Anabolic Therapies for Osteoporosis in Postmenopausal Women: Effectiveness and Value

Public Meeting – June 30, 2017
Welcome and Introduction

• California Technology Assessment Forum (CTAF)

• The Institute for Clinical and Economic Review (ICER)
Sources of Funding, 2017

Funding Sources - %

- Non-profit foundations: 78%
- Manufacturer grants, contracts and contributions: 10%
- Contributions from health plans and provider groups: 9%
- Government grants and contracts: 3%

ICER Policy Summit only
Welcome and Introduction

• Why are we here today?
  • Innovation promising substantial benefits to patients and their families

• "At times, and especially after a hip fracture, long-term care services are required for intensive rehabilitation. A good number of these patients are no longer able to live independently and need to move in with a family member, move to an assisted living or custodial care facility. This is an added concern for families who need to make and pay for these arrangements, or provide this care directly."
  
  --National Osteoporosis Foundation

• “I became unsure of myself. I was afraid to lift my own granddaughter, to do the DIY projects that I always do, for fear of fracturing. I was afraid to trust the BODY that I live in and that, beyond all else, was the worst of it!”
  
  -- Patient with osteoporosis
Welcome and Introduction

• Why are we here today?
  • Increasing health care costs affecting individuals, state and federal budgets
  • New mechanisms of action often raise questions about appropriate use, cost
  • Patients can have difficulty accessing drugs
    • Step therapy protocols
    • Requirements to switch drugs with new insurance
    • High out-of-pocket costs
  • Need for objective evaluation and public discussion of the evidence on effectiveness and value
Welcome and Introduction

How was the ICER report on anabolic therapies for osteoporosis developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis
- University of Washington cost-effectiveness modeling
- Public comment and revision
- Expert report reviewers
  - Douglas Bauer, MD
  - Teresa Fama, MD
  - Anna Tosteson, ScD
- How is the evidence report structured to support CTAF voting and policy discussion?
Goal:
Sustainable Access to High-Value Care for All Patients

Long-Term Value for Money
- Comparative Clinical Effectiveness
- Incremental cost-effectiveness
- Other Benefits or Disadvantages
- Contextual Considerations

Short-Term Affordability
- Potential Budget Impact
# Agenda

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:00am</td>
<td>Welcome and Opening Remarks</td>
</tr>
<tr>
<td>10:05 am</td>
<td>Presentation of the Evidence</td>
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<tr>
<td></td>
<td><strong>Evidence Review</strong>: Jeff Tice, MD</td>
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<td></td>
<td><strong>Cost Effectiveness</strong>: Lotte Steuten, MSc, PhD, University of Washington</td>
</tr>
<tr>
<td>10:55 am</td>
<td>Manufacturer Public Comment and Discussion</td>
</tr>
<tr>
<td>11:40 pm</td>
<td>Public Comments and Discussion</td>
</tr>
<tr>
<td>12:00 pm</td>
<td>Lunch</td>
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<tr>
<td>12:45 pm</td>
<td>CTAF Deliberation and Votes</td>
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<tr>
<td>1:45 pm</td>
<td>Break</td>
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<tr>
<td>2:00 pm</td>
<td>Policy Roundtable</td>
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<tr>
<td>3:30 pm</td>
<td>Reflections and Wrap Up</td>
</tr>
<tr>
<td>4:00 pm</td>
<td>Meeting Adjourned</td>
</tr>
</tbody>
</table>
Evidence Review

Jeffrey A. Tice, MD
Professor of Medicine
University of California San Francisco

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW
Key review team members:
Patricia Synnott, MALD, MS

Disclosures:
We have no conflicts of interest relevant to this report.
Topic in Context

• Weakening of the bone through loss of mineral content and quality that increases the risk for fracture
• 2-3 million fractures annually in US
• Cost: $20-$25 billion
• Underdiagnosed and undertreated
  • Women with fracture or BMD<-2.5: only 20-30% are evaluated and treated
  • 12 months after hip fracture: 2% had DXA, 15% treated with appropriate drug
Effect on Lives Can Be Profound

• Osteoporosis itself: silent
• Hip fracture
  • Hospitalization, skilled nursing facility for rehabilitation
  • Loss of independence
  • Mortality
• Vertebral fractures
  • Loss of height, kyphosis
  • Decreased respiratory function
  • Pain
Management

• Adequate calcium and vitamin D intake
• Weight bearing exercise
• Fall prevention
• T-score < -2.5 or prior vertebral/hip fracture
  • Oral bisphosphonate
  • Intolerant of oral bisphosphonate
    • Zoledronic acid
    • Denosumab
Harms of Therapies: Anti-Resorptive Drugs

• Bisphosphonates, denosumab
  • Osteonecrosis of the jaw
    • 96% in cancer treatment
  • Atypical femoral fractures
    • 1 per 110 hip fractures prevented

• Oral bisphosphonates: daily or weekly pill
  • Pill esophagitis

• Zoledronic acid: annual infusion
  • Infusion reaction: flu-like symptoms
    • 30% first infusion
    • 5% subsequent infusion
Scope of the Review

• Anabolic agents
  • Drugs that stimulate bone formation: teriparatide, abaloparatide, romosozumab
  • Population: postmenopausal women with osteoporosis
  • Comparator: zoledronic acid

• Caveat: Romosozumab consideration by the FDA delayed beyond 2017
  • Not included in comparative effectiveness
    • Not in network meta-analysis
    • Not in cost-effectiveness, budget impact models
Anabolic Therapies

• Teriparatide 20 mcg: FDA approval 11/26/2002
  • PTH analog
  • Given once daily via subcutaneous (SC) injection (pen)
• Abaloparatide 80 mcg: FDA approval 4/28/2017
  • PTHrP analog
  • Given once daily via SC injection (pen)
• Romosozumab 210 mg: FDA consideration delayed
  • Monoclonal antibody to sclerostin
  • Both anabolic and anti-resorptive
  • Given once monthly via SC injection
Fracture Outcomes

• Fragility: low impact fractures

• Morphometric Vertebral fractures
  • Compare lateral spine x-rays before and during therapy
  • Semiquantitative (SQ): radiologist using Genant scale
  • Quantitative (QM): place six points: 20% loss of height and 4 mm
  • Combination: SQ confirmed SQ, QM confirmed SQ, other

• Clinical vertebral fracture
  • ~35% of morphometric fractures

• Non-vertebral fragility fractures
  • Hip, forearm, humerus, pelvis
  • Exclude: skull, face, fingers, toes, pathologic fractures
Insights from Discussions with Patients

- NOF Survey Top Two Patient Concerns
  - Loss of independence
  - Loss of mobility

- Top caregiver concern
  - No longer being able to care for loved-one

- Why not taking prescribed medication
  - Concern about side effects

- Use of needles, need for refrigeration matter

- Insurance barriers are confusing

- Clinical trials don’t measure outcomes that matter to patients
Issues of Focus
## Key Clinical Trials

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study</th>
<th>Group</th>
<th>N</th>
<th>F/U, months</th>
<th>Age, years</th>
<th>BMI, kg/m²</th>
<th>Prior Fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neer 2001</td>
<td>Fracture Prevention Trial</td>
<td>Teriparatide</td>
<td>541</td>
<td>21</td>
<td>69</td>
<td>26.8</td>
<td>100% V</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>544</td>
<td>21</td>
<td>69</td>
<td>26.7</td>
<td></td>
</tr>
<tr>
<td>Prevrhal 2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miller 2016</td>
<td>ACTIVE</td>
<td>Abaloparatide</td>
<td>824</td>
<td>18</td>
<td>69</td>
<td>25.0</td>
<td>24% V</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Teriparatide*</td>
<td>818</td>
<td>18</td>
<td>69</td>
<td>25.2</td>
<td>63% any</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>821</td>
<td>18</td>
<td>69</td>
<td>25.1</td>
<td></td>
</tr>
<tr>
<td>Cosman 2016</td>
<td>FRAME</td>
<td>Romosozumab</td>
<td>3589</td>
<td>12</td>
<td>71</td>
<td>24.7</td>
<td>18% V</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>3591</td>
<td>12</td>
<td>71</td>
<td>24.7</td>
<td>22% non-V</td>
</tr>
<tr>
<td>Black 2007</td>
<td>HORIZON</td>
<td>Zoledronic acid</td>
<td>3889</td>
<td>36</td>
<td>73</td>
<td>25.1</td>
<td>63% V</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo</td>
<td>3876</td>
<td>36</td>
<td>73</td>
<td>25.4</td>
<td></td>
</tr>
</tbody>
</table>

Non-V: non-vertebral fracture, V: vertebral fracture
*Teriparatide was open label; fracture adjudication was done by central committee blinded to allocation status

Major difference between trials is prevalence of vertebral fractures at baseline
Network Diagram

- Placebo
  - Fracture Prevention Trial
  - HORIZON
- Teriparatide (ACTIVE)
- Zoledronic Acid (ACTIVE)
- Abaloparatide (ACTIVE)
### Relative Risk for Vertebral fractures

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Relative Risk</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abaloparatide (80 mcg)</td>
<td>0.76</td>
<td>(0.20 – 2.26)</td>
</tr>
<tr>
<td>Teriparatide (20 mcg)</td>
<td>0.44</td>
<td>(0.12 – 1.15)</td>
</tr>
<tr>
<td></td>
<td>0.57</td>
<td>(0.30 – 1.02)</td>
</tr>
<tr>
<td>Zoledronic Acid (5 mg)</td>
<td>0.13</td>
<td>(0.03 – 0.33)</td>
</tr>
<tr>
<td></td>
<td>0.17</td>
<td>(0.09 – 0.29)</td>
</tr>
<tr>
<td></td>
<td>0.30</td>
<td>(0.24 – 0.37)</td>
</tr>
<tr>
<td>Placebo</td>
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</tbody>
</table>
Caveats with NMA

• Fixed effects model: standard when few trials
  • Random effects model results wildly improbable
• Slightly different outcome measures
  • See next slide
• Teriparatide open-label in ACTIVE trial
• Different prevalence of vertebral fractures at baseline
  • Patients with prior fracture at higher risk for subsequent fracture
  • No effect modification by vertebral fracture status or other measures of risk for future fracture
Vertebral Fractures: NMA Versus Trials

<table>
<thead>
<tr>
<th>Drug</th>
<th>NMA Estimate</th>
<th>RCT Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abaloparatide</td>
<td>0.13 (0.03-0.33)</td>
<td>0.14 (0.05-0.39)&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>0.17 (0.09-0.29)</td>
<td>0.16 (0.08-0.33)&lt;sup&gt;2&lt;/sup&gt; 0.20 (0.08-0.47)&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Zoledronic acid</td>
<td>0.30 (0.24-0.37)</td>
<td>0.30 (0.24-0.38)&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>1</sup> ACTIVE Trial: SQ, confirmed with SQ  
<sup>2</sup> Fracture Prevention Trial: SQ alone originally (RR 0.35, 95% CI 0.22-0.55); SQ + QM Prevrhal 2009 used in NMA and presented in this table).  
<sup>3</sup> ACTIVE Trial: SQ, confirmed with SQ  
<sup>4</sup> Horizon Trial: QM, confirmed with SQ
### Non-Vertebral Fractures: NMA

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Risk Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abaloparatide (80 mcg)</td>
<td>0.83</td>
<td>(0.46 – 1.46)</td>
</tr>
<tr>
<td>Teriparatide (20 mcg)</td>
<td>0.82</td>
<td>(0.54 – 1.22)</td>
</tr>
<tr>
<td>Zoledronic Acid (5 mg)</td>
<td>0.75</td>
<td>(0.64 – 0.87)</td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
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</tbody>
</table>
## Non-Vertebral Fractures: NMA Versus Trials

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<tr>
<td>Abaloparatide</td>
<td>0.51 (0.28-0.85)</td>
<td>0.57 (0.32-1.00)</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>0.61 (0.41-0.88)</td>
<td>0.47 (0.25-0.88) 0.72 (0.42-1.22)</td>
</tr>
<tr>
<td>Zoledronic acid</td>
<td>0.75 (0.64-0.87)</td>
<td>0.75 (0.64-0.87)</td>
</tr>
</tbody>
</table>
Hip Fractures

- Zoledronic acid: relative risk (RR) 0.59 (0.42-0.83)
- Insufficient data for teriparatide and abaloparatide
  - Observational data for teriparatide comparing patients adherent for 2 years to those adherent less than 3 months
    - RR 0.55 (0.42-0.74)
Patient-Reported Outcomes

• No trial reports on loss of independence, activities of daily living (ADLs), instrumental ADLs, mobility, caregiver burden, or quality of life
Harms

- No differences from placebo in serious adverse events
- No differences from placebo in discontinuation due to adverse events except for abaloparatide more than teriparatide and placebo in ACTIVE trial (10% vs. 7% vs. 6%)
- More hypercalcemia with abaloparatide and teriparatide
- More injection site reactions with abaloparatide
Unpublished Studies

• VERO trial: 2 years teriparatide versus risedronate
  • 1360 women with prior vertebral fractures and T ≤ -1.5
  • V Fx: 5.4% versus 12.0%, HR 0.44, p<0.001
  • Non-V Fx: 4.0% versus 6.1%, HR 0.66, p=0.1

• ARCH trial: 1 year romosozumab then 1 year alendronate versus 2 years alendronate
  • 4093 women with hip T-score ≤ -2.5 and a vertebral fracture or hip T-score ≤ -2.0 and hip fracture or 2 vertebral fractures
  • V Fx: HR 0.50
  • Non-V Fx: HR 0.81
  • Increase in serious CVD events (2.5% versus 1.9%)
Other Benefits or Disadvantages and Contextual Considerations

• Both abaloparatide and teriparatide require daily SC injections vs. annual 15-minute infusion for zoledronic acid
• Burden for caregiver if they need to give daily injections
• Teriparatide requires refrigeration, abaloparatide does not require refrigeration after first dose per pen
• No other factors that differ between drugs
Controversies and Uncertainties

• No randomized-controlled trial data on hip fractures for abaloparatide or teriparatide: American College of Physicians (ACP) 2017 guidelines

• Lack of data on patient centered outcomes: independence and quality of life

• Primary outcome in trials: morphometric fractures – majority asymptomatic. Least relevant to patients.

• Heterogeneity of definitions for incident vertebral fractures

• Appropriate sequencing of therapy

• Definition of highest-risk population who should start with therapy other than oral bisphosphonate
Public Comments Received

• Heterogeneity of trial populations: is it appropriate to combine them in NMA?
  • Yes: there is no effect modification

• Anabolics work faster: shorter trials
  • Zoledronic significant reduction at 1 year (p<0.001)
  • See KM for zoledronic acid next slide
  • Need RCTs with fracture outcomes

• Zoledronic acid is inappropriate comparator
  • Parenteral, for highest-risk women. Feedback.

• Certain subgroups should receive anabolics
  • No clear evidence: Policy roundtable?
Horizon Trial: Zoledronic Acid Versus Placebo
Public Comments Received

- Heterogeneity of trial populations: is it appropriate to combine them in NMA?
  - Yes: there is no effect modification

- Anabolics work faster: shorter trials
  - Zoledronic significant reduction at 1 year ($p<0.001$)
  - See KM for zoledronic acid next slide
  - Need RCTs with fracture outcomes

- Zoledronic acid is inappropriate comparator
  - Parenteral, for highest-risk women. Feedback.

- Certain subgroups should receive anabolics
  - No clear evidence: Policy roundtable?
Summary

• NMA: abaloparatide and teriparatide reduce vertebral and non-vertebral fractures compared to placebo

• No significant differences from each other or zoledronic acid

• Minimal harms: more injection site reactions and hypercalcemia with abaloparatide

• Extensive real-world experience with teriparatide that supports RCT findings

• Both require daily SC injection
ICER Evidence Ratings for Abaloparatide and Teriparatide

• The evidence is promising, but inconclusive (P/I) for the net health benefit comparing abaloparatide and teriparatide to zoledronic acid

• There is moderate certainty that the drugs provide small or substantial net health benefit compared to no therapy (B+)

• There is insufficient evidence (I) for the two drugs compared to each other
Appendix Slides
# NMA Sensitivity Analyses: Morphometric Vertebral Fracture Comparisons to Placebo

<table>
<thead>
<tr>
<th>Drug</th>
<th>Study Publication RR (95% CrI)</th>
<th>Fixed Effects RR (95% CrI)</th>
<th>Random Effects, Vague Priors RR (95% CrI)</th>
<th>Random Effects, Informative Priors RR (95% CrI)</th>
<th>Frequentist Approach, Random Effects RR (95% CI)</th>
<th>Sensitivity Analysis Excluding Teriparatide Arm of ACTIVE Trial, Fixed Effects RR (95% CrI)</th>
<th>Sensitivity Analysis Using Neer 2001 Teriparatide Data, Fixed Effects, RR (95% CrI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abaloparatide (80 mcg)</td>
<td>0.14 (0.05 – 0.39)</td>
<td>0.13 (0.03 – 0.33)</td>
<td>0.13 (0.01 – 0.95)</td>
<td>0.13 (0.03 – 0.38)</td>
<td>0.13 (0.05 – 0.38)</td>
<td>0.13 (0.04 – 0.34)</td>
<td>0.14 (0.04 – 0.35)</td>
</tr>
<tr>
<td>Teriparatide* (20 mcg)</td>
<td>0.16 (0.08 – 0.33)</td>
<td>0.17 (0.09 – 0.29)</td>
<td>0.17 (0.03 – 0.75)</td>
<td>0.17 (0.09 – 0.34)</td>
<td>0.17 (0.10 – 0.30)</td>
<td>0.15 (0.07 – 0.28)</td>
<td>0.30 (0.19 – 0.45)</td>
</tr>
<tr>
<td>Zoledronic Acid (5 mg)</td>
<td>0.30 (0.24 – 0.38)</td>
<td>0.30 (0.24 – 0.37)</td>
<td>0.30 (0.03 – 1.94)</td>
<td>0.30 (0.15 – 0.55)</td>
<td>0.30 (0.24 – 0.38)</td>
<td>0.30 (0.24 – 0.37)</td>
<td>0.30 (0.24 – 0.38)</td>
</tr>
</tbody>
</table>

CI: confidence interval, CrI: credible interval, RR: relative risk
*Teriparatide results were calculated using Prevrhal, 2009 with the exception of the final column, which used data from Neer, 2001. Estimates in bold signify that the 95% credible interval does not contain 1.
## NMA Sensitivity Analyses: Non-Vertebral Fracture Comparisons to Placebo

<table>
<thead>
<tr>
<th>Drug</th>
<th>Study Publication RR (95% CrI)</th>
<th>Fixed Effects RR (95% CrI)</th>
<th>Random Effects, Vague Priors RR (95% CrI)</th>
<th>Random Effects, Informative Priors RR (95% CrI)</th>
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<th>Sensitivity Analysis Excluding Teriparatide Arm of ACTIVE Trial, Fixed Effects RR (95% CrI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abaloparatide (80 mcg)</td>
<td>0.57* (0.32 – 1.00)</td>
<td>0.51 (0.28 – 0.85)</td>
<td>0.50 (0.07 – 2.80)</td>
<td>0.50 (0.23 – 1.04)</td>
<td>0.50 (0.28 – 0.91)</td>
<td>0.55 (0.31 – 0.95)</td>
</tr>
<tr>
<td>Teriparatide (20 mcg)</td>
<td>0.47 (0.25 – 0.88)</td>
<td>0.61 (0.41 – 0.88)</td>
<td>0.60 (0.13 – 2.32)</td>
<td>0.60 (0.34 – 1.04)</td>
<td>0.61 (0.39 – 0.94)</td>
<td>0.45 (0.23 – 0.81)</td>
</tr>
<tr>
<td>Zoledronic Acid (5 mg)</td>
<td>0.75* (0.64 – 0.87)</td>
<td>0.75 (0.64 – 0.87)</td>
<td>0.75 (0.10 – 4.08)</td>
<td>0.75 (0.40 – 1.36)</td>
<td>0.75 (0.58 – 0.97)</td>
<td>0.75 (0.64 – 0.86)</td>
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</table>

CI: confidence interval, CrI: credible interval, NR: not reported, RR: relative risk

*Denotes use of hazard ratios instead of relative risks; RRs were not reported in the trial publication.

Estimates in bold signify that the 95% credible interval does not contain 1.
Cost Effectiveness

Lotte Steuten, MSc, PhD
Associate Professor
University of Washington
Key Review Team Members
Gregory Guzauskas, MSPH, PhD (UW)
David Veenstra, PharmD, PhD (UW)

Disclosures:
We have no conflicts of interest relevant to this report.
Objective

Estimate the cost-effectiveness of abaloparatide and teriparatide, each followed by treatment with a bisphosphonate (zoledronic acid) compared to treatment with zoledronic acid alone.
Methods in Brief
Overall Approach

- Target population: 70-year-old postmenopausal women
  - Fracture incidence similar to that observed in anabolic drug trials
- Lifelong time horizon summing:
  - Time in health states adjusted for quality of life (QoL) &
  - Costs associated with each health state
Key Model Assumptions

• From a post-fracture state, patients can transition to same or worse fracture state only (or death).
  • Fracture hierarchy: hip > clinical vertebral > other non-vertebral.

• Subject to the fracture hierarchy, patients may have an unlimited number of fractures.

• No serious adverse events modelled in base-case analysis.
  • Scenario analysis for IV infusion reactions of zoledronic acid

• All comparators’ adherence rates were 100% in base-case analysis
Treatment Sequence and Effect Over Time

- Initial tx (2-6 years depending on regimen)
- Post-anabolic zoledronic acid (6 years)
- Drug holiday: full tx effect maintenance (3 years)
- Tx effect decline (10 years)
- Remaining time horizon model (to 30 years)

Legend:
- Zoledronic acid (RR 0.59)
- Teriparatide (RR 0.48)
- Abaloparatide (RR 0.40)

Transition to next stage in treatment/efficacy sequence
Clinical Inputs – Fracture Relative Risks

• Annual RRs of fracture for each drug derived from:
  1. NMA: vertebral and non-vertebral fractures
  2. HORIZON and NMA: hip fractures
    • Zoledronic acid: RR from HORIZON trial
    • Anabolic agents: multiplied non-vertebral RR from NMA by ratio of hip to non-vertebral fracture RRs from HORIZON

• NMA RR estimates for vertebral fracture include both clinical and morphometric vertebral fractures:
  • Based on retrospective cohort analysis, we modelled a 35% proportion of overall vertebral fractures to be clinical vertebral fractures
Clinical Inputs – Baseline Fracture Risks

• Applied relative risk estimates from NMA to age-stratified baseline (placebo) estimates of annual probability of fracture to derive each comparator’s annual fracture probabilities.

• Age-stratified baseline annual fracture probabilities derived by calculating fracture risks of an average 70-year old patient
  • Using pooled data placebo arms of Fracture Prevention, ACTIVE, FRAME, and HORIZON trials.

• To model increasing fracture risk as patients age, we extrapolated pooled estimates from Melton et al.
  • Calibrated 10-year cumulative incidence of hip fracture to match the FRAX 10-year probability of hip fracture (9.5%)
Clinical Inputs – Post-Fracture Excess Mortality

• Excess mortality rate after hip fractures. When controlled for underlying health status, roughly 50% lower than studies that adjusted for age and gender only (Tosteson 2007).

  • Fracture-related excess mortality applied only to hip fractures in base case

  • Scenario analysis using 50% multiplier to excess mortality rates for vertebral and other fractures.
Clinical Inputs – Post-Fracture Disutility

• Age-stratified baseline utility estimates for patients with no new fracture based on study including non-institutionalized US adult population (Hanmer, 2006)

• EQ-5D utility multipliers applied to baseline estimates for each fracture and post-fracture health state.

• Utility multipliers derived from publicly-available literature and/or manufacturer-submitted data*
  • Utility multipliers for vertebral fracture applied to 35% of patients with clinical vertebral fracture
  • Non-clinical vertebral fractures had no utility multiplier applied in the base case analysis; explored in scenario analysis

Economic Inputs – Drug Costs

Zoledronic acid: average generic wholesale acquisition cost (WAC) of $306 (Redbook Online, 2017)

Teriparatide:
- Net price of $1,866.34 per pen (represents 38% discount from WAC).
- 28 doses per pen; approximately 13 pens / year.

Abaloparatide:
- Used list price of $1,625 per pen; applied 27% discount
- Net price of $1,186.25
- 30 doses per pen; approximately 12 pens / year
Economic Inputs – Fracture, Other Costs

• Derived from publicly available US cohort studies in representative populations.

• Specific estimates for fracture and post-fracture health states.
  • Costs for vertebral fracture applied to 35% of patients, reflecting proportion of clinical vertebral fractures
  • Non-clinical vertebral fractures had no fracture-related costs applied

• Included IV administration cost for zoledronic acid ($168); no administration cost for anabolic drugs

• Assumed supportive care costs to be similar among comparators
Results
## Base-Case Results

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Cost</th>
<th>QALYs</th>
<th>Life Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoledronic acid</td>
<td>$25,465</td>
<td>8.933</td>
<td>12.188</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>$68,905</td>
<td>8.979</td>
<td>12.193</td>
</tr>
<tr>
<td>Abaloparatide</td>
<td>$47,525</td>
<td>8.999</td>
<td>12.195</td>
</tr>
</tbody>
</table>

QALY: quality-adjusted life year

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Incr. Cost</th>
<th>Incr. QALYs</th>
<th>Incr. LYs</th>
<th>ICER vs. Zoledronic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teriparatide</td>
<td>$43,440</td>
<td>0.046</td>
<td>0.005</td>
<td>$941,537</td>
</tr>
<tr>
<td>Abaloparatide</td>
<td>$22,061</td>
<td>0.066</td>
<td>0.007</td>
<td>$333,892</td>
</tr>
</tbody>
</table>

ICER: incremental cost-effectiveness ratio, Incr.: incremental, LY: life year

<table>
<thead>
<tr>
<th>Lifetime Cumulative Fracture Probabilities</th>
<th>Zoledronic Acid</th>
<th>Teriparatide</th>
<th>Abaloparatide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip</td>
<td>0.24</td>
<td>0.21</td>
<td>0.19</td>
</tr>
<tr>
<td>Non-Vertebral</td>
<td>0.18</td>
<td>0.14</td>
<td>0.13</td>
</tr>
<tr>
<td>Other Non-Vertebral</td>
<td>0.54</td>
<td>0.50</td>
<td>0.46</td>
</tr>
</tbody>
</table>
One-Way Sensitivity Analyses

Teriparatide versus Zoledronic Acid

Abaloparatide versus Zoledronic Acid
Probabilistic Sensitivity Analysis

Cost Effectiveness Acceptability Curve (CEAC)

- Probability that Anabolic Therapy is Cost-Effective vs. Zoledronic Acid
- Green line represents Abaloparatide ICER, $333,892
- Blue line represents Teriparatide ICER, $941,537
- Dashed line indicates $150,000 Willingness to Pay Threshold
- 7.1% probability at $200,000
- 0% probability at $0

Willingness to Pay Per QALY Threshold

ICER
Scenario Analysis – Higher Baseline Fracture Risk

<table>
<thead>
<tr>
<th>Annual Fracture Probabilities Increase</th>
<th>Hip (0% - 100%)</th>
<th>Vert (0% - 100%)</th>
<th>Other Non-Vert (0% -100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip / Non-Vert / Other Vert (age 70-74)</td>
<td>0.006 - 0.012</td>
<td>0.034 - 0.068</td>
<td>0.024 - 0.048</td>
</tr>
<tr>
<td>Hip / Non-Vert / Other Vert (age 85+)</td>
<td>0.031 - 0.062</td>
<td>0.091 - 0.182</td>
<td>0.079 - 0.158</td>
</tr>
</tbody>
</table>

ICER Graph showing cost-effectiveness ratio (ICER) for Teriparatide and Abaloparatide as baseline fracture risk increases.
Scenario Analysis – Ramp-up Time to Full Zoledronic Acid Efficacy

![Graph showing ICER over time for Zoledronic Acid Efficacy with lines for Teriparatide and Abaloparatide. The x-axis represents time in years from 1 to 10, and the y-axis represents ICER in $1,000,000 to $0. The graph illustrates the ramp-up time for efficacy improvements for both drugs.]
Scenario Analysis – Comparison to No Treatment

• Reflects a scenario in which patients may not be able to take zoledronic acid

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Cost</th>
<th>QALYs</th>
<th>Life Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Treatment</td>
<td>$30,038</td>
<td>8.825</td>
<td>12.181</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>$73,162</td>
<td>8.886</td>
<td>12.182</td>
</tr>
<tr>
<td>Abaloparatide</td>
<td>$52,919</td>
<td>8.893</td>
<td>12.183</td>
</tr>
</tbody>
</table>

QALY: quality-adjusted life year

<table>
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<tr>
<th>Regimen</th>
<th>Incr. Cost</th>
<th>Incr. QALYs</th>
<th>Incr. LYs</th>
<th>ICER vs. No Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teriparatide</td>
<td>$43,124</td>
<td>0.060</td>
<td>0.002</td>
<td>$715,878</td>
</tr>
<tr>
<td>Abaloparatide</td>
<td>$22,881</td>
<td>0.067</td>
<td>0.002</td>
<td>$339,027</td>
</tr>
</tbody>
</table>

ICER: incremental cost-effectiveness ratio, Incr.: incremental, LY: life year
Limitations

• Fracture hierarchy prevents patients from having a fracture classified as less severe than their last fracture.
• Adherence not modeled due to a lack of data
• Base-case cost and cost-effectiveness results for anabolics reflect our current assumptions about drug prices.
Comments Received

• Baseline fracture risk inputs do not reflect a high-risk population
  • Scenario analysis

• Adverse events are not considered
  • Infusion-related events modelled in scenario

• There is an excess mortality risk for clinical vertebral and other fractures
  • Scenario analysis

• Morphometric fractures have a disutility
  • Scenario analysis
Summary

- The cost per additional QALY was estimated to be above $150,000 per QALY for each anabolic agent.
- This finding remained over a wide range of sensitivity and scenario analyses, including patients at even higher risk for fracture.
- Results were most sensitive to uncertainty in relative risk estimates for hip fracture, long-term fracture utility multipliers, and drug costs.
- When anabolic agents are compared to no treatment, results suggest that anabolic treatments would not produce incr. cost-effectiveness ratios <$150,000 /QALY.
Appendix Slides
## Clinical Inputs – Fracture Relative Risk Parameters

<table>
<thead>
<tr>
<th>Model Input</th>
<th>Default</th>
<th>Lower</th>
<th>Upper</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoledronic acid (baseline)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip Fracture</td>
<td>0.59</td>
<td>0.42</td>
<td>0.83</td>
<td>Black et al., HORIZON trial</td>
</tr>
<tr>
<td>Vertebral Fracture (all) *</td>
<td>0.30</td>
<td>0.24</td>
<td>0.37</td>
<td>NMA</td>
</tr>
<tr>
<td>Other Non-Vertebral Fractures</td>
<td>0.75</td>
<td>0.64</td>
<td>0.87</td>
<td>NMA</td>
</tr>
<tr>
<td>Teriparatide</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip Fracture</td>
<td>0.48</td>
<td>0.28</td>
<td>0.75</td>
<td>Derived from NMA and HORIZON</td>
</tr>
<tr>
<td>Vertebral Fracture (all)*</td>
<td>0.17</td>
<td>0.09</td>
<td>0.29</td>
<td>NMA</td>
</tr>
<tr>
<td>Other Non-Vertebral Fractures</td>
<td>0.61</td>
<td>0.41</td>
<td>0.88</td>
<td>NMA</td>
</tr>
<tr>
<td>Abaloparatide</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip Fracture</td>
<td>0.40</td>
<td>0.17</td>
<td>0.74</td>
<td>Derived from NMA and HORIZON</td>
</tr>
<tr>
<td>Vertebral Fracture (all)*</td>
<td>0.13</td>
<td>0.03</td>
<td>0.33</td>
<td>NMA</td>
</tr>
<tr>
<td>Other Non-Vertebral Fractures</td>
<td>0.51</td>
<td>0.28</td>
<td>0.85</td>
<td>NMA</td>
</tr>
</tbody>
</table>

*Relative risks for vertebral fractures were estimated from studies including morphometric vertebral fractures; 35% of estimated vertebral fractures were modeled as clinical vertebral fractures.
## Clinical Inputs - Baseline Annual Fracture Probabilities by Age Strata

<table>
<thead>
<tr>
<th>Fracture and Age (in years) Groups</th>
<th>Default</th>
<th>Lower</th>
<th>Upper</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hip Fracture</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 70-74</td>
<td>0.006</td>
<td>0.005</td>
<td>0.007</td>
<td>Pooled trials</td>
</tr>
<tr>
<td>Age 75-79</td>
<td>0.011</td>
<td>0.009</td>
<td>0.013</td>
<td>Pooled trials &amp; Melton/FRAX extrapolation</td>
</tr>
<tr>
<td>Age 80-84</td>
<td>0.023</td>
<td>0.019</td>
<td>0.028</td>
<td>Pooled trials &amp; Melton/FRAX extrapolation</td>
</tr>
<tr>
<td>Age 85+</td>
<td>0.031</td>
<td>0.025</td>
<td>0.038</td>
<td>Pooled trials &amp; Melton/FRAX extrapolation</td>
</tr>
<tr>
<td><strong>Vertebral Fracture (Clinical and Morphometric)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 70-74</td>
<td>0.034</td>
<td>0.027</td>
<td>0.041</td>
<td>Pooled trials</td>
</tr>
<tr>
<td>Age 75-79</td>
<td>0.046</td>
<td>0.037</td>
<td>0.055</td>
<td>Pooled trials &amp; Melton extrapolation</td>
</tr>
<tr>
<td>Age 80-84</td>
<td>0.076</td>
<td>0.061</td>
<td>0.091</td>
<td>Pooled trials &amp; Melton extrapolation</td>
</tr>
<tr>
<td>Age 85+</td>
<td>0.091</td>
<td>0.074</td>
<td>0.111</td>
<td>Pooled trials &amp; Melton extrapolation</td>
</tr>
<tr>
<td><strong>Other Non-Vertebral Fracture</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 70-74</td>
<td>0.024</td>
<td>0.019</td>
<td>0.029</td>
<td>Pooled trials</td>
</tr>
<tr>
<td>Age 75-79</td>
<td>0.037</td>
<td>0.030</td>
<td>0.044</td>
<td>Pooled trials &amp; Melton extrapolation</td>
</tr>
<tr>
<td>Age 80-84</td>
<td>0.053</td>
<td>0.042</td>
<td>0.063</td>
<td>Pooled trials &amp; Melton extrapolation</td>
</tr>
<tr>
<td>Age 85+</td>
<td>0.079</td>
<td>0.063</td>
<td>0.095</td>
<td>Pooled trials &amp; Melton extrapolation</td>
</tr>
</tbody>
</table>
Clinical Inputs – Mortality, Utilities

Fracture related excess mortality for hip

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Default</th>
<th>Lower</th>
<th>Upper</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 70-74</td>
<td>0.0025</td>
<td>0.0020</td>
<td>0.0029</td>
<td>Tosteson</td>
</tr>
<tr>
<td>Age 75-79</td>
<td>0.0075</td>
<td>0.0060</td>
<td>0.0090</td>
<td>Tosteson</td>
</tr>
<tr>
<td>Age 80-84</td>
<td>0.0336</td>
<td>0.0269</td>
<td>0.0403</td>
<td>Tosteson</td>
</tr>
<tr>
<td>Age 85+</td>
<td>0.0727</td>
<td>0.0581</td>
<td>0.0872</td>
<td>Tosteson</td>
</tr>
</tbody>
</table>

- Utility inputs by age strata
- Utility multipliers for fractures year 1 and years 2+

<table>
<thead>
<tr>
<th>Model Input</th>
<th>Default</th>
<th>Lower</th>
<th>Upper</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General Population Utilities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 70-79</td>
<td>0.770</td>
<td>0.616</td>
<td>0.924</td>
<td>Hanmer et al.</td>
</tr>
<tr>
<td>Age 80+</td>
<td>0.720</td>
<td>0.576</td>
<td>0.864</td>
<td>Hanmer et al.</td>
</tr>
<tr>
<td><strong>Utility Multipliers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip Fracture Year 1</td>
<td>0.700</td>
<td>0.560</td>
<td>0.840</td>
<td>Peasgood et al.</td>
</tr>
<tr>
<td>Hip Fracture Year 2+</td>
<td>0.800</td>
<td>0.640</td>
<td>0.960</td>
<td>Peasgood et al.</td>
</tr>
<tr>
<td>Clinical Vertebral Fracture Year 1</td>
<td>0.590</td>
<td>0.472</td>
<td>0.708</td>
<td>Peasgood et al.</td>
</tr>
<tr>
<td>Clinical Vertebral Fracture Year 2+</td>
<td>0.931</td>
<td>0.745</td>
<td>1.000</td>
<td>Kanis/Oleksik et al.</td>
</tr>
<tr>
<td>Other Non-Vertebral Fracture Year 1</td>
<td>0.902</td>
<td>0.722</td>
<td>1.000</td>
<td>Burstrom et al.</td>
</tr>
<tr>
<td>Other Non-Vertebral Fracture Year 2+</td>
<td>1.000</td>
<td>0.800</td>
<td>1.000</td>
<td>Assumption</td>
</tr>
</tbody>
</table>
# Economic Inputs – Drug Costs

<table>
<thead>
<tr>
<th>Drug Name, Labeled Dose, Administration Route</th>
<th>Strength (Pen Size)</th>
<th>WAC/Pen</th>
<th>Net Price*</th>
<th>Base-Case Tx Duration</th>
<th>Acquisition Cost Per Tx Course†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teriparatide 20 mcg SC QD</td>
<td>250 mcg/ml (2.4 ml)</td>
<td>$2,997.90</td>
<td>$1,866.34‡</td>
<td>2 years</td>
<td>$48,691</td>
</tr>
<tr>
<td>Abaloparatide 80 mcg SC QD</td>
<td>3,120 mcg/1.56 ml</td>
<td>$1,625</td>
<td>$1,186.25§</td>
<td>2 years</td>
<td>$29,312</td>
</tr>
<tr>
<td>Zoledronic Acid 5 mg IV Q year</td>
<td>5 mg/100 ml</td>
<td>$306 #</td>
<td>$306#</td>
<td>6 years</td>
<td>$1,837</td>
</tr>
</tbody>
</table>

*Net price is the estimated price after discounts and rebates from WAC. No discounts have been applied to generic zoledronic acid.

†Acquisition cost of initial drug using net price (or average generic WAC for zoledronic acid) and assuming full course of treatment; costs would be lower if a modeled patient died before completing a course of therapy.

Costs do not include the additional costs of post-anabolic zoledronic acid therapy.

‡Price per pen including 38% discount

§Price per pen based on announced list price and assumed 27% discount

#Annual dose cost based on average generic WAC
## Economic Inputs – Fracture Costs

<table>
<thead>
<tr>
<th>Model Input</th>
<th>Default</th>
<th>Lower</th>
<th>Upper</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip Fracture Cost</td>
<td>$44,395</td>
<td>$35,516</td>
<td>$53,274</td>
<td>Bonafede</td>
</tr>
<tr>
<td>Post-Hip Fracture Annual Cost</td>
<td>$10,835</td>
<td>$8,668</td>
<td>$13,002</td>
<td>Parthan</td>
</tr>
<tr>
<td>Clinical Vertebral Fracture Cost</td>
<td>$27,906</td>
<td>$22,325</td>
<td>$33,487</td>
<td>Bonafede</td>
</tr>
<tr>
<td>Post-Clinical Vertebral Fracture Annual Cost</td>
<td>$309</td>
<td>$247</td>
<td>$371</td>
<td>Parthan</td>
</tr>
<tr>
<td>Other Non-Vertebral Fracture Cost</td>
<td>$12,764</td>
<td>$10,211</td>
<td>$15,317</td>
<td>Bonafede</td>
</tr>
<tr>
<td>Post-Other Non-Vertebral Fracture Annual Cost</td>
<td>$0</td>
<td>$0</td>
<td>$0</td>
<td>Assumption</td>
</tr>
</tbody>
</table>
Background on Inclusion of Vert/Other Excess Mortality, from Johnell et al.

<table>
<thead>
<tr>
<th>Age</th>
<th>Clinical Vertebral, y1</th>
<th>Shoulder and Forearm, y1</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-74</td>
<td>7.42</td>
<td>6.05</td>
</tr>
<tr>
<td>75-79</td>
<td>5.46</td>
<td>5.07</td>
</tr>
<tr>
<td>80-84</td>
<td>3.73</td>
<td>4.06</td>
</tr>
<tr>
<td>85+</td>
<td>2.36</td>
<td>2.51</td>
</tr>
</tbody>
</table>

- Relative risks were multiplied by the age-stratified background mortality of the US population.
- Because these inputs were not controlled for comorbidity, we applied a 50% reduction.
## Scenario Analysis – Inclusion of Excess Mortality Due to Clinical Vertebral and Other Non-Vertebral Fractures* 

<table>
<thead>
<tr>
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<td>12.062</td>
</tr>
<tr>
<td>Abaloparatide</td>
<td>$47,260</td>
<td>8.917</td>
<td>12.080</td>
</tr>
</tbody>
</table>

QALY: quality-adjusted life year

<table>
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<tr>
<th>Regimen</th>
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<th>Incr. LYs</th>
<th>ICER vs. No Treatment</th>
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</thead>
<tbody>
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<td>0.067</td>
<td>0.035</td>
<td>$649,845</td>
</tr>
<tr>
<td>Abaloparatide</td>
<td>$22,209</td>
<td>0.098</td>
<td>0.053</td>
<td>$226,259</td>
</tr>
</tbody>
</table>

ICER: incremental cost-effectiveness ratio, Incr.: incremental, LY: life year

Manufacturer Public Comment and Discussion
# Speakers

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jorge Arellano, MSc, MPhil</td>
<td>Executive Director Global Health Economics Therapy Area Lead: Bone, Nephrology, and Supportive Oncology Care</td>
<td>Amgen</td>
</tr>
<tr>
<td>John Krege, MD, FAHA</td>
<td>Medical Fellow</td>
<td>Eli Lilly</td>
</tr>
<tr>
<td>Lorraine Fitzpatrick, MD</td>
<td>Chief Medical Officer</td>
<td>Radius Health</td>
</tr>
</tbody>
</table>
Public Comment and Discussion
Conflicts of interest:

- Receipt or potential receipt of anything of monetary value, including but not limited to, salary or other payments for services such as consulting fees or honoraria in excess of $5,000

Dr. Dore serves on speakers bureaus, advisory boards, and as a consultant for:

- Amgen
- Eli Lilly
- Novartis
- Radius Health
Benjamin Leder, MD  
American Society for Bone and Mineral Research; Massachusetts General Hospital  
Chair, Professional Practice Committee (ASBMR)

Conflicts of interest:

• Manufacturer support of research in the clinical area of this meeting

Dr. Leder has received support (medication supply) from the following manufacturers on an investigator-initiated trial:
• Amgen
• Eli Lilly
No conflicts of interest disclosed
Lunch Meeting will resume at 12:45 pm
Voting Questions

WIFI: TCEGuest
0. Which US President was born on July 4?

A. George Washington
B. Calvin Coolidge
C. John Quincy Adams
D. George W. Bush
1. For postmenopausal women with osteoporosis and a high risk of fracture, is the evidence adequate to demonstrate that the net health benefit of treatment with teriparatide (Forteo®, Eli Lilly and Co.), is greater than that of treatment with zoledronic acid?

A. Yes
B. No
2. For postmenopausal women with osteoporosis and a high risk of fracture, is the evidence adequate to demonstrate that the net health benefit of treatment with abaloparatide (Tymlos™, Radius Health Inc.), is greater than that of treatment with zoledronic acid?

A. Yes
B. No
3. For postmenopausal women with osteoporosis and a high risk of fracture, is the evidence adequate to distinguish between the net health benefit of teriparatide and abaloparatide?

A. Yes
B. No
4. 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 with teriparatide followed by zoledronic acid versus treatment with zoledronic acid alone for postmenopausal women with osteoporosis at high risk for fracture?

A. Low
B. Intermediate
C. High
5. 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 with abaloparatide followed by zoledronic acid versus treatment with zoledronic acid alone for postmenopausal women with osteoporosis at high risk for fracture?

A. Low
B. Intermediate
C. High
Break
Meeting will resume at 2:00 pm
Policy Roundtable
## Policy Roundtable Participants

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
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<tbody>
<tr>
<td>Victoria Dang, PharmD</td>
<td>Director, CDAG Program Performance, UnitedHealthcare Medicare and Retirement</td>
<td>United Healthcare employee and stockholder</td>
</tr>
<tr>
<td>Matthew Drake, MD, PhD</td>
<td>Consultant, Division of Endocrinology, Department of Medicine; Associate Professor of Medicine, Mayo Clinic</td>
<td>None</td>
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<tr>
<td>Deborah Kado, MD, MS</td>
<td>Professor, Department of Family Medicine and Public Health; Osteoporosis Clinic Director, Department of Medicine; Deputy Director of Clinical Research and Education, Sam and Rose Stein Institute for Research on Aging, University of California, San Diego</td>
<td>Scientific Advisory Board: Amgen (romosozumab), Kalytera</td>
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<td>John Krege, MD, FAHA</td>
<td>Medical Fellow, Eli Lilly and Co.</td>
<td>Lilly employee and stockholder</td>
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<tr>
<td>Shireen Fatemi, MD, FACE, FACP</td>
<td>Healthy Bones Regional Co-Lead, Kaiser Permanente Southern California; National Clinical Lead for Osteoporosis, Kaiser Permanente; Assistant Area Medical Director, Kaiser Permanente Panorama City</td>
<td>None</td>
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<tr>
<td>Stuart L. Silverman, MD, FACP, FACR</td>
<td>Clinical Professor of Medicine, Cedars-Sinai Medical Center and UCLA School of Medicine; Medical Director, Osteoporosis Medical Center Clinical Research Center; Member, National Bone Health Alliance Osteoporosis Messaging Group</td>
<td>Advisory Board, Speaker: Amgen, Lilly, Radius Consultant: Amgen Research Grants: Amgen, Lilly, Novartis, Pfizer, Roche Former Officer: Kalytera</td>
</tr>
<tr>
<td>Roselyne Smith</td>
<td>Patient</td>
<td>None</td>
</tr>
<tr>
<td>Martin Zagari, MD</td>
<td>Vice President, Global Health Economics, Amgen, Inc.</td>
<td>Amgen employee, officer, and stockholder</td>
</tr>
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CTAF Panel Reflections
Next Steps

• Meeting recording posted to ICER website next week
• Final Report published on/about July 14
  • Includes description of CTAF votes, deliberation; policy roundtable discussion
• Materials available at
  https://icer-review.org/topic/osteoporosis/
Adjourn