Anti B-Cell Maturation Antigen CAR T-cell and Antibody Drug Conjugate Therapy for Heavily Pre-Treated Relapsed and Refractory Multiple Myeloma: Effectiveness and Value

Public Meeting — April 16, 2021

Meeting materials available at: https://icer.org/assessment/multiple-myeloma-2021/#timeline
Patient and Clinical Experts

• **Tom Bellfort**, Patient Expert
  - No financial conflicts to disclose.

• **David Mitchell**, Founder, Patients For Affordable Drugs, Patient Expert
  - David Mitchell is on the Board of Directors of Friends of Cancer Research which receives grants from BMS, Bluebird Bio, and Janssen. He received honoraria from the FDA for his service on the Oncologic Drugs Advisory Committee and was part of a class action suit against Celgene to which he received a service award.

• **Anita D’Souza, MD, MS**, Associate Professor of Medicine, Medical College of Wisconsin
  - Dr. Anita D’Souza has received institutional research funding from Sanofi, TeneoBio, Takeda, and Caelum. Dr. D’Souza reports advisory board roles with Akcea, Imbrium Therapeutics and Pfizer and received consulting honoraria from Janssen.

• **S. Vincent Rajkumar, MD**, Edward W. and Betty Knight Scripps Professor of Medicine, Mayo Clinic, Rochester, MN
  - Dr. S. Vincent Rajkumar has held a position as a member of the Board of Directors for the International Myeloma Foundation.
There is not a day that goes by that I am not aware that I have Multiple Myeloma. I know that while the current combo is working, it won't work forever. I will then be refractory to all three major lines of treatment. That means I will have to look at ASCT [autologous stem cell transplantation] and/or one of the new classes of drugs which come with greater toxicities. I know that without new drugs I will run out of options.

David, Multiple Myeloma Patient
Why Are We Here Today?

- What happens the day these treatments are approved by the FDA?
- Patients can have difficulty accessing drugs
  - Coverage eligibility
  - Costs (out-of-pocket and insurance premiums)
- What happens to patients and others in the health care “system”?
When There Isn’t Enough Money For Health Insurance

Leonard Edloe, Richmond, Virginia

The Whitmans, Bird City, Alaska

Luke Breen, Minneapolis, Minnesota
Organizational Overview

- Midwest Comparative Effectiveness Public Advisory Council
- The Institute for Clinical and Economic Review (ICER)
Sources of Funding, 2021
https://icer.org/who-we-are/independent-funding/

- Nonprofit Foundations: 68%
- Manufacturer Contributions: 12%
- Health Plans and Provider Group Contributions: 9%
- Government Contributions: 10%
- Other*: 1%

ICER Policy Summit and non-report activities only

*Individual / matching contributions and speech stipends
How was the ICER report developed?

• Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
• Internal ICER staff evidence analysis
• The University of Colorado, Anschutz Medical Campus cost-effectiveness modeling
• Public comment and revision
• Expert reviewers
  • Elizabeth Franklin, PhD, MSW, President, Cancer Support Community
  • S. Vincent Rajkumar, MD, Edward W. and Betty Knight Scripps Professor of Medicine, Mayo Clinic
  • Ravi Vij, MD, MBA, Professor, Department of Medicine, Washington University School of Medicine in St. Louis
• How is the evidence report structured to support CEPAC voting and policy discussion?
Value Assessment Framework: Long-Term Value for Money

- Special Social/Ethical Priorities
- Benefits Beyond “Health”
- Total Cost Overall
  Including Cost Offsets
- Health Benefits:
  Return of Function, Fewer Side Effects
- Health Benefits:
  Longer Life
## Agenda

<table>
<thead>
<tr>
<th>Time (CST)</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:00am – 10:20am</td>
<td>Meeting Convened and Opening Remarks</td>
</tr>
<tr>
<td></td>
<td>Steven D. Pearson, MD, MSc, President, ICER</td>
</tr>
<tr>
<td>10:20am – 10:50am</td>
<td>Presentation of the Clinical Evidence</td>
</tr>
<tr>
<td></td>
<td>Sei Lee, MD, MAS, Associate Professor of Medicine</td>
</tr>
<tr>
<td></td>
<td>University of California San Francisco</td>
</tr>
<tr>
<td>10:50am – 11:20am</td>
<td>Presentation of the Economic Model</td>
</tr>
<tr>
<td></td>
<td>R. Brett McQueen, PhD, Assistant Professor</td>
</tr>
<tr>
<td></td>
<td>University of Colorado, Anschutz Medical Campus</td>
</tr>
<tr>
<td>11:20am – 11:50am</td>
<td>Public Comments and Discussion</td>
</tr>
<tr>
<td>11:50am – 12:30pm</td>
<td>Lunch Break</td>
</tr>
<tr>
<td>12:30pm – 1:45pm</td>
<td>Midwest CEPAC Vote on Clinical Effectiveness and Value</td>
</tr>
<tr>
<td>1:45pm – 2:00pm</td>
<td>Break</td>
</tr>
<tr>
<td>2:00pm – 3:30pm</td>
<td>Policy Roundtable</td>
</tr>
<tr>
<td>3:30pm – 4:00pm</td>
<td>Reflections from Midwest CEPAC</td>
</tr>
<tr>
<td>4:00pm</td>
<td>Meeting Adjourned</td>
</tr>
</tbody>
</table>
Presentation of the Clinical Evidence

Sei J. Lee, MD, MAS
Division of Geriatrics
University of California, San Francisco
Key Collaborators

• Molly Beinfeld, MPH, Research Lead, Evidence Synthesis, ICER
• Noemi Fluetsch, MPH, Research Assistant, HEOR, ICER
• Belen Herce-Hagiwara, BA, Research Assistant, Evidence Synthesis, ICER

Disclosures:

We have no conflicts of interest relevant to this report.
Background

- Multiple Myeloma (MM)
  - Hematologic cancer of plasma cells, affecting 150,000 Americans
  - Median age at diagnosis: 69
  - Black Americans 2x more likely to be affected than White Americans

- Relapsed Refractory MM
  - Currently approved therapies are not curative
  - Patients cycle through multiple combinations of treatments, resulting in significant side effects and high cost
  - High unmet need
What Patients and Advocates Told Us

Patient Concerns

- Fatigue, weakness
- Financial strain
- Impact on caregivers
Usual Care Treatments

• Three broad classes of commonly used treatments:
  • Monoclonal antibodies (daratumumab or isatuximab)
  • Immunomodulators (lenalidomide or pomalidomide)
  • Proteasome inhibitors (bortezomib, carfilzomib or ixazomib)

• Triple-class refractory: patients whose disease is unresponsive to each of these classes of treatments

• Quad- and Penta- refractory: patients whose disease is unresponsive to 4 or 5 commonly used MM medications (including at least 1 medication from each class above)
Anti-BCMA Therapies

• B-cell maturation antigen (BCMA) is an attractive target for MM
  • Over-expressed on plasma cells but minimally expressed on other cells
  • Appears to be essential for the survival of long-lived plasma cells
B-Cell Maturation Antigen (BCMA) Therapies Under Review

• Interventions:
  • Chimeric antigen receptor T (CAR-T) cell therapies:
    • Idecabtagene vicleucel (‘ide-cel’, Abecma®, BMS and bluebird bio)
    • Ciltacabtagene autoleucel (‘cilta-cel’, Janssen and Legend biotech)
  • Antibody-drug conjugate (IV):
    • Belantamab mafodotin (Blenrep®, GSK)

• Comparators:
  • Usual care regimens
CAR-T Process (ide-cel and cilta-cel)

**LEUKAPHERESIS**
Collect patient’s white blood cells

**MANUFACTURING PROCESS**
- Isolate and activate T cells
- Engineer T cells with CAR gene
- Grow and expand number of T cells

**INFUSION**
Infuse same patient with engineered T cells

Image: dana-farber.org
Antibody-Drug Conjugate: Belantamab mafodotin

• Belantamab mafodotin is made up of two parts linked together: an antibody (belantamab) that binds to BCMA on the surface of plasma cells, delivering the drug (mafodotin) that accumulates in and kills the plasma cells

Image: blenrep.com
Scope of Comparative Clinical Effectiveness

**Ide-cel or Cilta-cel vs Usual Care**

- Adults with triple- or quad-refractory MM who have received at least three prior lines of therapy

**Belantamab vs Usual Care**

- Adults with triple-, quad- or penta-refractory MM who have received at least four prior lines of therapy
Outcomes Assessed

• Overall response
• Progression free survival
• Overall survival
• Health-related quality of life
• Harms
Insights from Discussions with Patients

• **Fatigue and weakness:** "The weakness is the worst thing...it interferes with your ability to exercise and take care of yourself."

• **Financial strain:** "That first year I went into debt and had to refinance my home. I was 3 years from paying off my house and I had to start over."

• **Impact on Caregivers:** [The irritability caused by dexamethasone led to] “a temporary estrangement with my spouse because of my short temper.”
Clinical Evidence
Clinical Evidence: Triple- or Quad-Refractory MM (3+ prior lines of treatment)
Overview of Key Phase II, Open-Label Single-Arm Trials

<table>
<thead>
<tr>
<th>Key Trials</th>
<th>N</th>
<th>Age (years)</th>
<th>Follow-Up Duration (months)</th>
<th>As Treated, Overall Response Rate</th>
<th>Intention to Treat, Overall Response Rate</th>
<th>Median Progression Free Survival (months)</th>
<th>Median Overall Survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KarMMa† Ide-cel</td>
<td>149</td>
<td>61</td>
<td>13.3</td>
<td>94/128 (73%)</td>
<td>94/149 (63%)</td>
<td>8.6</td>
<td>19.4</td>
</tr>
<tr>
<td>CARTITUDE-1 Cilta-cel</td>
<td>126</td>
<td>61</td>
<td>12.4</td>
<td>94/97 (97%)</td>
<td>94/126 (75%)</td>
<td>&gt;12.4</td>
<td>&gt;12.4</td>
</tr>
<tr>
<td>MAMMOTH* Overall Usual Care</td>
<td>275</td>
<td>65</td>
<td>10.6</td>
<td>--</td>
<td>31%</td>
<td>3.4</td>
<td>9.3</td>
</tr>
</tbody>
</table>

† 28 patients were retreated after disease progression
*Retrospective chart review
# Clinical Evidence: Triple-, Quad-, or Penta-Refractory MM (4+ prior lines of treatment)

## Overview of Key Phase II, Open-Label Single-Arm Trials

<table>
<thead>
<tr>
<th>Key Trials</th>
<th>N</th>
<th>Age (years)</th>
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<th>As Treated, Overall Response Rate</th>
<th>Intention to Treat, Overall Response Rate</th>
<th>Median Progression Free Survival (months)</th>
<th>Median Overall Survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DREAMM-2 Belantamab</td>
<td>97</td>
<td>65</td>
<td>13</td>
<td>--</td>
<td>32%</td>
<td>2.8</td>
<td>13.8</td>
</tr>
<tr>
<td>MAMMOTH* Subcohort Usual Care</td>
<td>Triple/quad: 148</td>
<td>59</td>
<td>10.6</td>
<td>--</td>
<td>28%</td>
<td>NR</td>
<td>Triple/quad: 9.2 Penta: 5.6</td>
</tr>
</tbody>
</table>

*Retrospective chart review
## Patient-Reported Outcomes: Mean Change From Baseline in Health-Related Quality of Life*§

<table>
<thead>
<tr>
<th>Intervention (Trial)</th>
<th>Time from Baseline (N)</th>
<th>Physical Functioning</th>
<th>Fatigue†</th>
<th>Pain†</th>
<th>Global Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ide-cel (KarMMa)</td>
<td>9 months (N=59)</td>
<td>13.2‡</td>
<td>-22.8‡</td>
<td>-23.8‡</td>
<td>15.4‡</td>
</tr>
<tr>
<td>Cilta-cel (CARTITUDE-1)</td>
<td>6 months (N=30)</td>
<td>NR</td>
<td>-9.2‡</td>
<td>-8.9‡</td>
<td>NR</td>
</tr>
<tr>
<td>Belantamab (DREAMM-2)</td>
<td>6 months (N=19)</td>
<td>-0.1</td>
<td>3.6</td>
<td>2.6</td>
<td>-4.7</td>
</tr>
</tbody>
</table>

* Selected EORTC QLQ-C30 Sub-domains (Change of 10 points is usually considered clinically significant)
† Negative changes indicate a reduction in pain or fatigue
‡ statistically significant, p<0.05
§ Data are digitized
# Harms

<table>
<thead>
<tr>
<th>Ide-cel and Cilta-cel</th>
<th>Belantamab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytokine release syndrome (CRS): 84-95% overall</td>
<td></td>
</tr>
<tr>
<td>- 31%-39% Grade 2+ (hypoxia/hypotension, usu. hospitalization)</td>
<td></td>
</tr>
<tr>
<td>- Lasted median 4-5 days</td>
<td></td>
</tr>
<tr>
<td>- 52-69% require tocilizumab</td>
<td></td>
</tr>
<tr>
<td>Neurotoxicity: 18-21%</td>
<td></td>
</tr>
<tr>
<td>Treatment-related deaths: 3-6%</td>
<td></td>
</tr>
<tr>
<td>Ocular toxicity and visual decline:</td>
<td></td>
</tr>
<tr>
<td>- 46% 2+ lines worsening on Snellen chart in more affected eye</td>
<td></td>
</tr>
<tr>
<td>- 18% had worse than 20/50 BCVA in better eye</td>
<td></td>
</tr>
<tr>
<td>- Median duration of visual decline 22-33 days</td>
<td></td>
</tr>
</tbody>
</table>

BCVA: Best Correct Visual Acuity
Uncertainty and Controversies

- Concern about cilta-cel treatment-related deaths
- Data for cilta-cel is immature and preliminary, resulting in substantial uncertainty
- The PFS/OS ratio for belantamab is an outlier compared to all other MM treatments
Potential Other Benefits/Harms and Contextual Considerations

• **Benefit:** Anti-BCMA therapies offer a novel mechanism of action, making it more likely that this treatment would benefit patients who are refractory to all current treatments.

• **Harms:** Anti-BCMA therapies may worsen disparities, since previous treatments with high cost and high side effects requiring treatment at specialized centers have often worsened disparities.
Public Comments Received

• For belantamab, the ocular toxicities are temporary and reversible

• Published data on ide-cel and cilta-cel rely on "as treated" analyses. Intention-to-treat analyses are more likely to lead to unbiased comparisons to usual care

• There is insufficient data to compare anti-BCMA treatments to each other
## ICER Evidence Ratings

<table>
<thead>
<tr>
<th>Intervention</th>
<th>ICER Evidence Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Triple-or Quad-Refractory MM (3+ prior lines of therapy)</strong></td>
<td></td>
</tr>
<tr>
<td>Ide-cel vs Usual Care</td>
<td>B+</td>
</tr>
<tr>
<td>Cilta-cel vs Usual Care</td>
<td>B+</td>
</tr>
<tr>
<td>Ide-cel vs Cilta-cel</td>
<td>I</td>
</tr>
<tr>
<td><strong>Triple-, Quad- or Penta-Refractory MM (4+ prior lines of therapy)</strong></td>
<td></td>
</tr>
<tr>
<td>Belantamab vs Usual Care</td>
<td>P/I</td>
</tr>
</tbody>
</table>

B+: incremental or better, high certainty of at least a small net health benefit
I: insufficient
P/I: promising but inconclusive, small likelihood of a negative net health benefit
Summary

• For the CAR-T therapies for MM (ide-cel and cilta-cel), current evidence suggests a high likelihood of at least small benefit compared to usual care, with a possibility of substantial benefit

• For belantamab mafodotin, current evidence suggests equivalence or small benefit compared to usual care. Current evidence cannot exclude the possibility of small net harm
Questions?
Long-Term Cost-Effectiveness

R. Brett McQueen, PhD
Assistant Professor
University of Colorado Anschutz Medical Campus
Key Review Team Members

• **R. Brett McQueen, PhD**, Assistant Professor, University of Colorado Anschutz Medical Campus
• **Eric Gutierrez, MPH**, Statistical Analyst, University of Colorado Anschutz Medical Campus
• **Sue Kwon, BS**, Graduate Research Assistant, University of Colorado Anschutz Medical Campus
• **Melanie D. Whittington, PhD**, Associate Director of Health Economics, ICER

**Disclosures:**

Financial support provided to the University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences from the Institute for Clinical and Economic Review (ICER)

R. Brett McQueen has no conflicts to disclose defined as more than $10,000 in healthcare company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care manufacturers or insurers.
Objective

• Assess the lifetime cost-effectiveness of ide-cel, cilta-cel, and belantamab as compared to relevant comparator treatments
Methods in Brief
Methods Overview

• **Time Horizon:** Patient lifetime

• **Setting:** United States

• **Perspective:** Health care sector (direct medical care and drug costs); modified societal

• **Cycle Length:** 1 month

• **Discount Rate:** 3% per year (costs and outcomes)

• **Outcomes:** Total costs, life years, quality-adjusted life years (QALY), equal value of life years gained (evLYG), incremental cost-effectiveness ratio (cost per life-year gained, cost per QALY gained, cost per evLYG, cost per month of progression-free survival (PFS) gained)
Model Schematic

*Includes up-front decision tree to account for patient disposition from leukapheresis and through CAR-T infusion.
## Model Cohort Characteristics

<table>
<thead>
<tr>
<th>Triple or Quad-Refractory Refractory MM</th>
<th>Ide-cel</th>
<th>Cilta-cel</th>
<th>Triple or Quad-Refractory Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age</td>
<td>61</td>
<td>61</td>
<td>60</td>
</tr>
<tr>
<td>Percent Male</td>
<td>59%</td>
<td>59%</td>
<td>57%</td>
</tr>
<tr>
<td>Refractory status, %</td>
<td>Anti-CD38 Ab-refractory: 94% Triple-refractory: 84%</td>
<td>Triple-refractory: 88%</td>
<td>Anti-CD38 Ab-refractory: 100%</td>
</tr>
<tr>
<td>Median prior lines of treatment</td>
<td>6</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Source</td>
<td>KarMMa; Munshi et al. 2020</td>
<td>CARTITUDE-1; Madduri et al. 2020</td>
<td>MAMMOTH; Gandhi et al. 2019</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Triple/Quad/Penta-Refractory MM</th>
<th>Belantamab</th>
<th>Triple/Quad/Penta-Refractory Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age</td>
<td>65</td>
<td>59</td>
</tr>
<tr>
<td>Percent Male</td>
<td>53%</td>
<td>56%</td>
</tr>
<tr>
<td>Refractory status, %</td>
<td>Anti-CD38 Ab-refractory: 92% - 100% (dependent on dose)</td>
<td>Anti-CD38 Ab-refractory: 100%</td>
</tr>
<tr>
<td>Median prior lines of treatment</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Source</td>
<td>DREAMM-2; Lonial et al. 2020</td>
<td>MAMMOTH; Gandhi et al. 2019</td>
</tr>
</tbody>
</table>
Key Model Assumptions

• Parametric curve functions were fit separately for each population/treatment and were used to extrapolate the data over a lifetime horizon

• Recent observational evidence on patients using a mix of therapies was used to estimate PFS and OS of relevant comparators

• For CAR-T therapies, patients received at least one full single course of therapy. A proportion of patients were re-treated and assigned the full costs associated with CAR-T, including infusion and other resource utilization

• Discontinuation of CAR-T due to an AE or manufacturing failure before receiving infusion, receive comparator treatment benefits, risks, and costs
# Key Model Inputs: Survival and Mortality

<table>
<thead>
<tr>
<th>Survival Estimate</th>
<th>Ide-cel (KarMMa)</th>
<th>Cilta-cel (CARTITUDE-1)</th>
<th>MAMMOTH Triple- or Quad-Refractory (Comparator to CAR-Ts)*</th>
<th>Belantamab (DREAMM-2)</th>
<th>MAMMOTH Triple/Quad/Penta-Refractory (Comparator to Belantamab)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression-free survival</td>
<td>Median: 8.8 months</td>
<td>Median not reached; 12 month PFS 77% used in model</td>
<td>PFS curve fit to proportional relationship reported in previous meta-analyses Median: 3.4 months</td>
<td>Median: 2.8 months</td>
<td>PFS curve fit to proportional relationship reported in previous meta-analyses Median: 2.6 months</td>
</tr>
<tr>
<td>Overall survival</td>
<td>Median: 19.4 months</td>
<td>Median not reached</td>
<td>Median: 9.2 months</td>
<td>Median: 13.7 months</td>
<td>Median: 7.7 months</td>
</tr>
</tbody>
</table>

* Comparator to belantamab weights outcomes from both populations exposed to three or more lines of therapy and populations exposed to four or more lines of therapy.
### Key Model Inputs: Intervention Costs

<table>
<thead>
<tr>
<th>Intervention (Dosage)</th>
<th>WAC/List Price</th>
<th>Net Price</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ide-cel</td>
<td>$419,500 per infusion</td>
<td>N/A</td>
<td>REDBOOK</td>
</tr>
<tr>
<td>Cilta-cel</td>
<td>Assumed same as ide-cel</td>
<td>N/A</td>
<td>Assumption</td>
</tr>
<tr>
<td>Belantamab</td>
<td>$8,277 per 100mg package ($21,520 - $32,280 per month)</td>
<td>$20,434 - $24,829 per month</td>
<td>REDBOOK</td>
</tr>
<tr>
<td>Comparator therapies per month</td>
<td>N/A net prices used</td>
<td>$20,434 - $24,829 per month</td>
<td>Multiple</td>
</tr>
</tbody>
</table>
Key Model Inputs: Administration and Monitoring Utilization

- **Stage 1**: prior to and during therapy administration
  - Ide-cel: leukapheresis, *92% infused, 22% re-treated*, and intensive AE treatment and monitoring in inpatient settings
  - Cilta-cel: leukapheresis, *86% infused, 22% re-treated* (assumption based on ide-cel), and intensive AE treatment and monitoring in inpatient settings
  - Belantamab: ophthalmic examinations at baseline and prior to each dose
- **Stage 2**: post-therapy monitoring and progression-free
  - Complete blood count testing, liver function testing, treatment-specific outpatient visits
- **Stage 3**: progressed disease
  - 4 cycles of subsequent treatment administration, complete blood count testing, liver function testing
## Key Model Inputs: Utilities

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Three or More Lines of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression-free on Therapy and Responding</td>
<td>0.78</td>
</tr>
<tr>
<td>Progression-free off Therapy and Responding</td>
<td>0.82</td>
</tr>
<tr>
<td>Progressed Disease/not Responding to Treatment</td>
<td>0.71</td>
</tr>
<tr>
<td>Source</td>
<td>Delforge et al (KarMMa), 2020</td>
</tr>
</tbody>
</table>

- Disutilities varied from -0.04 to -0.31 for adverse events
- Utility for grade 3 or 4 CRS = 0 for duration of 15 days
Results
## Base-Case Results: Ide-cel

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Intervention Cost</th>
<th>Other Non-intervention costs*</th>
<th>Total Cost</th>
<th>Time Spent in PFS State (months)</th>
<th>QALYs</th>
<th>evLYGs</th>
<th>Life Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ide-Cel</td>
<td>$466,000</td>
<td>$180,000</td>
<td>$646,000</td>
<td>16.24</td>
<td>2.24</td>
<td>2.40</td>
<td>2.97</td>
</tr>
<tr>
<td>CAR-T Comparator Market Basket</td>
<td>$153,000</td>
<td>$123,000</td>
<td>$276,000</td>
<td>5.75</td>
<td>1.08</td>
<td>1.08</td>
<td>1.50</td>
</tr>
</tbody>
</table>

CAR-T: chimeric antigen receptor T-cells, evLYG: equal-value of life years gained, QALYs: quality-adjusted life years gained, PFS: progression-free survival.
*Other non-intervention costs include costs for monitoring, progressed treatment costs, physician visits, adverse event management (first two cycles only) and monthly laboratory costs for complete blood count and liver testing.
## Preliminary Base-Case Results: Cilta-cel

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Intervention Cost</th>
<th>Other Non-intervention costs*</th>
<th>Total Cost</th>
<th>Time Spent in PFS State (months)</th>
<th>QALYs</th>
<th>evLYGs</th>
<th>Life Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cilta-Cel† (preliminary)</td>
<td>$445,000</td>
<td>$172,000</td>
<td>$617,000</td>
<td>25.82</td>
<td>3.40</td>
<td>3.74</td>
<td>4.52</td>
</tr>
<tr>
<td>CAR-T Comparator Market Basket</td>
<td>$153,000</td>
<td>$123,000</td>
<td>$276,000</td>
<td>5.75</td>
<td>1.08</td>
<td>1.08</td>
<td>1.50</td>
</tr>
</tbody>
</table>

CAR-T: chimeric antigen receptor T-cells, evLYG: equal-value of life years gained, QALYs: quality-adjusted life years gained, PFS: progression-free survival.

*Other non-intervention costs include costs for monitoring, progressed treatment costs, physician visits, adverse event management (first two cycles only) and monthly laboratory costs for complete blood count and liver testing.

†Using placeholder price for cilta-cel.
## Base-Case Results: Belantamab

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Intervention Cost</th>
<th>Other Non-intervention costs*</th>
<th>Total Cost</th>
<th>Time Spent in PFS State (months)</th>
<th>QALYs</th>
<th>evLYGs</th>
<th>Life Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belantamab</td>
<td>$152,000</td>
<td>$102,000</td>
<td>$254,000</td>
<td></td>
<td>1.15</td>
<td>1.19</td>
<td>1.60</td>
</tr>
<tr>
<td>Belantamab Comparator</td>
<td>$118,000</td>
<td>$99,000</td>
<td>$218,000</td>
<td></td>
<td>0.78</td>
<td>0.79</td>
<td>1.08</td>
</tr>
</tbody>
</table>

CAR-T: chimeric antigen receptor T-cells, evLYG: equal-value of life years gained, QALYs: quality-adjusted life years gained, PFS: progression-free survival.

*Other non-intervention costs include costs for monitoring, progressed treatment costs, physician visits, adverse event management (first two cycles only) and monthly laboratory costs for complete blood count and liver testing.
## Base-Case Incremental Results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comparator</th>
<th>Cost per QALY Gained</th>
<th>Cost per evLYG gained</th>
<th>Cost per Life Year Gained</th>
<th>Cost per additional PFS month gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ide-Cel</td>
<td>CAR-T Comparator Market Basket</td>
<td>$319,000</td>
<td>$280,000</td>
<td>$250,000</td>
<td>$35,000</td>
</tr>
<tr>
<td>Cilta-cel</td>
<td>CAR-T Comparator Market Basket</td>
<td>$147,000</td>
<td>$128,000</td>
<td>$113,000</td>
<td>$17,000</td>
</tr>
<tr>
<td>(preliminary)*</td>
<td>Belantamab Comparator Market Basket</td>
<td>$98,000</td>
<td>$93,000</td>
<td>$70,000</td>
<td>$18,000</td>
</tr>
</tbody>
</table>

evLYG: equal-value of life years gained, QALY: quality-adjusted life year, LY: life years.
*Using placeholder price for cilta-cel
• Key drivers across all model findings included progression-free survival for the active interventions, the unit price of the comparator market basket of therapies, and utility of PFS (on or off treatment)
# Probabilistic Sensitivity Analysis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cost-Effective at $50,000 per QALY</th>
<th>Cost-Effective at $100,000 per QALY</th>
<th>Cost-Effective at $150,000 per QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ide-cel</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>3%</td>
</tr>
<tr>
<td>Cilta-cel</td>
<td>0%</td>
<td>0%</td>
<td>64%</td>
</tr>
<tr>
<td>Belantamab</td>
<td>17%</td>
<td>50%</td>
<td>78%</td>
</tr>
</tbody>
</table>

QALY: quality-adjusted life year
Scenario Analysis: Assuming no additional charge for CAR-T retreatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comparator</th>
<th>Cost per QALY Gained</th>
<th>Cost per evLYG</th>
<th>Cost per Life Year Gained</th>
<th>Cost per Month of PFS Gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ide-cel</td>
<td>CAR-T Comparator Market Basket</td>
<td>$247,000</td>
<td>$217,000</td>
<td>$194,000</td>
<td>$27,000</td>
</tr>
<tr>
<td>Cilta-cel (preliminary)*</td>
<td>CAR-T Comparator Market Basket</td>
<td>$110,000</td>
<td>$96,000</td>
<td>$85,000</td>
<td>$13,000</td>
</tr>
</tbody>
</table>

evLYG: equal-value of life years gained, QALY: quality-adjusted life year, LY: life years
*Using placeholder price for cilta-cel
Scenario Analysis: Adjusting the proportional relationship between PFS and OS for belantamab

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Comparator</th>
<th>Cost per QALY Gained</th>
<th>Cost per evLYG</th>
<th>Cost per Life Year Gained</th>
<th>Cost per Month of PFS Gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belantamab</td>
<td>Belantamab Comparator Market Basket</td>
<td>Dominated (more costly, less effective)</td>
<td>Dominated (more costly, less effective)</td>
<td>Dominated (more costly, less effective)</td>
<td>$17,000</td>
</tr>
</tbody>
</table>

evLYG: equal-value of life years gained, QALY: quality-adjusted life year, LY: life years, PFS: progression-free survival
Limitations

• Given the lack of a quantitative indirect treatment comparison to inform these analyses, caution should be used when interpreting cost-effectiveness estimates.

• Specific to cilta-cel, interpretation of the cost-effectiveness findings should be noted as very preliminary.

• Survival extrapolations can differ substantially between parametric models; scenario analyses around alternative extrapolations found large variation in incremental cost-effectiveness ratios.
Comments Received

• Underestimation of observed survival for ide-cel and comparators

• Update the model to reflect re-treatment of CAR-T therapies

• Utilization and monitoring around belantamab vision complications such as keratopathy
Conclusions

• Findings suggest CAR-T therapies provide clinical benefit in terms of gains in QALYs and LYs over current treatment options
  • Ide-cel meets commonly cited cost-effectiveness thresholds with discounts of > 37%
  • Preliminary evidence on cilta-cel meets commonly cited thresholds given limited evidence

• Findings for belantamab suggest current list pricing is within commonly cited cost-effectiveness thresholds
  • Given uncertainties with the PFS-OS relationship and other parameters, updated data should be generated and incorporated into future modeling analyses
Questions?
Kyna Gooden, PhD
Director, Worldwide Health Economics and Outcomes Research, Bristol-Myers Squibb

Conflicts of Interest:

• Dr. Kyna Gooden is a full-time employee of Bristol-Myers Squibb.
Ira Gupta, MD
Vice President & Medicine Development Leader, GlaxoSmithKline R&D, Oncology

Conflicts of Interest:

• Dr. Ira Gupta is a full-time employee of GlaxoSmithKline.
Public Comment and Discussion
Conflicts of Interest:

• No financial conflicts to disclose.
Lunch

Meeting will resume at 12:30pm CST
Voting Questions
Clinical Evidence
**Patient Population for question 1:** Patients with triple-, quad- or penta-refractory multiple myeloma who have tried at least four prior lines of treatment. Our characterization of the population is consistent with the FDA label.

1. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of belantamab mafodotin is superior to that provided by usual care*?

   A. Yes

   B. No

*usual care is represented by the regimens employed for the relevant populations in the MAMMOTH observational study.
**Patient Population for questions 2-4:** Patients with triple- or quad-refractory multiple myeloma who have tried at least three prior lines of treatment. Our characterization of the population for both ide-cel and cilta-cel is consistent with the entry criteria in the key studies.

2. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of *idecabtagene vicleucel* (ide-cel) is superior to usual care*?

   A. Yes
   
   B. No

*usual care is represented by the regimens employed for the relevant populations in the MAMMOTH observational study.
Patient Population for questions 2-4: Patients with triple- or quad-refractory multiple myeloma who have tried at least three prior lines of treatment. Our characterization of the population for both ide-cel and cilta-cel is consistent with the entry criteria in the key studies.

3. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of ciltacabtagene autoleucel (cilta-cel) is superior to usual care*?

A. Yes

B. No

*usual care is represented by the regimens employed for the relevant populations in the MAMMOTH observational study.
Patient Population for questions 2-4: Patients with triple- or quad-refractory multiple myeloma who have tried at least three prior lines of treatment. Our characterization of the population for both ide-cel and cilta-cel is consistent with the entry criteria in the key studies.

4. Is the evidence adequate to distinguish the net health benefit of idecabtagene vicleucel (ide-cel) from ciltacabtagene autoleucel (cilta-cel)?

A. Yes

B. No
Patient Population for questions 2-4: Patients with triple- or quad-refractory multiple myeloma who have tried at least three prior lines of treatment. Our characterization of the population for both ide-cel and cilta-cel is consistent with the entry criteria in the key studies.

4a. If the answer to question 4 is yes, which therapy has the greater net health benefit?

A. idecabtagene vicleucel (ide-cel)
B. ciltacabtagene autoleucel (cilta-cel)
Potential Other Benefits and Contextual Considerations
5. When making judgments of overall long-term value for money, what is the relative priority that should be given to any effective treatment for triple-class refractory multiple myeloma, on the basis of the following contextual considerations:

**Acuity of need for treatment based on the severity of the condition being treated**

A. Very low priority
B. Low priority
C. Average priority
D. High priority
E. Very high priority
6. When making judgments of overall long-term value for money, what is the relative priority that should be given to any effective treatment for triple-class refractory multiple myeloma, on the basis of the following contextual considerations:

Magnitude of the lifetime impact of the condition being treated

A. Very low priority
B. Low priority
C. Average priority
D. High priority
E. Very high priority
Please vote separately for each treatment under review on the following potential other benefits or disadvantages:

7. What are the relative effects of belantamab mafodotin versus usual care* on the following outcomes that inform judgment of the overall long-term value for money of belantamab mafodotin?

**Patients’ ability to achieve major life goals related to education, work, or family life**

A. Major negative effect  
B. Minor negative effect  
C. No difference  
D. Minor positive effect  
E. Major positive effect

*usual care is represented by the regimens employed for the relevant populations in the MAMMOTH observational study.
8. What are the relative effects of belantamab mafodotin versus usual care* on the following outcomes that inform judgment of the overall long-term value for money of belantamab mafodotin?

Caregivers’ quality of life and/or ability to achieve major life goals related to education, work, or family life

A. Major negative effect
B. Minor negative effect
C. No difference
D. Minor positive effect
E. Major positive effect

*usual care is represented by the regimens employed for the relevant populations in the MAMMOTH observational study.
9. What are the relative effects of **belantamab mafodotin** versus usual care* on the following outcomes that inform judgment of the overall long-term value for money of belantamab mafodotin?

**Society’s goal of reducing health inequities**

A. Major negative effect
B. Minor negative effect
C. No difference
D. Minor positive effect
E. Major positive effect

*usual care is represented by the regimens employed for the relevant populations in the MAMMOTH observational study.
Please vote separately for each treatment under review on the following potential other benefits or disadvantages:

10. What are the relative effects of **idecabtagene vicleucel** (ide-cel) and **ciltacabtagene autoleucel** (cilta-cel) versus usual care on the following outcomes that inform judgment of the overall long-term value for money of ide-cel and cilta-cel?

**Patients’ ability to achieve major life goals related to education, work, or family life**

A. Major negative effect
B. Minor negative effect
C. No difference
D. Minor positive effect
E. Major positive effect

*usual care is represented by the regimens employed for the relevant populations in the MAMMOTH observational study.*
Please vote separately for each treatment under review on the following potential other benefits or disadvantages:

11. What are the relative effects of idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) versus usual care* on the following outcomes that inform judgment of the overall long-term value for money of ide-cel and cilta-cel?

Caregivers’ quality of life and/or ability to achieve major life goals related to education, work, or family life

A. Major negative effect
B. Minor negative effect
C. No difference
D. Minor positive effect
E. Major positive effect

*usual care is represented by the regimens employed for the relevant populations in the MAMMOTH observational study.
12. What are the relative effects of *idecabtagene vicleucel* (ide-cel) and *ciltacabtagene autoleucel* (cilta-cel) versus usual care* on the following outcomes that inform judgment of the overall long-term value for money of ide-cel and cilta-cel?

Patients’ ability to manage and sustain treatment given the complexity of regimen

A. Major negative effect
B. Minor negative effect
C. No difference
D. Minor positive effect
E. Major positive effect

*usual care is represented by the regimens employed for the relevant populations in the MAMMOTH observational study.*
13. What are the relative effects of idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) versus usual care* on the following outcomes that inform judgment of the overall long-term value for money of ide-cel and cilta-cel?

Society’s goal of reducing health inequities

A. Major negative effect
B. Minor negative effect
C. No difference
D. Minor positive effect
E. Major positive effect
Long-term Value for Money
14. Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment at current pricing with **belantamab mafodotin** versus usual care*?

A. Low long-term value for money at current prices

B. Intermediate long-term value for money at current prices

C. High long-term value for money at current prices

*usual care is represented by the regimens employed for the relevant populations in the MAMMOTH observational study.
15. Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment at current pricing with *idecabtagene vicleucel* (ide-cel) versus usual care*?

A. Low long-term value for money at current prices

B. Intermediate long-term value for money at current prices

C. High long-term value for money at current prices

*usual care is represented by the regimens employed for the relevant populations in the MAMMOTH observational study.
Break

Meeting will resume at 2:00pm CST
## Policy Roundtable

<table>
<thead>
<tr>
<th>Policy Roundtable Member</th>
<th>Conflicts of Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tom Bellfort</strong>, Patient Expert</td>
<td>No conflicts to disclose.</td>
</tr>
<tr>
<td><strong>Harold Carter, PharmD</strong>, Vice President, Pharma Contracting, Strategy &amp; Wholesale Markets, Express Scripts</td>
<td>Harold Carter is a full-time employee of Express Scripts.</td>
</tr>
<tr>
<td><strong>Anita D’Souza, MD, MS</strong>, Associate Professor of Medicine, Medical College of Wisconsin</td>
<td>Anita D’Souza has received institutional research funding from Sanofi, TeneoBio, Takeda, and Caelum. Dr. D’Souza reports advisory board roles with Akcea, Imbrium Therapeutics and Pfizer and received consulting honoraria from Janssen.</td>
</tr>
<tr>
<td><strong>Ira Gupta, MD</strong>, Vice President &amp; Medicine Development Leader, GlaxoSmithKline R&amp;D, Oncology</td>
<td>Ira Gupta is a full-time employee of GSK.</td>
</tr>
<tr>
<td><strong>David Mitchell</strong>, Patient Expert Founder, Patients For Affordable Drugs</td>
<td>David Mitchell is on the Board of Directors of Friends of Cancer Research which receives grants from BMS, Bluebird Bio, and Janssen. He received honoraria from the FDA for his service on the Oncologic Drugs Advisory Committee and was part of a class action suit against Celgene to which he received a service award.</td>
</tr>
<tr>
<td><strong>S. Vincent Rajkumar, MD</strong>, Edward W. and Betty Knight Scripps Professor of Medicine, Mayo Clinic, Rochester, MN</td>
<td>S. Vincent Rajkumar has held a position as a member of the Board of Directors for the International Myeloma Foundation.</td>
</tr>
<tr>
<td><strong>Melissa Pozotrgo, PharmD, BCOP</strong> Senior Clinical Oncology Pharmacist, Oncology Analytics Inc.</td>
<td>Melissa Pozotrgo is a full-time employee of Oncology Analytics.</td>
</tr>
</tbody>
</table>
Next Steps

• Meeting recording posted to ICER website next week

• Final Report published on or around May 11, 2021
  • Includes description of the Midwest CEPAC votes, deliberation, policy roundtable discussion

• Materials available at: https://icer.org/assessment/multiple-myeloma-2021/#timeline
Adjourn