Pharmacoeconomic Analyses and Oncology Pharmacy: Optimizing Multiple Myeloma Value for Patients and Plans

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Outline

- The Value Proposition in Oncology
- The Evidence Gap and Uncertainty
- Pharmacoeconomic Evidence and Studies in Multiple Myeloma
- Future Considerations for Pharmacoeconomic Evaluations of Multiple Myeloma Therapies
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Historically, payers felt that
- “Oncology is different”
- Cost-effectiveness threshold higher
  - $50,000 / QALY for most therapies
  - $100,000 / QALY for cancer therapies

Currently, oncology is “less different” but still unique
- Oncology therapies still hold the promise for
  - Extending life
  - Enhancing quality of life (QoL)

QALY=Quality-adjusted life year.
Oncology Value Proposition

• Evidence requirements
  – Outcomes, NOT surrogates
  – Clinically meaningful
  – Patient-centered outcomes
  – Clinical outcomes aligned with cost analysis to provide context for payers

• Cost is always an issue
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Evidence Gap: Pervasiveness of Off-Label Use

- National Comprehensive Cancer Network (NCCN) estimates ½ to ¾ of all cancer drugs used off-label\(^1\)
- Survey of oncologists identified at least 87 distinct anticancer therapies used outside labeled indications\(^2\)

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Evidence Gap: Limitations of Current Evidence

- Four compendia are approved to provide Medicare and other payers with guidance
- A 2009 systematic review of major compendia:
  - “Lack transparency, cite little current evidence, and lack systematic methods...”\(^1\)
- Some argue that useful evidence is simply not being generated
  - Compendia have to aggregate poor information

Evidence Gap: Limitations of Current Evidence (cont’d)

- Evidence is not always “patient-centered”
  - Nor is it “payer-applicable”
- Patients increasingly have proportional co-pays that make them a “payer”
- Traditional clinical trials may not provide the evidence that is most meaningful to patient
  - Impact of treatment on daily activities, etc.
- There is a need for patient-reported outcomes (PROs)
  - Quality of life, etc.
- There is a need for more payer involvement in study design
Evidence Gap: Methodological Concerns

- **Limitations of observational and retrospective analyses**
  - Studies often lack randomization
  - Selection bias is frequently present
  - PROs are not always available

- **Limitations with randomized clinical trials**
  - Patients often not typical of enrollee population
  - Treatment typically reflects academic medical centers, NOT community oncology practice

PRO=Patient-reported outcomes.
Evidence Gap: Decision-Making

- Patients have a vital need to access the most effective and safe cancer care, but often unclear which therapies meet this criteria
- Oncologists have few treatment options supported by strong evidence
- Payers must make coverage and reimbursement decisions with little reliable evidence
  - Conflicting pressure from multiple sides
- Use of safe and effective therapies may be limited by lack of data
Filling the Evidence Gap

• It’s important to fill the right gap/answer the right question
• Simultaneously “too little” and “too much” info
Data From Randomized Clinical Trials

Scientific Evidence

Evidence Needed for Definitive Answer on Patient Outcome

Threshold for Action
Best Case Situation
Threshold for Action vs Definitive Answer

Scientific Evidence

Evidence Needed for Definitive Answer on Patient Outcome

Threshold for Action
Climbing Over the Threshold for Action

Evidence Needed for Definitive Answer on Patient Outcome

Scientific Evidence

Clinical trials

Threshold for Action

Other data sources
Addressing the Evidence Gaps and Uncertainty

Can it work? Does it work? Is it worth it?

CER = Comparative Effectiveness Research.
RCTs = Randomized Controlled Trials.
EBM = Evidence-based Medicine.
HTA = Health Technology Assessment.

Summary: Evidence Gap

• Significant off-label use of oncology therapies
• Oncologists have few treatment options supported by strong evidence
  – Evidence is not always “patient-centered”
  – There is a need for more payer involvement in study design
• Payers must make coverage and reimbursement decisions with little reliable evidence
• It’s important to fill the right gap/answer the right question
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What is the Cost Associated with Improved Survival?

Overall Survival of Multiple Myeloma Patients From Time of Diagnosis

Survival

Time from diagnosis (months)

Relevant Considerations for Multiple Myeloma Pharmacoeconomic Analyses

- Treatment costs range from minimal to very expensive
- Treatment effectiveness limited to a few studies
- Lack of large scale clinical trial evidence to direct the use of newer therapies
  - Use often guided by data from small trials
- Short duration of treatment
- Limited life span after initial diagnosis
  - Small difference in effectiveness (denominator of cost-effectiveness ratio) results in large incremental cost-effectiveness ratios
Relevant Costs for Multiple Myeloma Pharmacoeconomic Analyses

- Treatment costs mimic treatments
  - Induction chemotherapy
  - High-dose chemotherapy supported by autologous peripheral stem cell transplantation (ASCT)
  - Long-term bisphosphonates
  - Allogeneic bone marrow transplantation
  - Interferon-α maintenance
## Cost of Autologous Stem Cell Transplantation

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Costs</td>
<td>$146,890</td>
<td>$32,160</td>
<td>$38,186</td>
<td>$32,320</td>
<td>$112,999 vs $95,215</td>
<td>$34,000 vs $9500</td>
</tr>
</tbody>
</table>

MP = melphalan plus prednisone.  
CCT = combination chemotherapy.  

*Cost converted from Euros to US dollars.

Issues With Estimating Costs for Multiple Myeloma

- Treatment regimens constantly changing
- Combination therapies are common
- Treatment algorithms affect duration of use, indirectly affecting costs
# Budget Impact Model for Multiple Myeloma

<table>
<thead>
<tr>
<th>Cost Component</th>
<th>Bortezomib</th>
<th>Bortezomib/ Doxorubicin</th>
<th>Lenalidomide/ Dexamethasone</th>
<th>Thalidomide/ Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Costs</td>
<td>$22,734</td>
<td>$34,794</td>
<td>$64,806</td>
<td>$37,281</td>
</tr>
<tr>
<td>Medical Costs</td>
<td>$5,886</td>
<td>$7,041</td>
<td>$1,623</td>
<td>$1,397</td>
</tr>
<tr>
<td>AE Costs</td>
<td>$5,209</td>
<td>$6,094</td>
<td>$5,243</td>
<td>$7,910</td>
</tr>
<tr>
<td>Total</td>
<td>$33,829</td>
<td>$47,929</td>
<td>$71,672</td>
<td>$46,588</td>
</tr>
</tbody>
</table>

This model assumes the following methods:

1. Direct medical costs compared using one therapeutic course of bortezomib, bortezomib/liposomal doxorubicin, thalidomide/low-dose dexamethasone, and lenalidomide/low-dose dexamethasone treatment with drug costs from the 2007 Red Book,
2. Duration of therapy was based on published median duration therapy protocols and dosages, and
3. Recommended prophylaxis for herpes zoster and DVT/PE are based on NCCN guidelines.


Formal Value Assessments in Multiple Myeloma

- Few systematic studies
- Several studies on individual products
  - Few active comparator studies
  - Inconsistent methods so indirect comparisons are a challenge
Bortezomib for the Treatment of Multiple Myeloma Patients at First Relapse

Issue date: October 2007
Review date: October 2010

**Bortezomib monotherapy for relapsed multiple myeloma**

This guidance was developed using the single technology appraisal process
Comparison of Estimated Survival Difference Between Bortezomib and HDD

HDD=High Dose Dexamethasone.

National Institute for Health and Clinical Excellence Appraisal Guidance #129.
### Bortezomib vs High-Dose Dexamethasone (HDD): Cost per Life-Year Gained (LYG)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Bortezomib</th>
<th>HDD</th>
<th>Difference: Bortezomib vs HDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean overall survival, months</td>
<td>35.7</td>
<td>24.5</td>
<td>11.2</td>
</tr>
<tr>
<td>Mean discounted overall survival</td>
<td>32.5</td>
<td>22.6</td>
<td>9.9</td>
</tr>
<tr>
<td>% Alive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>87%</td>
<td>72%</td>
<td>15%</td>
</tr>
<tr>
<td>2 years</td>
<td>65%</td>
<td>45%</td>
<td>20%</td>
</tr>
<tr>
<td>5 years</td>
<td>23%</td>
<td>12%</td>
<td>11%</td>
</tr>
<tr>
<td>Costs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bortezomib and/or HDD</td>
<td>$33,778</td>
<td>$132</td>
<td>$33,645</td>
</tr>
<tr>
<td>Other care</td>
<td>$23,106</td>
<td>$16,081</td>
<td>$7023</td>
</tr>
<tr>
<td>Total</td>
<td>$56,889</td>
<td>$16,210</td>
<td>$40,669</td>
</tr>
<tr>
<td>Cost per discounted LYG</td>
<td></td>
<td></td>
<td><strong>$49,372</strong></td>
</tr>
</tbody>
</table>

• Cost per life year gained: $49,372 ($44,887–$59,000)*

*Costs converted from UK pound sterling to US dollars.

National Institute for Health and Clinical Excellence Appraisal Guidance #129.
NICE Recommendations: Bortezomib Monotherapy

- Bortezomib monotherapy is recommended for the treatment of progressive multiple myeloma (MM) in patients with the following characteristics:
  - Experiencing a first relapse after one prior therapy
  - Have undergone, or are unsuitable for, bone marrow transplantation

- Guidance on the use of bortezomib
  - Response is measured using serum M protein after a maximum of 4 cycles of treatment
  - Treatment is continued only when complete or partial response observed (ie, reduction in serum M protein of ≥50%, or where serum M protein is unmeasurable)

NICE=National Institute for Health and Clinical Excellence.
NICE Recommendations: Bortezomib Monotherapy (con’t)

• In the UK, the full cost of bortezomib is returned (by the manufacturer) to patients who have less than a partial response.
• Patients receiving bortezomib monotherapy who fail to meet these criteria should have the option to continue therapy until they and their clinicians consider it appropriate to stop.
Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy
Key Findings

- **Lenalidomide vs dexamethasone***
  - Two or more prior therapies
    - $48,751 per QALY
  - Thalidomide failure subgroup
    - $46,474 per QALY

- **Recommended patient access scheme (treatment beyond 26 cycles paid for by the manufacturer)**

QALY=Quality-Adjusted Life Year.

*Costs converted from UK pound Sterling to US dollars.

NICE Technology Appraisal Guidance #171.
Summary: Pharmacoeconomic Evidence

- **Treatment regimens constantly changing**
  - Algorithms used to guide treatment and payment can become outdated quickly
- **Robust clinical trial evidence of treatment effectiveness is limited**
  - Few active comparator studies
  - Inconsistent methods; indirect comparisons are a challenge
- **Pharmacoeconomic analysis of cost/benefit often hindered by limited clinical data**
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Study Design and Reporting of Results Affect PE Studies and Decision-Making

- **Current treatment strategies**
- **Direct or indirect evidence**
  - No direct trials comparing treatments
  - Comparison groups different
- **Means or medians?**
  - Survival curves typically presented as medians
  - Cost-effectiveness results based on means or medians
- **Patient cost-sharing influences**
  - Utilization
  - Cost-effectiveness

PE=Pharmacoeconomic.
Future Evidence Needs for Economic Evaluations of Multiple Myeloma Treatments

- **Subgroup of responders**
  - Prospective identification of subgroups

- **Cost-effectiveness varies by treatment population**
  - Technologies perhaps not cost-effective for everyone
  - Very cost-effective for the responsive patient
• To enhance the quality of pharmacoeconomic data in multiple myeloma, future clinical trials
  – Must be designed in a way that supports both clinical and pharmacoeconomic endpoints
  – Should examine the impact of patient cost-sharing on clinical outcomes
  – Identify subgroups of responders