecular profiles</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Double hit genetics, n (%)</strong></td>
<td>57 (53%)</td>
<td>55 (56%)*</td>
</tr>
<tr>
<td><strong>SKY92 risk signature present, n (%)</strong></td>
<td>82 (77%)</td>
<td>72 (72%)*</td>
</tr>
<tr>
<td><strong>Both Double hit and SKY92, n (%)</strong></td>
<td>33 (31%)</td>
<td>28 (29%)*</td>
</tr>
</tbody>
</table>

* in relation to 98 patients with complete GEP and genetic profiles

## Comparable clinical & molecular characteristics
Extended Follow-up: End of Dara-VR Consolidation 2
OPTIMUM vs. Myeloma XI: PFS

Median follow-up 41.2 months
Extended Follow-up: End of Dara-VR Consolidation
OPTIMUM vs. Myeloma XI: OS

Median follow-up 41.2 months
### Dose Reductions during Consolidation 2

**n=80 patients, including earlier reductions**  
Trial protocol encouraged early reductions (grade 1 AR)

<table>
<thead>
<tr>
<th>Modification of therapy</th>
<th>Daratumumab</th>
<th>Bortezomib</th>
<th>Lenalidomide</th>
</tr>
</thead>
<tbody>
<tr>
<td>No modification</td>
<td>79 (98.8%)</td>
<td>48 (69.0%)</td>
<td>46 (57.5%)</td>
</tr>
<tr>
<td>Hematological toxicity</td>
<td>0 (0%)</td>
<td>11 (28.8%)</td>
<td>17 (21.3%)</td>
</tr>
<tr>
<td>Non-Hematological toxicity</td>
<td>0 (0%)</td>
<td>26 (32.5%)</td>
<td>20 (25.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1.3%)</td>
<td>1 (1.3%)</td>
<td>3 (3.8%)</td>
</tr>
</tbody>
</table>
Summary

- Collaborative trial designed with patients to address unmet need within healthcare system requirements
- Extended intensified consolidation with Dara-VR(d) is an effective treatment option for UHiR MM and PCL patients
- Continued improvement of PFS for OPTIMUM vs. Myeloma XI UHiR patients
- Early positive OS signal for OPTIMUM vs Myeloma XI UHiR patients
- Ongoing intensive consolidation required individualised dose reductions, but was tolerable for most patients, with cytopenia and infection main AEs
- OPTIMUM design explicitly balanced intensity and toxicity vs. high unmet need
- Successful recruitment suggests high unmet need for better diagnostics and therapy
- Results support allocation of resources to unmet need in restricted healthcare systems
Defining the optimum duration of lenalidomide maintenance after autologous stem cell transplant – data from the Myeloma XI trial.

Charlotte Pawlyn¹,², Tom Menzies³, Faith Davies⁴, Ruth de Tute⁵, Rowena Henderson³, Gordon Cook³,⁶, Matthew Jenner⁷, John Jones⁸, Martin Kaiser¹,², Mark Drayson⁹, Roger Owen⁸, David Cairns³, Gareth Morgan⁴, Graham Jackson¹⁰

¹) The Institute of Cancer Research, London, UK; ²) The Royal Marsden Hospital, London, UK; ³) Clinical Trials Research Unit, Leeds Institute of Clinical Trials Research, University of Leeds, Leeds, UK; ⁴) Perlmutter Cancer Center, NYU Langone Health, New York, US; ⁵) HMDS, Leeds Cancer Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; ⁶) Leeds Cancer Centre, Leeds Teaching Hospitals NHS Trust, Leeds, UK; ⁷) University Hospital Southampton NHS Foundation Trust, Southampton, UK; ⁸) Kings College Hospital NHS Foundation Trust, London, UK; ⁹) Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, UK; ¹⁰) Department of Haematology, University of Newcastle, Newcastle-upon-Tyne, UK

On behalf of the Myeloma XI Trial Management Group and NCRI Haem-Onc Clinical Studies Group
Lenalidomide maintenance after ASCT

**PFS**

<table>
<thead>
<tr>
<th>Study</th>
<th>Ratio (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFM 2005-02</td>
<td>0.63 (0.43, 0.84)</td>
<td>33.93</td>
</tr>
<tr>
<td>CALGB 100104</td>
<td>0.38 (0.29, 0.50)</td>
<td>20.94</td>
</tr>
<tr>
<td>GIMEMA-RVMM-P1209</td>
<td>0.50 (0.31, 0.80)</td>
<td>7.86</td>
</tr>
<tr>
<td>Myeloma XI</td>
<td>0.48 (0.40, 0.58)</td>
<td>37.28</td>
</tr>
<tr>
<td>Overall (I-squared = 21.0%, p = 0.284)</td>
<td>0.47 (0.41, 0.54)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

**OS**

<table>
<thead>
<tr>
<th>Study</th>
<th>Ratio (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFM 2005-02</td>
<td>0.91 (0.72, 1.15)</td>
<td>33.18</td>
</tr>
<tr>
<td>CALGB 100104</td>
<td>0.56 (0.42, 0.76)</td>
<td>28.38</td>
</tr>
<tr>
<td>GIMEMA-RVMM-P1209</td>
<td>0.72 (0.37, 1.38)</td>
<td>10.52</td>
</tr>
<tr>
<td>Myeloma XI</td>
<td>0.69 (0.52, 0.93)</td>
<td>28.38</td>
</tr>
<tr>
<td>Overall (I-squared = 54.6%, p = 0.085)</td>
<td>0.72 (0.56, 0.91)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis.

**Myeloma XI**

**Induction**
- NDMM TE
  - Myeloma XI induction protocols and ASCT

**Maintenance**
- Lenalidomide
  - 10mg/day, days 1-21/28

**Observation**

Planned to continue till disease progression

**N=1248**
- Median follow up: 44.7 months (IQR 32.4-62.7)

**Exclusion criteria**
- Failure to respond to lenalidomide as induction IMiD or progressive disease
- Previous or concurrent active malignancies
- Dialysis dependent renal failure

Pawlyn et al ASH 2022, Abstract 570
Outcomes from maintenance randomisation – overall population

PFS

LEN control

Hazard Ratio 0.52*

PFS2

LEN control

Hazard Ratio 0.66*

Pawlyn et al ASH 2022, Abstract 570

*p<0.05
Outcomes from maintenance randomisation

Genetic risk status

LEN

control

HR 0.40*

HR/UHR

LEN

control

HR 0.50*

S

R

HR 0.50*

MRD status

LEN

control

HR 0.72*

MRD -ve

LEN

control

HR 0.37*

MRD +ve

MRD status was assessed by flow cytometry (median sensitivity $4 \times 10^5$)

*p<0.05

Pawlyn et al ASH 2022, Abstract 570
Multiple landmark analyses

Induction

Randomisation

Maintenance

Observation

Lenalidomide
10mg/day, days 1-21/28

N=1248
Median follow up: 44.7 months
(IQR 32.4-62.7)

NDMM
Myeloma XI induction protocols and ASCT

PFS
• Overall
• By risk
• By MRD status

To PD

Median duration of lenalidomide therapy 28 cycles (range 1-96)
• Patients still on therapy 330/730 (45%)
Outcomes from multiple landmarks – overall population

PFS

2 years
LEN
control
HR 0.51*

3 years
LEN
control
HR 0.47*

4 years
LEN
control
HR 0.56*

5 years
LEN
control
HR 0.83

PFS2

2 years
LEN
control
HR 0.70*

3 years
LEN
control
HR 0.65*

4 years
LEN
control
HR 0.54*

5 years
LEN
control
HR 0.64

*p<0.05

Pawlyn et al ASH 2022, Abstract 570
Outcomes from multiple landmarks – by MRD status

2 years

MRD -ve

LEN control HR 0.63*

MRD +ve

LEN control HR 0.34*

3 years

LEN control HR 0.65

LEN control HR 0.28*

4 years

LEN control HR 0.68

LEN control HR 0.14*

5 years

LEN control HR 0.43

* p<0.05

Pawlyn et al ASH 2022, Abstract 570
Can this help us personalise therapy?

MRD +ve – continue maintenance to progression

MRD –ve:

- MRD -ve
- MRD -ve

6 months

Evidence that there is benefit from 2.5 further years of lenalidomide therapy before treatment effect may diminish.

Lenalidomide
10mg/day, days 1-21/28

Observation

Pawlyn et al ASH 2022, Abstract 570
Can this help us personalise therapy?

MRD +ve – continue maintenance to progression

MRD –ve:

- Evidence that there is benefit from 2.5 further years of lenalidomide therapy before treatment effect may diminish

Lenalidomide
10mg/day, days 1-21/28

Future trials?

Myeloma XI

1 year

2 years

3 years

Pawlyn et al ASH 2022, Abstract 570
Conclusions

• These data suggest an ongoing PFS benefit associated with continuing lenalidomide maintenance beyond at least 4-5 years in the overall patient population

• Even in patients with sustained MRD negativity, there is evidence of benefit from continuing lenalidomide maintenance for at least 3 years in total
  • Randomised trials to address the impact of stopping lenalidomide maintenance in patients with sustained MRD negativity could be considered, at no earlier than 3 years

• In patients who are MRD +ve these data support continuing lenalidomide until disease progression

• No evidence of cumulative haematological toxicity was identified

• These findings emphasise the need for long term follow up of maintenance studies to enable the exploration of such questions
  • There is a planned powered OS update of Myeloma XI in 2023

Pawlyn et al ASH 2022, Abstract 570
Relapsed disease

Bispecific antibodies

- BCMA-CD3
- Elranatamab
- GPRC5D-CD3
- Talquetamab

Antibody drug conjugates

- CD38-attenuated IFNα
- Modakafusp alfa
Elranatamab

MagnetisMM-3 Study

- MagnetisMM-3 is an open-label, multicenter, non-randomized, phase 2 study

### Patients with RRMM

**Key inclusion criteria:**
- Refractory to ≥1 each of the following: proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody
- ECOG performance status ≤2
- Creatinine clearance ≥30 mL/min
- Platelets ≥25 × 10^9/L
- ANC ≥1.0 × 10^9/L
- Hemoglobin ≥8 g/dL

### Primary endpoint

- ORR by BICR

### Secondary endpoints

- Duration of response
- CR rate
- ORR
- ORR by baseline extramedullary disease status
- Duration of CR
- Time-to-response
- PFS
- MRD-negativity rate
- OS
- Safety
- Pharmacokinetics

---

Bahlis N et al ASH 2022, Abstract 159
Elranatamab – MagnetisMM-3

ORR, 61.0% (95% CI, 51.8–69.6)

- ≥CR: 27.6%
- CR (14.6)
- sCR (13.0)
- VRGPR (27.5)
- PR (5.7)

Cohort A (n=123)

Progression-Free Survival per BICR

Median OS not yet reached

Bahlis N et al ASH 2022, Abstract 159
**Elranatamab – MagnetisMM-3**

**AEs of Special Interest: CRS and ICANS**

- The step-up priming regimen successfully mitigated the rate and severity of CRS, and the CRS profile was predictable

<table>
<thead>
<tr>
<th>TEAE of special interest</th>
<th>12/32 mg step-up regimen (n=119)*</th>
<th>CRS</th>
<th>ICANS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with TEAE, n (%)</td>
<td>67 (56.3)</td>
<td>4 (3.4)</td>
<td>0 (0.8)</td>
</tr>
<tr>
<td>Maximum Grade 1</td>
<td>50 (42.0)</td>
<td>1 (0.8)</td>
<td>0 (0.8)</td>
</tr>
<tr>
<td>Maximum Grade 2</td>
<td>17 (14.3)</td>
<td>3 (2.5)</td>
<td>0 (0.8)</td>
</tr>
<tr>
<td>Maximum Grade ≥3</td>
<td>0</td>
<td>0 (0.8)</td>
<td>0 (0.8)</td>
</tr>
<tr>
<td>Patients with &gt;1 TEAE, n (%)</td>
<td>18 (15.1)</td>
<td>1 (0.8)</td>
<td>0 (0.8)</td>
</tr>
<tr>
<td>Median time to onset of TEAE, d (range)</td>
<td>2.0 (1.0–9.0)</td>
<td>2.5 (1.0–4.0)</td>
<td></td>
</tr>
<tr>
<td>Median time to resolution of TEAE, d (range)</td>
<td>2.0 (1.0–19.0)</td>
<td>2.0 (1.0–6.0)</td>
<td></td>
</tr>
<tr>
<td>Patients who received tocilizumab or steroids, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>27 (22.7)</td>
<td>2 (1.7)</td>
<td>0 (0.8)</td>
</tr>
<tr>
<td>Steroids</td>
<td>10 (8.4)</td>
<td>2 (1.7)</td>
<td>0 (0.8)</td>
</tr>
<tr>
<td>Permanent discontinuation due to AE, n (%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Patients who received 1 step-up priming dose of 44 mg in Wk 1 were excluded from this CRS and ICANS analysis (n=4); * Includes tocilizumab and etrolizumab

CRS and ICANS which were graded by American Society for Transplant and Cellular Therapy criteria (Lee DW, et al. Biol Blood Marrow Transplant 2019;25:82)

AE=adverse event; CRS=cytokine release syndrome; ICANS=immune effector cell-associated neurotoxicity syndrome; TEAE=treatment-emergent adverse event

Bahlis N et al ASH 2022, Abstract 159
Elranatamab – MagnetisMM-3

AEs of Special Interest: Infections

- Infections were reported in 66.7% (Grade 3/4, 35.0%) of patients
  - Median time to first onset of infections was 47.5 (range, 1.0–295.0) days
- COVID-19 related TEAEs were reported in 31 (25.2%) patients
  - 2 (1.6%) patients died due to COVID-19 pneumonia, both considered unrelated to treatment by the investigator
- 8 (6.5%) patients had an infection that led to permanent discontinuation of elranatamab
  - Most common infection TEAEs leading to treatment discontinuation were septic shock (n=2) and sepsis (n=2)
- Among patients with quantitative IgG data (n=101), 76 (75.2%) patients had IgG level <400 mg/dL during the study
- Overall, 50 (40.7%) patients received IVIG during the study

<table>
<thead>
<tr>
<th>Cohort A (N=123)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any grade</td>
<td>Grade 3/4</td>
</tr>
<tr>
<td>Infection TEAEs in ≥5% of patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COVID-19 related</td>
<td>31 (25.2)</td>
<td>14 (11.4)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>22 (17.9)</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>15 (12.2)</td>
<td>7 (5.7)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>11 (8.9)</td>
<td>4 (3.3)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>11 (8.9)</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>TEAEs of interest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumocystis jirovecii pneumonia</td>
<td>6 (4.9)</td>
<td>5 (4.1)</td>
</tr>
<tr>
<td>CMV infection reactivation</td>
<td>6 (4.9)</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>CMV infection</td>
<td>4 (3.3)</td>
<td>0</td>
</tr>
</tbody>
</table>

* Includes preferred terms in COVID-19 (narrow) standardized MedDRA queries.

Administration of antibacterial and/or antiviral agents for infection prophylaxis was permitted for patients at increased risk of infection in accordance with local standard of care practice and/or institutional guidelines. AE=adverse event; CMV=cytomegalovirus; IgG=immunoglobulin G; IVIG=intravenous immunoglobulin; MedDRA=Medical Dictionary for Regulatory Activities Terminology; TEAE=treatment-emergent adverse event.
Talquetamab – MonumenTAL-1

- Talquetamab is a novel first-in-class, off-the-shelf, T-cell redirecting bispecific antibody directed against a new antigen target called GPRC5D\(^1,2\).

- GPRC5D is a novel antigen target in myeloma that is highly expressed on malignant plasma cells with limited expression in normal human tissues,\(^3-6\) including hematopoietic stem cells\(^7\).

- Talquetamab has shown an ORR of 64–70% with QW and Q2W dosing in the MonumenTAL-1 study (NCT03399799/NCT04634552)\(^8\).

- Updated results from the MonumenTAL-1 study are presented, including all patients treated at each RP2D for the first time, as well as a cohort of patients with prior CAR-T cell or bispecific antibody treatment.

Chari AJ et al ASH 2022, Abstract 157

Phase 1 experience – 232 pt, 70% ORR and 10.2m median PFS
Talquetamab – MonumenTAL-1

**ORR 63%**
72% prior CART
44% prior bispecific

**RP2D 0.4 mg/kg QW SC**
Prior anti-BCMA ADC treatment allowed
T-cell redirection therapy naive
(Phase 1 [n=21] + Phase 2 [n=122]; N=143)

**RP2D 0.8 mg/kg Q2W SC**
Prior anti-BCMA ADC treatment allowed
T-cell redirection therapy naive
(Phase 1 [n=36] + Phase 2 [n=109]; N=145)

**Prior T-cell redirection (QW and Q2W)**
Previously exposed to T-cell redirection therapies
Dosed with either 0.4 mg/kg weekly SC or 0.8 mg/kg Q2W SC
(Phase 1 [n=17] + Phase 2 [n=34]; N=51)

Chari AJ et al ASH 2022, Abstract 157
Talquetamab – MonumenTAL-1

**Hematologic adverse events**

<table>
<thead>
<tr>
<th>AEs (≥20% of any RP2D cohort), n (%)</th>
<th>0.4 mg/kg SC QW*(n=143)</th>
<th>0.8 mg/kg SC Q2W*(n=145)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Grade</td>
<td>Grade 3/4</td>
<td>Any Grade</td>
</tr>
<tr>
<td>Anemia</td>
<td>64 (44.8)</td>
<td>45 (31.5)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>49 (34.3)</td>
<td>44 (30.8)</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>40 (28.0)</td>
<td>37 (25.9)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>39 (27.3)</td>
<td>29 (20.3)</td>
</tr>
</tbody>
</table>

- Most high-grade AEs were cytopenias
- Cytopenias were generally limited to the first few cycles

**Infections**

- At 0.4 mg/kg QW and 0.8 mg/kg Q2W:
  - Infections occurred in 57.3% and 50.3%:
  - Grade 3/4 in 16.8% and 11.7%:
  - 5 (3.5%) and 4 (2.8%) patients had opportunistic infections:
    - 13 (9.1%) and 16 (11.0%) patients had COVID-19:
      - Grade 3/4 in 0.7% and 2.1%:
      - 2 patients died from COVID-19:
- 13.3% and 9.7% of patients received IVlg, respectively.

**Maximum CRS Grade**

- Grade 2: 21 (14.7%)
- Grade 3: 3 (2.1%)

**Maximum ICANS Grade**

- Grade 2: 25 (17.2%)
- Grade 3: 1 (0.7%)

**Low rates of grade 3/4 nonhematologic AEs were observed**

- Low rates of discontinuation due to AEs were observed with QW (4.9%) and Q2W (6.2%) schedules

- Most common AEs were CRS, skin-related events, nail-related events, and dysgeusia:
  - Rates of high-grade skin, nail, and rash-related events were low:
  - Dysgeusia was managed with supportive care, and at times with dose reduction:
- At 0.4 mg/kg QW and at 0.8 mg/kg Q2W:
  - 8.4% and 13.8% had dose delays due to AEs:
  - 14.7% and 6.2% had dose reductions due to AEs:
- At time of data cut-off, no patients in these cohorts died due to drug-related AEs

Chari AJ et al ASH 2022, Abstract 157
Talquetamab – MonumenTAL-1

- Treatment at both doses led to durable responses
  - Median DOR not reached for those patients who achieved ≥CR

**DOR, 0.4 mg/kg SC QW**

- mDOR: NE (20.2–NE)
- mDOR: 9.3 (6.8–12.7)

**DOR, 0.8 mg/kg SC Q2W**

- mDOR: NE (10.6–NE)
- mDOR: 13.0 (10.6–NE)

mPFS: 7.5 months (95% CI: 5.7–9.4; 33% censored)

11.9 months (95% CI: 8.4–NE; 61% censored)

Chari AJ et al. ASH 2022, Abstract 157
Infections with bispecific antibodies

10 trials
790 patients

Hypogamaglobulinemia 48.5%

Mazahreh F et al ASH 2022, Abstract 1909
Outline

Bispecific antibodies
- BCMA-CD3
  - Teclistamab
  - Elranatamab
- GPRC5D-CD3
  - Talquetamab

Antibody drug conjugates
- CD38-attenuated IFNα
  - Modakafusp alfa
Modakafusp alfa is a first-in-class, innate immunity enhancer that functions through targeted next-generation IFN signaling

Modakafusp alfa
Binds with high affinity to unique epitope of CD38

Signals through IFNAR to:
- Activate innate and adaptive immune cells
- Elicit direct anti-proliferative/apoptotic signals to tumor cells

Modakafusp alfa is a first-in-class, immune-targeting, attenuated cytokine. It consists of 2 attenuated interferon (IFN)α2b molecules genetically fused to the Fc portion of an anti-CD38 IgG4 monoclonal antibody (mAb), allowing targeted delivery of IFNα to innate and adaptive immune cells, as well as myeloma cells.
First-in-human, phase 1/2 study of modakafusp alfa in heavily pre-treated patients with RRMM

100 patients enrolled

Key eligibility criteria:
• ≥3 prior lines of MM therapy
• Refractory to, or intolerant of ≥1 PI and ≥1 IMID
• Anti-CD38 mAb washout of 90 days required for patients with ≥5 months of therapy in escalation phase

ClinicalTrials.gov identifier: NCT03215030

Data cutoff date: May 30, 2022

*Not required for patients enrolled into the expansion phase
IMID: immunomodulatory drug; mAb, monoclonal antibody; MTD, maximum tolerated dose; OBD, optimal biological dose; PI, proteasome inhibitor; QW, weekly; Q2 or Q4W, every 2 or 4 weeks; RRMM, relapsed/refractory MM

ClinicalTrials.gov identifier: NCT03215030

Escalation phase (n=56) 3+3 design

- Q4W schedule (28-day cycles)
  - 0.75–6.0 mg/kg

- Q3W schedule (21-day cycles)
  - 0.4–0.75 mg/kg

- Q2W schedule (28-day cycles)
  - 0.2–0.4 mg/kg

- 'Modified QW' schedule (28-day cycles)
  - QW cycles 1–2, Q2W cycles 3–6, Q4W cycle ≥7
  - 0.001–0.75 mg/kg

Expansion phase (n=44)

- Q4W schedule
  - 1.5 mg/kg
  - All patients in 1.5 mg/kg Q4W cohorts: n=30

- Q3W schedule
  - 0.4 mg/kg

Objectives
Primary: Safety and tolerability
Secondary included:
• OBD and/or MTD
• Preliminary anti-tumor activity

97% prior anti-CD38, 93% refractory
50% prior anti-BCMA
Median 7 prior lines

Vogl D et al ASH 2022, Abstract 565
Modakafusp alfa 1.5 mg/kg Q4W (n=30) adverse events were primarily hematologic

- 26 (87%) patients have discontinued treatment; 19 (73%) due to PD and 4 (15%) due to TEAEs
- Median duration of exposure: 4 cycles (range: 1–24)
- Thrombocytopenia and neutropenia mainly occurred in cycles 1–2, with counts usually recovering over time
- One patient had a grade 3 bleeding event and remained on study for 6 cycles until progressing
- Four patients had grade 3 infections (pneumonia, n=4; sinusitis, n=1)
- Aside from IRRs, there were no constitutional or neuropsychiatric effects typical of IFNα therapy

<table>
<thead>
<tr>
<th>TEAE</th>
<th>Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>27</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>30</td>
</tr>
<tr>
<td>Anemia</td>
<td>13</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>37</td>
</tr>
<tr>
<td>Fatigue</td>
<td>37</td>
</tr>
<tr>
<td>IRRs</td>
<td>37</td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>33</td>
</tr>
<tr>
<td>Headache</td>
<td>30</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>24</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>17</td>
</tr>
<tr>
<td>Cough</td>
<td>27</td>
</tr>
<tr>
<td>Back pain</td>
<td>27</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>10</td>
</tr>
</tbody>
</table>

*All-grade TEAEs reported in >25% of patients or at grade ≥3 severity in ≥10% of patients, excluding leukopenia. Percentages may not sum due to rounding.

PD, progressive disease; TEAE, treatment-emergent adverse event

Vogl D et al ASH 2022, Abstract 565
Responses were observed with modakafusp alfa 1.5 mg/kg Q4W regardless of prior therapies or refractory status

Median PFS 5.7m
Median duration of response 12.5m

Vogl D et al ASH 2022, Abstract 565
Safety and efficacy in the MTD cohort
3.0 mg/kg Q4W (n=7)

Most common* TEAEs

<table>
<thead>
<tr>
<th>Condition</th>
<th>Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>71</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>71</td>
</tr>
<tr>
<td>Anemia</td>
<td>67</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>67</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>57</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>57</td>
</tr>
<tr>
<td>Nausea</td>
<td>57</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>57</td>
</tr>
<tr>
<td>IRRs</td>
<td>43</td>
</tr>
<tr>
<td>Chills</td>
<td>43</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>29</td>
</tr>
<tr>
<td>AST increased</td>
<td>29</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>29</td>
</tr>
<tr>
<td>Fatigue</td>
<td>29</td>
</tr>
<tr>
<td>Wheezing</td>
<td>29</td>
</tr>
<tr>
<td>Pruritus</td>
<td>29</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>29</td>
</tr>
<tr>
<td>Hypertension</td>
<td>29</td>
</tr>
</tbody>
</table>

*All-grade TEAEs reported in ≥25% of patients. Percentages may not sum due to rounding.

Best responses

ORR 43%

Study - 1.5 vs 3mg/kg ongoing
### Table 1. Prior therapies

<table>
<thead>
<tr>
<th></th>
<th>All patients (N = 101)</th>
<th>Patients with prior anti-BCMA therapy (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of prior therapies, median (range)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stem cell transplantation, n (%)</td>
<td>6 (3–10)</td>
<td></td>
</tr>
<tr>
<td>PI, n (%)</td>
<td>76 (77.2)</td>
<td></td>
</tr>
<tr>
<td>IMiD agent, n (%)</td>
<td>101 (100)</td>
<td></td>
</tr>
<tr>
<td>POM as last prior regimen, n (%)</td>
<td>101 (100)</td>
<td></td>
</tr>
<tr>
<td>Anti-CD38 mAb, n (%)</td>
<td>37 (36.6)</td>
<td></td>
</tr>
<tr>
<td>Anti-BCMA therapy, n (%)</td>
<td>22 (21.6)</td>
<td></td>
</tr>
<tr>
<td>Antibody-drug conjugate, n (%)</td>
<td>3 (3.0)</td>
<td></td>
</tr>
<tr>
<td>CAR T cell therapy, n (%)</td>
<td>8 (7.9)</td>
<td></td>
</tr>
</tbody>
</table>

*LEN and POM, BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; IMiD, immunomodulatory drug; LEN, lenalidomide; mAb, monoclonal antibody; PI, proteasome inhibitor; POM, pomalidomide.

### Table 2. Summary of responses to MEZI + DEX

<table>
<thead>
<tr>
<th>Response, n (%)</th>
<th>All patients (N = 101)</th>
<th>Patients with prior anti-BCMA therapy (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR*</td>
<td>40 (36.6)</td>
<td>12 (30.8)</td>
</tr>
<tr>
<td>sCR</td>
<td>2 (2.0)</td>
<td>0</td>
</tr>
<tr>
<td>CR</td>
<td>3 (3.0)</td>
<td>2 (5.1)</td>
</tr>
<tr>
<td>VGFR</td>
<td>16 (17.6)</td>
<td>6 (15.4)</td>
</tr>
<tr>
<td>PR</td>
<td>17 (16.6)</td>
<td>4 (10.3)</td>
</tr>
<tr>
<td>MR</td>
<td>8 (7.9)</td>
<td>0</td>
</tr>
<tr>
<td>SD</td>
<td>38 (37.6)</td>
<td>21 (53.8)</td>
</tr>
<tr>
<td>PD</td>
<td>10 (9.9)</td>
<td>4 (10.3)</td>
</tr>
<tr>
<td>NE/Missing</td>
<td>5 (5.0)</td>
<td>2 (5.1)</td>
</tr>
<tr>
<td><strong>DOR, median (95% CI), months</strong></td>
<td>8.3 (5.4–NR)</td>
<td>6.9 (4.0–NR)</td>
</tr>
<tr>
<td><strong>PFS, median (95% CI), months</strong></td>
<td>4.8 (3.2–6.3)</td>
<td>3.7 (2.3–4.9)</td>
</tr>
</tbody>
</table>

*Defined as PR or better.

BCMA, B-cell maturation antigen; CI, confidence interval; CR, complete response; DEX, dexamethasone; DOR, duration of response; MEZI, meziglotinib; MR, minimal response; NE, not evaluable; NR, not reached; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; RRNM, relapse refractory multiple myeloma; sCR, stringent complete response; SD, stable disease; VGFR, very good partial response.
Conclusions

• Personalizing therapy remains important
  – High-risk, frail etc

• Therapies with new modes of actions show impressive response rates in RRMM
  – Balance efficacy and toxicity
    • CRS, infections etc

• Determine the most appropriate place in disease to use

• Determine the day to day practicalities of how to introduce therapies into clinical practice
Acknowledgements

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