Bispecific Therapy

FROM CLINICAL TRIALS TO REAL-WORLD EXPERIENCE - THERAPEUTIC CONSIDERATIONS AND LOGISTICAL STRATEGIES
Faculty

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Learning Objectives

1. Discuss the pharmacology and pharmacokinetics of current T-cell engaging bispecific antibodies (BsAbs).

2. Review data supporting the use of current T-cell engaging bispecific antibodies (BsAbs) in hematological malignancies.

3. Describe common side effects associated with T-cell engaging bispecific antibodies (BsAbs) including cytokine release syndrome.

4. Outline logistical challenges that can occur with the administration of T-cell engaging bispecific antibodies (BsAbs) and summarize therapeutic strategies that can be utilized.
Introduction

• Bispecific antibodies represent a novel treatment approach for the treatment of hematologic malignancies

• Contain 2 different antigen-binding sites in 1 molecule

• Activate peripheral and intratumoral endogenous immune cells

• Redirects cytotoxic T lymphocytes by targeting CD3 and cell surface antigens on cancer cells

Bispecific Antibodies (BsAbs)

IgG-based (Fc format)
- Large molecular weight
- Fc-mediated effector function
- Increased solubility and stability
- Increased serum half-life and affinity

Non-IgG based (Fv format)
- Lack of Fc fragments
- Easy to produce
- Low immunogenicity
- Increased permeability to tumor tissues

# B-cell Lymphoma Bispecific FDA Approval Timeline

<table>
<thead>
<tr>
<th>2022</th>
<th>2023</th>
</tr>
</thead>
<tbody>
<tr>
<td>December 2022:</td>
<td>June 2023:</td>
</tr>
<tr>
<td><strong>Mosunetuzumab-axgb</strong></td>
<td><strong>Glofitamab-gxbm</strong></td>
</tr>
<tr>
<td>• <strong>Indication</strong>: R/R FL ≥2 L</td>
<td>• <strong>Indication</strong>: R/R DLBCL NOS or LBCL arising from FL after ≥2 L</td>
</tr>
<tr>
<td>• <strong>Study</strong>: GO29781</td>
<td>• <strong>Study</strong>: NP30179</td>
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<tr>
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<td>May 2023:</td>
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<td></td>
<td><strong>Epcoritamab-bysp</strong></td>
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<tr>
<td></td>
<td>• <strong>Indication</strong>: R/R DLBCL NOS (DLBCL from indolent lymphoma, HGBCL) after ≥2 L</td>
</tr>
<tr>
<td></td>
<td>• <strong>Study</strong>: EPCORE™ NHL-1</td>
</tr>
</tbody>
</table>
Mosunetuzumab – axgb

**Indication:** relapsed or refractory follicular lymphoma, after two or more lines of systemic therapy

**Mechanism of action:** targets CD3 on T-cells and CD20 expressed on the surface of B-cells

**Approval Date:** December 2022
# Mosunetuzumab – axgb

## Clinical Trial Data

### Inclusion Criteria
- Grade 1-3a follicular lymphoma
- Relapsed/refractory to ≥ 2 lines of therapy
  - Anti-CD20
  - Alkylating agent
- Adults (≥ 18 years)
- ECOG 0-1
- Hepatic and renal function WNL

### Dosing schedule

<table>
<thead>
<tr>
<th>Cycle 1</th>
<th>Cycle 2-12</th>
<th>Cycle 3 and beyond</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Day 1: 1mg</td>
<td>• Day 1 60mg</td>
<td>• Day 1 30mg</td>
</tr>
<tr>
<td>• Day 8: 2mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Day 15: 60mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Premedication (required for C1/2)
  - Acetaminophen
  - Anti-histamine
  - Steroid
- Duration of treatment
  - 8 cycles (21 day)
  - CR – discontinue
  - PR/SD – continue for 9 more cycles

### Endpoints
- Primary endpoint: CR
- Secondary Endpoints: ORR, DOR, PFS, OS, Safety

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Lancet Oncol 2022, 23:1055-1065
# Mosunetuzumab – axgb

## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=90</th>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td>60 (53-67)</td>
</tr>
<tr>
<td><strong>FLIPI risk score 1-4</strong></td>
<td>86 (96%)</td>
</tr>
<tr>
<td><strong>Bulky disease (&gt;6cm)</strong></td>
<td>31 (34%)</td>
</tr>
<tr>
<td><strong>Median previous lines of therapy</strong></td>
<td></td>
</tr>
<tr>
<td>2 previous lines of therapy</td>
<td>34 (38%)</td>
</tr>
<tr>
<td>3 previous lines of therapy</td>
<td>28 (31%)</td>
</tr>
<tr>
<td>&gt; 3 previous lines of therapy</td>
<td>28 (31%)</td>
</tr>
<tr>
<td><strong>Double refractory (both anti-CD20 AND alkylator therapy)</strong></td>
<td>48 (53%)</td>
</tr>
<tr>
<td><strong>PI3K inhibitors</strong></td>
<td>17 (19%)</td>
</tr>
<tr>
<td><strong>Immunomodulatory agents</strong></td>
<td>13 (14%)</td>
</tr>
<tr>
<td><strong>Chimeric antigen receptor T-cell therapy</strong></td>
<td>3 (3%)</td>
</tr>
<tr>
<td><strong>Prior autologous stem cell transplant</strong></td>
<td>19 (21%)</td>
</tr>
<tr>
<td><strong>POD24 (progression of disease within 24 months)</strong></td>
<td>47 (52%)</td>
</tr>
</tbody>
</table>

Budde LE et al Lancet Oncol July 2022,23:1055-1065
Mosunetuzumab – axgb

Results

CR: **60%** (95% CI 49.1-70.2) vs 36%

ORR: **80%** (95% CI 70.3-87.7) vs 56%

24month PFS: **51.4%** vs 23.5%
Mosunetuzumab – axgb

Results

<table>
<thead>
<tr>
<th></th>
<th>Grade 1-2 (%)</th>
<th>Grade 3-4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>37</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>Pruritis</td>
<td>21</td>
<td>0</td>
</tr>
<tr>
<td>ICANS</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Grade 1-2 (%)</th>
<th>Grade 3-4 (%)</th>
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</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>2</td>
<td>26</td>
</tr>
</tbody>
</table>

  - Median time of onset = 70 days (31 – 106)
  - Median duration= 8 days
  - No incidence of FN
  - GCSF support (69%)

<table>
<thead>
<tr>
<th></th>
<th>All Grade (n)</th>
<th>Grade 3-4 (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
<td>18</td>
<td>13</td>
</tr>
</tbody>
</table>

  - UTI (n=3)
  - Epstein-Barr viremia (n=2)
  - Pneumonia (n=2)
  - Septic shock (n=2)
  - Covid and other (n=9)
Mosunetuzumab – axgb
Safety – CRS data

CRS: 40 patients (44%)

Onset of CRS:
- 5 hours (C1D1)
- 27 hours (C1D15)

Duration of CRS
- 3 days

CRS: Cytokine Release Syndrome

Budde LE et al. Lancet Oncol July 2022;23:1055-1065
Mosunetuzumab – axgb
Pharmacotherapy Considerations

Administration:
- Intravenous Infusion
- Hospitalization is not required (23% hospitalized in the trial)

Pre-medications:
- Corticosteroid: Dexamethasone 20 mg IV or methyprednisolone 80mg IV at least 1 hour prior
- Antihistamine: Diphenhydramine 50mg IV/PO at least 30 mins prior to infusion
- Antipyretic: Acetaminophen 500 to 1,000 mg IV/PO at least 30 mins prior to infusion
  - Recommended for cycle 1 and 2

Consider prophylactic medications
- Consider G-CSF as applicable
- Consider Pneumocystis jirovecii pneumonia (PJP) and herpes virus prophylaxis
**Indication:** relapsed or refractory diffuse large B-cell Lymphoma NOS (DLBCL from indolent lymphoma, HGBCL) after ≥2 L after two or more lines of systemic therapy

**Mechanism of action:** targets CD3 on T-cells and CD20 expressed on the surface of B-cells

**Approval Date:** May 2023
Epcoritamab – bysp
Clinical Trial Data

### Inclusion Criteria

- Relapsed or refractory CD20+ large B-cell lymphoma (LBCL) after two or more lines of systemic therapy
- Adult patients
- ECOG 0-2

### Dosing schedule

#### Cycle 1:

- Day 1: 0.16mg
- Day 8: 0.8mg
- Day 15: 48 mg
- Day 22: 48mg

#### Cycle 2-3

- Day 1,8,15,22: 48mg

#### Cycle 4-9:

- Day 1,15: 48 mg

#### Cycle 10 and beyond:

- Day 1: 48 mg

### Premedication (required for C1)

- Acetaminophen
- Anti-histamine
- Steroid (Day 1-4, 8-11, 15-18, 22-25)

### Endpoints

- **Primary endpoint:** ORR
- **Secondary Endpoints:** CR, DOR, PFS, OS, Safety

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ORR = Overall Response Rate, CR = Complete Response, DOR = Duration of response, PFS = Progression Free Survival, OS = Overall Survival

J Clin Oncol. 2023 Apr 20;41(12):2238-2247.
## Epcoritamab – bysp

### Baseline Characteristics

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<tr>
<th>Characteristic</th>
<th>N=157</th>
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<tbody>
<tr>
<td>Age</td>
<td>64 (20-83)</td>
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<tr>
<td>Median previous lines of therapy</td>
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<tr>
<td>2 previous lines of therapy</td>
<td>46 (29%)</td>
</tr>
<tr>
<td>3 previous lines of therapy</td>
<td>50 (32%)</td>
</tr>
<tr>
<td>&gt; 3 previous lines of therapy</td>
<td>61 (39%)</td>
</tr>
<tr>
<td>Double hit/triple-hit lymphoma</td>
<td>13/99 (13.1%)</td>
</tr>
<tr>
<td>Refractory to &gt;/= 2 lines of therapy</td>
<td>119 (76%)</td>
</tr>
<tr>
<td>Prior CAR T-cell therapy</td>
<td>61 (39%)</td>
</tr>
<tr>
<td>Progressed within 6 months of CAR T-cell therapy</td>
<td>46/61 (75%)</td>
</tr>
</tbody>
</table>
Epcoritamab – bysp

Results

ORR: **63.1%** (95% CI 55-70.6)
CR: **38.9%** (95% CI 31.2-46.9)
Duration of Response: 12 months (6.6 –NR)
PFS months: 4.4 (3-7.9)
OS months: not reached (11.3- NR)
Time to response: 1.4 months (1-8.4)

ORR= Objective Response Rate; CR: Complete response; PFS: Progression-free survival; NR: not reached

J Clin Oncol. 2023 Apr 20;41(12):2238-2247.
# Epcoritamab – bysp

## Results

<table>
<thead>
<tr>
<th></th>
<th>Any Grade(%)</th>
<th>Grade &gt; 3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyrexia</td>
<td>23.6</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>22.9</td>
<td>1.9</td>
</tr>
<tr>
<td>Pruritis</td>
<td>21</td>
<td>0</td>
</tr>
<tr>
<td>ICANS</td>
<td>6.4</td>
<td>0.6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Any Grade(%)</th>
<th>Grade &gt; 3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>21.7</td>
<td>14.6</td>
</tr>
<tr>
<td>Febrile Neutropenia (2.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GCSF support (10%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*J Clin Oncol. 2023 Apr 20;41(12):2238-2247.*
Epcoritamab – bysp

Safety - CRS

- Onset of CRS: 20 hrs (C1D1) 27 hours (C1D15)
- Duration of CRS: 3 days
- 49.7% (any grade)

CRS: Cytokine Release Syndrome
Epcoritamab – bysp
Pharmacotherapy Considerations

Administration:
- Subcutaneous administration
- Hospitalization required for Day 15 (24 hours)

Pre-medications:
- Corticosteroid: Dexamethasone 15 mg or prednisone 100mg (and for 3 consecutive days after)
- Antihistamine: Diphenhydramine 50mg
- Antipyretic: Acetaminophen 500 to 1,000 mg
  - Recommended for cycle 1; steroids can be continued for C2 if previous CRS

Consider prophylactic medications
- Consider G-CSF as applicable
- Recommend Pneumocystis jirovecii pneumonia (PJP) and consider herpes virus prophylaxis
Glofitamab-gxbm
Glofitamab-gxbm
Clinical Pharmacology

**Indication**
Glofitamab-gxbm is approved by the Food and Drug Administration for relapsed or refractory DLBCL, NOS or LBCL arising from follicular lymphoma, after two or more lines of systemic therapy.

**Mechanism of action**
Glofitamab-gxbm is a bispecific T-cell engaging antibody that targets CD3 and CD20 in a novel 2:1 tumor–T-cell binding configuration, resulting in T-cell activation and proliferation, cytokine secretion, and lysis of CD20-expressing B cells.

DLBCL, NOS = Diffuse large B-cell lymphoma, not otherwise specified; LBCL= Large B-cell lymphoma
Glofitamab-gxbm Clinical Trial

Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma

An open-label, multicenter, multicohort, single-arm clinical trial

- Median age 67 years (range: 21-90)
- Diagnosis of DLBCL, NOS in 80% of patients, 20% had transformed follicular lymphoma
- Median number of prior therapies was 3 (range 2-7), 55% of patients had primary refractory disease, 83% with refractory to last previous therapy, 19% with prior autologous stem cell transplant, and 30% with prior CAR T-cell therapy

**ITT Population Enrolled:** 3L+ DLBCL NOS, trFL, HGBCL, and PMBCL N=155

**Safety-evaluable Population** N=154

**Columvi Safety-Evaluable Population** N=145

**Columvi Efficacy Population:** 3L+ DLBCL NOS and trFL N=132

**Assessed for eligibility:** N=154

**Discontinued treatment:** N=9

**Reasons for discontinuation:**
- AE: N=3
- Physician decision: N=1
- Withdrawal: N=2
- Death: N=2
- Other: N=1

13 HGBCL and PMBCL patients treated with COLUMVI excluded from efficacy population


DLBCL, NOS = Diffuse large B-cell lymphoma, not otherwise specified; CAR-T = Chimeric antigen receptor
# Glofitamab-gxbm Clinical Trial
## Pivotal Phase II – Design

### Inclusion Criteria
- DLBCL, NOS or LBCL arising from FL
- ECOG PS 0-1
- ≥2 prior therapies including:
  - anti-CD20 antibody
  - anthracycline agent

### Dosing schedule

<table>
<thead>
<tr>
<th>Cycle 1</th>
<th>Cycle 2-12</th>
</tr>
</thead>
</table>
| • Pretreatment with Obinutuzumab 1000 mg (Day 1)  
  • Glofitamab-gxbm step-up dosing:  
    - 2.5 mg (Day 8)  
    - 10 mg (Day 15) | • Glofitamab-gxbm 30 mg on Day 1 every 3 weeks for 11 cycles |

### Endpoints
- Primary endpoint:  
  - CR rate by IRC
- Secondary endpoints:  
  - ORR  
  - DOCR  
  - DOR

Day 8: Hospitalize all patients during and for 24 hours post-infusion  
Day 15: Hospitalize patients who experienced CRS during step-up dose 1 for 24 hours  
Cycles 2-12: Hospitalize patients who experienced CRS with previous infusion for 24 hours

Dickinson MJ, et al. Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2022;387(24):2220-2231; Columvi (Glofitamab) [durable remissions achieved with a unique T-cell engaging bispecific antibody brochure]. M-US-00017815 (v1.15); Printed in USA: CA; Genentech Inc; June 2023; Columvi (Glofitamab) [Formulary Dossier] Genentech Inc; 2023

DLBCL, NOS = Diffuse large B-cell lymphoma, not otherwise specified; LBCL = Large B-cell lymphoma; FL = Follicular lymphoma; CR = Complete response; IRC = Independent review committee; ORR = Overall response rate; DOCR = Duration of complete response; DOR = Duration of response
Glofitamab-gxbm
Clinical Trial
Pivotal Phase II – Efficacy Results

Overall Response Rate
(n=74/132; 95% CI: 47%-65%)
- 13% of patients experienced partial response (n=17/132; 95% CI: 8%-22%)

Complete Response
(n=57/132; 95% CI: 35%-52%)

TIME TO RESPONSE

Median time to response
Median time to CR
42 days (2 cycles)
42 days (2 cycles)

-6.5-MONTH TREATMENT DURATION*

PROBABILITY (%)

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100

mDOCR not reached (NR)*
(95% CI: 16.8-NR)

mDOR: 18.4 months* (95% CI: 11.4-NR)

mDOCR = Median duration of complete response; mDOR = Median duration of response

*From date of first response (CR or PR) until disease progression or death due to any cause.

Glofitamab-gxbm
Clinical Trial
Pivotal Phase II – Safety Results

- Serious adverse reactions occurred in 48% to which in ≥2% of patients included CRS, COVID-19 infection, sepsis, and tumor flare
- Fatal adverse reactions occurred in 5% of patients from COVID-19 infection (3.4%), sepsis (1.4%), and delirium (0.6%)
- ARs led to dose interruptions in 19% of patients, most frequently (≥2%) from neutropenia and thrombocytopenia
- ARs leading to treatment discontinuation were reported in 7% of patients – included infection, delirium, neutropenia, CRS
- ICANS reactions were also observed
  - All Grade: 7 (4.8%); Grade ≥3: 2 (2.1%)
Glofitamab-gxbm
Clinical Trial
Pivotal Phase II – CRS

CRS Incidence by grade and cycle

- CRS of any grade occurred in 70% of patients
  - CRS Grade 1 occurred in 52% of patients, 14% Grade 2, 2.8% Grade 3, and 1.4% Grade 4
  - Grade 1-2 CRS event was observed in 94.1% of patients
  - Grade 3 or 4 CRS was only observed during Cycle 1
  - Recurrent CRS occurred in 34% of all patients

- The median time to onset of CRS
  - C1D8: 14hrs (5-74hrs), C1D15: 29hrs (7-125hrs), C2D1: 28hrs (2-62hrs)

- CRS after any dose resolved in 98% of cases, with a median duration of 2 days (range: 1-14 days)

CRS: Cytokine Release Syndrome
Observed CRS with dexamethasone premedication

Mandatory dexamethasone premedication led to a lower incidence of any grade CRS than treatment with any glucocorticoid.


CRS: Cytokine Release Syndrome
Pharmacotherapy Considerations

**Administration:**
- Administer only as an intravenous infusion through a dedicated infusion line that includes a sterile 0.2-micron in-line filter
- Cycles 1-2: over 4 hours
- Cycles 3-12: over 2 hours
  - Patients experiencing cytokine release syndrome (CRS): Cycles 1-2: over 8 hours; Cycles 3-12: over 4 hours
- Patients should be hospitalized during and for 24 hours after completion of infusion of step-up dose 1 (2.5 mg on Cycle 1 Day 8)

**Pre-medications:**
- Corticosteroid: Dexamethasone 20 mg IV at least 1 hour prior to infusion
- Antihistamine: Diphenhydramine 50 IV/PO at least 30 minutes prior to infusion
- Antipyretic: Acetaminophen 500 to 1,000 mg orally at least 30 minutes prior to infusion
  - Dexamethasone required for Cycles 1-3; may be administered in Cycles 4-12 if any CRS experienced with the previous dose

**Consider prophylactic medications**
- Antiviral agent to prevent herpes simplex virus reactivation
- Anti-PJP agent to prevent pneumocystis jiroveci pneumonia infection
- Anti-CMV agent to present cytomegalovirus infection

**Contraindications, Warnings and Precautions**
- US Boxed Warning: Cytokine release syndrome
- Warnings and Precautions: Neurologic toxicity, serious infections, tumor flare, embryo-fetal toxicity
- Contraindications: None
## Multiple Myeloma Bispecific Antibody FDA Approval Timeline

<table>
<thead>
<tr>
<th>2022</th>
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</tr>
</thead>
<tbody>
<tr>
<td>October 2022:</td>
<td>August 2023:</td>
</tr>
<tr>
<td><strong>Teclistamab-cqyv</strong></td>
<td><strong>Talquetamab-tgvs</strong></td>
</tr>
<tr>
<td><em>Indication</em>: Relapsed/Refractory Multiple Myeloma after at least 4 prior lines of therapy</td>
<td><em>Indication</em>: Relapsed/Refractory Multiple Myeloma after at least 4 prior lines of therapy</td>
</tr>
<tr>
<td><em>Study</em>: MajesTEC-1</td>
<td><em>Study</em>: MMY1001 (MonumenTAL-1) Trial</td>
</tr>
<tr>
<td>August 2023:</td>
<td>August 2023:</td>
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<tr>
<td><strong>Elranatamab-bcmm</strong></td>
<td><strong>Elranatamab-bcmm</strong></td>
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<tr>
<td><em>Indication</em>: Relapsed/Refractory Multiple Myeloma after at least 4 prior lines of therapy</td>
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</tr>
<tr>
<td><em>Study</em>: MagnetisMM-3 trial</td>
<td><em>Study</em>: MagnetisMM-3 trial</td>
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</table>
Talquetamab-tgvs
Talquetamab-tgvs
Clinical Pharmacology

**Indication**
Talquetamab-tgvs is approved by the Food and Drug Administration for the treatment of adults with relapsed or refractory multiple myeloma who have received at least 4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

**Mechanism of action**
Talquetamab-tgvs is a bispecific T-cell engaging antibody that targets CD3 and G protein-coupled receptor class C group 5 member D (GPRC5D), resulting in the lysis of malignant plasma cells that occurs via T-cell recruitment and activation.
232 patients met study criteria and received talquetamab-tgvs subcutaneous (n=130) or IV (n=102)
- Subcutaneous doses had a more favorable pharmacokinetics, safety, and efficacy profile and was selected for phase 2 of the study
  - N=30 - 405 µg/kg weekly
  - N=44 - 800 µg/kg every 2 weeks

<table>
<thead>
<tr>
<th></th>
<th>Talquetamab 405 µg/kg QW (n = 30)</th>
<th>Talquetamab 800 µg/kg Q2W (n = 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age – years (range)</td>
<td>62 (46–80)</td>
<td>64 (47–84)</td>
</tr>
<tr>
<td>Median time since diagnosis – years (range)</td>
<td>5.6 (1.7–19.6)</td>
<td>6.4 (0.8–21.3)</td>
</tr>
<tr>
<td>Median lines of previous therapy – no. (range)</td>
<td>6 (2–14)</td>
<td>5 (2–17)</td>
</tr>
<tr>
<td>Previous stem-cell transplantation – no. (%)</td>
<td>27 (90)</td>
<td>33 (75)</td>
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<tr>
<td>Previous therapy exposure – no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triple-class exposure</td>
<td>30 (100)</td>
<td>43 (98)</td>
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<tr>
<td>Penta-drug exposure</td>
<td>24 (80)</td>
<td>30 (68)</td>
</tr>
<tr>
<td>Refractory status – no. (%)</td>
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<tr>
<td>Immunomodulatory drug</td>
<td>28 (93)</td>
<td>42 (95)</td>
</tr>
<tr>
<td>Proteasome inhibitor</td>
<td>25 (83)</td>
<td>36 (82)</td>
</tr>
<tr>
<td>Anti-CD38 monoclonal antibody</td>
<td>30 (100)</td>
<td>39 (89)</td>
</tr>
<tr>
<td>Triple-class refractory</td>
<td>23 (77)</td>
<td>33 (75)</td>
</tr>
<tr>
<td>Penta-drug refractory</td>
<td>6 (20)</td>
<td>9 (20)</td>
</tr>
<tr>
<td>Refractory to last line of therapy</td>
<td>26 (87)</td>
<td>39 (89)</td>
</tr>
</tbody>
</table>
Talquetamab-tgvs
Clinical Trial
Phase II – Design

**Inclusion Criteria**
- Relapse/refractory with proteasome inhibitor, anti-CD38, immunomodulator as prior therapy
- ECOG PS 0-1

**Dosing schedule**

<table>
<thead>
<tr>
<th>Weekly step-up dosing schedule</th>
<th>Weekly dosing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 (step-up dose 1): 10 µg/kg</td>
<td>405 µg/kg once weekly</td>
</tr>
<tr>
<td>Day 4 (step-up dose 2): 60 µg/kg</td>
<td>Starting 1 week after the first treatment dose and weekly thereafter</td>
</tr>
<tr>
<td>Day 7 (first treatment dose): 405 µg/kg</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Biweekly (every 2 weeks) step-up dosing schedule</th>
<th>Biweekly (every 2 weeks) dosing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 (step-up dose 1): 10 µg/kg</td>
<td>800 µg/kg every 2 weeks</td>
</tr>
<tr>
<td>Day 4 (step-up dose 2): 60 µg/kg</td>
<td>Starting 2 weeks after the first treatment dose and every 2 weeks thereafter</td>
</tr>
<tr>
<td>Day 7 (step-up dose 3): 300 µg/kg</td>
<td></td>
</tr>
<tr>
<td>Day 10 (first treatment dose): 800 µg/kg</td>
<td></td>
</tr>
</tbody>
</table>

Patients should be hospitalized for 48 hours after administration of all doses within the step-up dosing schedule
Subcutaneous injection into abdomen (preferred) or thigh

**Endpoints**

- **Primary endpoint:**
  - Frequency and severity of ARs

- **Secondary endpoints:**
  - ORR
  - DOR
  - TTR
  - PFS

ARs=Adverse reactions; ORR=Overall response rate; DOR=Duration of response; TTR=Time to respond; PFS=Progression free survival

# Talquetamab-tgvs Clinical Trial
## Phase II – Efficacy Results

<table>
<thead>
<tr>
<th>Overall Response – no. (%)</th>
<th>Talquetamab 405 µg/kg QW (n = 30)</th>
<th>Talquetamab 800 µg/kg Q2W (n = 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best Response – no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S-CR</td>
<td>7 (23.3)</td>
<td>5 (11.4)</td>
</tr>
<tr>
<td>CR</td>
<td>0</td>
<td>5 (11.4)</td>
</tr>
<tr>
<td>VGPR</td>
<td>10 (33.3)</td>
<td>13 (29.5)</td>
</tr>
<tr>
<td>PR</td>
<td>4 (13.3)</td>
<td>5 (11.4)</td>
</tr>
<tr>
<td>SD</td>
<td>9 (30.0)</td>
<td>13 (29.5)</td>
</tr>
<tr>
<td>PD</td>
<td>0</td>
<td>3 (6.8)</td>
</tr>
</tbody>
</table>

- **Median time to response – months (range)**
  - 0.9 (0.2-3.8) for 405 µg/kg QW
  - 1.2 (0.3-6.8) for 800 µg/kg Q2W

- **Median time to CR – months (range)**
  - 9.3 (1.7-17.1) for 405 µg/kg QW
  - 2.3 (2.1-6.8) for 800 µg/kg Q2W

- **Median response duration – months (95% CI)**
  - 10.2 (3.0-NR) for 405 µg/kg QW
  - 7.8 (4.6-NR) for 800 µg/kg Q2W

- **Progression-free survival (patients)**
  - 10/21 for 405 µg/kg QW
  - 19/28 for 800 µg/kg Q2W

---

S-CR=Stringent complete response; CR=Complete response; VGPR=Very good partial response; PR=Partial response; SD=Stable disease; PD=Progressive disease

## Talquetamab-tgvs Clinical Trial Phase II – Safety Results

### Hematologic – no. (%)

<table>
<thead>
<tr>
<th>Event</th>
<th>Talquetamab 405 µg/kg QW</th>
<th>Any Grade</th>
<th>Grade 3-4</th>
<th>Talquetamab 800 µg/kg Q2W</th>
<th>Any Grade</th>
<th>Grade 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse event</td>
<td>30 (100)</td>
<td>26 (87)</td>
<td>44 (100)</td>
<td>38 (86)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>18 (60)</td>
<td>9 (30)</td>
<td>19 (43)</td>
<td>10 (23)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>20 (67)</td>
<td>18 (60)</td>
<td>16 (36)</td>
<td>14 (32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>12 (40)</td>
<td>12 (40)</td>
<td>17 (39)</td>
<td>17 (39)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>11 (37)</td>
<td>7 (23)</td>
<td>10 (23)</td>
<td>5 (11)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukopenia</td>
<td>12 (40)</td>
<td>9 (30)</td>
<td>8 (18)</td>
<td>6 (14)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Non-Hematologic – no. (%)

<table>
<thead>
<tr>
<th>Event</th>
<th>Talquetamab 405 µg/kg QW</th>
<th>Any Grade</th>
<th>Grade 3-4</th>
<th>Talquetamab 800 µg/kg Q2W</th>
<th>Any Grade</th>
<th>Grade 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>6 (20)</td>
<td>0</td>
<td>11 (25)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>7 (23)</td>
<td>0</td>
<td>4 (9)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dry mouth</td>
<td>9 (30)</td>
<td>0</td>
<td>25 (57)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>19 (64)</td>
<td>N/A</td>
<td>25 (57)</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysphagia</td>
<td>11 (37)</td>
<td>0</td>
<td>12 (27)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>9 (30)</td>
<td>0</td>
<td>7 (16)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>9 (30)</td>
<td>0</td>
<td>7 (16)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased weight</td>
<td>9 (30)</td>
<td>0</td>
<td>14 (32)</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin-related event</td>
<td>20 (67)</td>
<td>0</td>
<td>31 (70)</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nail-related event</td>
<td>17 (57)</td>
<td>0</td>
<td>12 (27)</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash-related event</td>
<td>14 (47)</td>
<td>0</td>
<td>13 (30)</td>
<td>7 (16)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>10 (33)</td>
<td>0</td>
<td>8 (18)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased AST</td>
<td>3 (10)</td>
<td>0</td>
<td>15 (34)</td>
<td>3 (7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased ALT</td>
<td>6 (20)</td>
<td>1 (3)</td>
<td>13 (30)</td>
<td>3 (7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>8 (27)</td>
<td>5 (17)</td>
<td>8 (18)</td>
<td>3 (7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased GGT</td>
<td>6 (20)</td>
<td>1 (3)</td>
<td>10 (23)</td>
<td>3 (7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### CRS grade – no. (%)

<table>
<thead>
<tr>
<th>Event</th>
<th>Talquetamab 405 µg/kg QW</th>
<th>Any Grade</th>
<th>Grade 3-4</th>
<th>Talquetamab 800 µg/kg Q2W</th>
<th>Any Grade</th>
<th>Grade 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRS grade – no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>23 (76.7)</td>
<td>35 (79.5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>18 (60.0)</td>
<td>25 (56.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>4 (13.3)</td>
<td>10 (22.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 4</td>
<td>1 (3.3)</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Median time to CRS – days (range)

<table>
<thead>
<tr>
<th>Event</th>
<th>Talquetamab 405 µg/kg QW</th>
<th>Any Grade</th>
<th>Grade 3-4</th>
<th>Talquetamab 800 µg/kg Q2W</th>
<th>Any Grade</th>
<th>Grade 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time to CRS</td>
<td>2 (1-22)</td>
<td>2 (1-5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Median CRS duration – days (range)

<table>
<thead>
<tr>
<th>Event</th>
<th>Talquetamab 405 µg/kg QW</th>
<th>Any Grade</th>
<th>Grade 3-4</th>
<th>Talquetamab 800 µg/kg Q2W</th>
<th>Any Grade</th>
<th>Grade 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median CRS duration</td>
<td>2 (1-3)</td>
<td>2 (1-5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CRS= Cytokine Release Syndrome

## Talquetamab-tgvs Clinical Trial Phase II – Safety Results

<table>
<thead>
<tr>
<th></th>
<th>Talquetamab 405 µg/kg QW</th>
<th>Talquetamab 800 µg/kg Q2W</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 neurotoxic event – no. (%)</td>
<td>3 (10.0)</td>
<td>2 (4.5)</td>
</tr>
<tr>
<td>Anosmia</td>
<td>0</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td>Aphasia</td>
<td>1 (3.3)</td>
<td>0</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>1 (3.3)</td>
<td>0</td>
</tr>
<tr>
<td>Confusional state</td>
<td>1 (3.3)</td>
<td>1 (2.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Talquetamab 405 µg/kg QW</th>
<th>Talquetamab 800 µg/kg Q2W</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 infection – no. (%)</td>
<td>14/30 (47%)</td>
<td>15/44 (34)</td>
</tr>
<tr>
<td>Grade 3-4</td>
<td>2/30 (7%)</td>
<td>3/44 (7)</td>
</tr>
<tr>
<td>Opportunistic infection</td>
<td>2/30 (7%)</td>
<td>2/44 (5)</td>
</tr>
</tbody>
</table>

### Administration:
- Subcutaneous injection
- Patients should be hospitalized for 48 hours after administration of each step-up dose (including first treatment dose)

### Pre-medications:
- Corticosteroid: Dexamethasone 16 mg IV/PO 1-3 hours prior to infusion
- Antihistamine: Diphenhydramine 50 IV/PO 1-3 hours prior to infusion
- Antipyretic: Acetaminophen 650 to 1,000 mg IV/PO 1-3 hours prior to infusion
- Recommended 1-3 prior to each step-up dose and repeated step-up doses or cytokine release syndrome

### Consider prophylactic medications
- Antiviral agent to prevent herpes simplex virus reactivation
- Anti-PJP agent to prevent pneumocystis jiroveci pneumonia infection

### Contraindications, Warnings and Precautions
- US Boxed Warning: Cytokine release syndrome, neurologic toxicity
- Warnings and Precautions: Oral toxicity and weight loss, infections, cytopenias, skin toxicity, hepatotoxicity, embryo-fetal toxicity
- Contraindications: None

### REMS
Prescribers, pharmacies, and healthcare settings must be enrolled to dispense to patients
### Talquetamab-tgvs
#### Recommended Management

<table>
<thead>
<tr>
<th>Oral and Mucosal Changes: Can affect weight loss over time</th>
<th>Skin and Nail related adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Symptomatic management with mouth rinses, pain management, nutrition consult</td>
<td>• Skin management: oral and topical glucocorticoid. If refractory, consult dermatology</td>
</tr>
<tr>
<td></td>
<td>• Nail management : Nail soaks, topical moisturizers, and topical steroids</td>
</tr>
</tbody>
</table>
Teclistamab-cqyv
Clinical Pharmacology

**Indication**
Adult patients with RRMM after at least 4 prior lines of therapy including iMiD, PI, and anti-CD38 antibody

**Mechanism of action**
bispecific T-cell engaging antibody that binds to the CD3 receptor expressed on the surface of T-cells and B-cell maturation antigen (BCMA) expressed on the surface of multiple myeloma cells and some healthy B-lineage cells

Bridge between myeloma cells and CD3 receptor on T-cells → T-cell activation leads to myeloma cell death

RRMM: Relapsed/refractory multiple myeloma; iMiD: immunomodulatory drug; PI: proteasome inhibitor;
Teclistamab-cqyv
MajesTEC-1: Phase 1/2 single arm, open-label, multicenter trial

### Inclusion Criteria
- RRMM
- Previously received ≥3 lines of prior therapy, progressive and measurable disease
- ECOG 0-1
- N = 165

Previous BCMA-targeted therapy excluded

### Subcutaneous injection into abdomen (preferred) or thigh

<table>
<thead>
<tr>
<th>Step-up dosing schedule</th>
<th>Weekly dosing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 (step-up dose 1): 0.06 mg/kg</td>
<td>1.5 mg/kg once weekly</td>
</tr>
<tr>
<td>Day 4 (step-up dose 2): 0.3 mg/kg</td>
<td>Starting 1 week after the first treatment dose and weekly thereafter</td>
</tr>
<tr>
<td>Day 7 (first treatment dose): 1.5 mg/kg</td>
<td></td>
</tr>
</tbody>
</table>

Patients should be hospitalized for 48 hours after administration of all doses within the step-up dosing schedule

### Baseline Characteristics

<table>
<thead>
<tr>
<th>Median age 64 years; 58.2% male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median number of previous lines of therapy: 5</td>
</tr>
<tr>
<td>High-risk cytogenetic profile: 25.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relapsed/Refractory status</th>
</tr>
</thead>
<tbody>
<tr>
<td>77.6% triple-class refractory</td>
</tr>
<tr>
<td>30.3% penta-drug refractory</td>
</tr>
<tr>
<td>89.7% resistance to last therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prior Cancer Therapy Regimen:</th>
</tr>
</thead>
<tbody>
<tr>
<td>81.8% prior Auto-SCT</td>
</tr>
</tbody>
</table>

### Endpoints
- **Primary endpoint:** ORR (PR or better)
- **Secondary endpoints:** DOR, VGPR or better, CR or better, time to response, PFS, OS, MRD negativity, safety, PKs, immunogenicity

Teclistamab-cqyv

Safety

<table>
<thead>
<tr>
<th>Adverse Events (N = 165)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CRS (all grade), %</td>
<td>72</td>
</tr>
<tr>
<td>Grade 1</td>
<td>50.3</td>
</tr>
<tr>
<td>Grade 2</td>
<td>21.2%</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0.6%</td>
</tr>
<tr>
<td>Median time to CRS onset after most recent dose, days (range)</td>
<td>2 (1-6)</td>
</tr>
<tr>
<td>ICANS, %</td>
<td>3</td>
</tr>
<tr>
<td>Infections, %</td>
<td>76.4</td>
</tr>
<tr>
<td>Neutropenia, %</td>
<td>70.9</td>
</tr>
<tr>
<td>Anemia, %</td>
<td>52.1</td>
</tr>
<tr>
<td>Thrombocytopenia, %</td>
<td>40</td>
</tr>
<tr>
<td>Hypogammaglobulinemia, %</td>
<td>74.5</td>
</tr>
</tbody>
</table>

Other common ADRs (≥20%): pyrexia, musculoskeletal pain, injection site reaction, fatigue, nausea, headache, pneumonia, and diarrhea.

Onset of CRS: 2 days (range 1-6)
Duration of CRS: 2 days (range 1-9)

72% (any grade)
- Grade 1: 50.3%
- Grade 2: 21.2%
- Grade 3: 1%
- Grade 4: 0


CRS: Cytokine Release Syndrome
Teclistamab-cqyv

Efficacy

Median follow up: 14.1 mo

MRD negativity*:
46% (patients with CR or better)

*threshold of 10^-5

Teclistamab-cqyv

Efficacy

Teclistamab-cqyv

Administration:
- Subcutaneous injection
- Patients should be hospitalized for 48 hours after administration of each step-up dose (including first treatment dose)

Pre-medications:
- Administer the following 1-3 hours before each step-up dose (including step-up dose 1, step-up dose 2, and the first treatment dose)
- Corticosteroid (oral or intravenous dexamethasone 16 mg)
- H1RA (oral or IV diphenhydramine 50 mg or equivalent)
- Antipyretics (oral or IV acetaminophen 650 mg to 1,000 mg or equivalent)

Duration of therapy:
- Continue until disease progression or unacceptable toxicity

Prophylactic/supportive care therapy
- Anti-PJP agent to prevent pneumocystis jiroveci pneumonia infection
- Antiviral agent to prevent herpes simplex virus reactivation

REMS program
Prescribers, pharmacies and healthcare settings must be enrolled to dispense to patients

Black Box Warnings:
- CRS
- Neurologic toxicities

H1RA: Histamine 1 receptor antagonist
Teclistamab-cqyv
Dosing Considerations

Step-up dose #2 and the first treatment dose may be given between 2 - 4 days after the previous dose.

Option to switch to Q2W (Q4W*) dosing if:
• ≥PR after ≥4 cycles (Phase 1)
• ≥CR for ≥6 months (Phase 2)

*Patients could further switch to monthly dosing if they demonstrated continued response on the Q2W schedule.
Elranatamab-bcmm
Clinical Pharmacology

**Indication**
Adult patients with RRMM after at least 4 prior lines of therapy including iMiD, PI, and anti-CD38 antibody

**Mechanism of action**
Bispecific B-cell maturation antigen (BCMA)-directed T-cell engaging antibody that binds BCMA on plasma cells, plasmablasts, and multiple myeloma cells and CD3 on T-cells leading to cytolysis of the BCMA-expressing cells → Elranatamab-bcmm activated T-cells, caused proinflammatory cytokine release, and resulted in multiple myeloma cell lysis.
Elranatamab-bcmm
MagnetisMM-3: Phase 2 single-arm, open-label, multicenter trial

**Baseline Characteristics (Cohort A)**
- Median age 68 years; 55% male
- Median number of previous lines of therapy: 5
- High-risk cytogenic profile: 25%

**Endpoints**
- **Primary endpoint:** ORR (PR or better)
- **Secondary endpoints:** DOR, DOR CR or better, time to response, PFS, OS, MRD negativity, PFS, safety, PK immunogenicity

**Inclusion Criteria**
- RRMM
- Previously received 4+ lines of prior therapy, progressive and measurable disease
- ECOG 0-2
- N = 187
  - Cohort A: No prior BCMA-directed therapy N=123
  - Cohort B: Prior BCMA-directed therapy N=64

**Subcutaneous injection into abdomen (preferred) or thigh**

<table>
<thead>
<tr>
<th>Priming doses</th>
<th>Weeks 2-24</th>
<th>Weeks 25+</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step-up Dosing</strong></td>
<td><strong>Weekly Dosing</strong></td>
<td><strong>Responders (patients who achieve PR or better lasting at least 2 months): Biweekly (every 2 weeks) Dosing</strong></td>
</tr>
<tr>
<td>Day 1: 12 mg</td>
<td>Day 8: 76 mg</td>
<td>Day 1: 12 mg</td>
</tr>
<tr>
<td>Day 4: 32 mg</td>
<td><strong>76 mg once weekly</strong></td>
<td><strong>76 mg every 2 weeks</strong></td>
</tr>
<tr>
<td><strong>First Treatment Dose</strong></td>
<td><strong>Starting 1 week after the first treatment dose and weekly thereafter</strong></td>
<td><strong>Starting 1 week after the first treatment dose and weekly thereafter</strong></td>
</tr>
</tbody>
</table>

Patients should be hospitalized for 48 hours after administration of first step-up dose, and for 24 hours after second step-up dose.

Elranatamab-bcmm
Safety

<table>
<thead>
<tr>
<th>Safety</th>
<th>Adverse Events (N = 123/119*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRS (all grade), %</td>
<td>56.3*</td>
</tr>
<tr>
<td>Grade 1</td>
<td>42*</td>
</tr>
<tr>
<td>Grade 2</td>
<td>14.3*</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
</tr>
<tr>
<td>Median time to CRS onset after most recent dose, days (range)</td>
<td>2 (1-9)</td>
</tr>
<tr>
<td>ICANS, %</td>
<td>3.4</td>
</tr>
<tr>
<td>Infections, %</td>
<td>42</td>
</tr>
<tr>
<td>Neutropenia, %</td>
<td>48.8</td>
</tr>
<tr>
<td>Anemia, %</td>
<td>48.8</td>
</tr>
<tr>
<td>Thrombocytopenia, %</td>
<td>30.9</td>
</tr>
</tbody>
</table>

Other common ADRs (≥20%): fatigue, injection site reaction, diarrhea, musculoskeletal pain, decreased appetite, rash, cough, nausea, pyrexia

*patients who received 2 step up doses
Elranatamab-bcmm

Safety - CRS

N=119
CRS: 56.3%

Median onset of CRS:
  • 2 days (1-9)

Median time to resolution
  • 2 days (1-19)

Elranatamab-bcmm

Efficacy

(Cohort A)

Median follow up: 14.7 mo

MRD negativity*: 89.7% (patients with CR or better)

*threshold of $10^{-5}$

Elranatamab-bcmm

Efficacy

Elranatamab-bcmm

Administration
- Subcutaneous injection
- Patients should be hospitalized for 48 hours after administration of first step-up dose, and for 24 hours after administration of the second step-up dose

Pre-medications
- Administer the following 1 hour before each step-up dose (including the first treatment dose)
  - Corticosteroid (oral or intravenous dexamethasone, 20 mg or equivalent)
  - Antihistamine (oral diphenhydramine 25 mg or equivalent)
  - Antipyretics (oral acetaminophen 650 mg or equivalent)

Duration of therapy
- Continue until disease progression or unacceptable toxicity

Prophylactic/supportive care therapy
- Antiviral agent to prevent herpes simplex virus reactivation
- Anti-PJP agent to present pneumocystis jiroveci pneumonia infection

REMS program
- Prescribers, pharmacies and healthcare settings must be enrolled to dispense to patients

FOR THE PATIENT
Call your healthcare provider or get emergency help right away if you have any of these symptoms:

- Fever 100.4°F (38°C) or higher
- Trouble breathing
- Chills
- Dizziness or light-headedness
- Fast heartbeat
- Headache
- Agitation, trouble staying awake, confusion or disorientation, seeing or hearing things that are not real

Black Box Warnings:
- CRS
- Neurologic toxicities

Elranatamab-bcmm (prescribing information), Pfizer Inc. August 2023.
Toxicity & Management
Cytokine Release Syndrome

Fever

Hypotension

Hypoxia
Neurotoxicity

- ICE score
- Level of consciousness
- Seizure
- Motor finding
- Elevated ICP or cerebral edema
- Other Symptoms: headache, peripheral neuropathy, dizziness

Mitigation Strategies

- Premedication
  - Steroids, antihistamine, acetaminophen

- Step-up dosing

- Bridging therapies
  - Obinutuzumab prior to CD20 bispecifics

- Alternative routes
  - SQ mosunetuzumab reduced peak IL-6 levels

References:
Management

Grade adapted strategies
Supportive care
Hospitalization / ICU monitoring
IL-6 mAb
Corticosteroids

Real World Considerations

Flagging patient's charts via smart zone alert
Staff competency and training
Toxicity management guidelines for all products vs individual products management

- Smart Zone Design
  - Goal is to notify ED or urgent care provider a BMT physician needs to be consulted for possible management of unique toxicities (CRS, ICANS)
  - Alert set up to fire in **ED and urgent care encounters** for **ED and urgent care providers, nursing, and support staff** upon registration and alert clears automatically after **48 hours**
  - **Any bispecific antibody** (blina, tec, talq, elrana, mosun, epcor) in **any status** (active, complete, discontinued, future) ordered within past **365 days**
  - Go live tentative 7/5
Inpatient - Logistical Strategies and Therapeutic Considerations

MCI clinic notifies the oncology unit charge nurse of any direct/unplanned admissions:
- Implementation of a shared Team’s worksheet for direct admissions – updates daily
  - Allows time for the allocation of bispecific T-cell antibody

Patients are hospitalized as per the package insert recommendations:
- Exceptions based on specific patient case

CRS/ICANS monitoring:
- CRS laboratories: LDH, ferritin, and CRP daily; vital signs multiple times per day
- Neurology checks every 4 hours and ICE assessment done every shift
- Institutional management is in progress, but managed per package insert/trial protocol

Patients without sign or symptoms of CRS/ICANS are discharge home to continue therapy outpatient:
- Medication reconciliation and education is performed by transition of care pharmacist/specialist
- Clinical staff pharmacist emails outpatient team for the procurement of medication for the following cycle
MCC IPOP program

Inpatient-Outpatient program with APP assessment on days of administration for Cycle 1-2

Close monitoring, lab follow-up, lower threshold for admission

IPOP pharmacist dedicated for education, medication reviews
## MCC

<table>
<thead>
<tr>
<th>Bispecific Antibody</th>
<th>Scheduled Hospitalization</th>
<th>Outpatient Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elranatamab</td>
<td>C1 Day 1,3</td>
<td>C1 Day 8,15,22</td>
</tr>
<tr>
<td>Epcoritamab</td>
<td>C1 Day 15</td>
<td>C1 Day 1,2,8,9,22,23</td>
</tr>
<tr>
<td>Glofitamab</td>
<td>C1 Day 8</td>
<td>C1 Day 15,16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C2 Day 1,2</td>
</tr>
<tr>
<td>Mosunetuzumab</td>
<td>-</td>
<td>C1 Day 1,8,15,16</td>
</tr>
</tbody>
</table>
Thank You

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Syeda Saba Kareem Pharm.D BCOP – Moffitt Cancer Center