Examining the Clinical and Cost Implications of Current and Future Value-Based HER2+ Breast Cancer Care

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Disclosures

Dr. Cardarelli, PharmD: None
Dr. McGuire, MD: None

Learning Objectives

- Describe the clinical and economic impact of breast cancer in the United States and factors that impact prognosis
- Identify strategies to aid providers in adhering to guidelines and evidence-based recommendations for the diagnosis, treatment, and management of patients with HER2+ breast cancer
- Apply recent clinical/cost data, value-based guidance, and individualized care strategies to formulary and patient access discussions for HER2+ breast cancer
- Differentiate among reference drugs, biosimilars, and generic drugs in terms of their manufacturing processes, clinical considerations, regulatory parameters, interchangeability, safety/efficacy, cost-benefit, and patient impact

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Breast Cancer Statistics

- Approximately 2600 new cases of invasive breast cancer are expected to be diagnosed in men in 2016
- A man’s lifetime risk of breast cancer is approximately 1 in 1000
- Approximately 1 in 8 US women (approximately 12%) will develop invasive breast cancer over the course of her lifetime
- Approximately 40,450 women in the United States were expected to die of breast cancer in 2015
- For women in the United States, breast cancer death rates are higher than those for any other cancer other than lung cancer
- Breast cancer is more common in black women than white women
- The risk of breast cancer developing in women and of women dying of breast cancer is lower in Asian, Hispanic, and Native-American women
- A woman’s risk of breast cancer approximately doubles if she has a first-degree relative (e.g., mother, sister, daughter) who has been diagnosed with breast cancer
- Approximately 85% of breast cancers occur in women who have no family history of breast cancer
- Approximately 20% of breast cancers are HER2+

HER2+ = human epidermal growth factor receptor 2.


Risk Factors

- Age
- Family history
- Hormones/childbirth
  - Began menopause after age 55 years
  - Never had children or had first child after age 30 years
  - Used hormone therapy after menopause
  - History of radiation to the chest area
  - Previous abnormal breast biopsy results
  - Obesity
- Oral contraceptive use
- Diet high in saturated fats
- Excessive alcohol use
- Sedentary lifestyle
- Began menopause after age 55 years
- Never had children or had first child after age 30 years
- Used hormone therapy after menopause
- History of radiation to the chest area
- Previous abnormal breast biopsy results
- Obesity

Economic Burden of Breast Cancer

- Direct costs for breast cancer in 2010 were $16.5 billion
- Lifetime per-patient costs ranged from $20,000 to $120,000
- Average direct costs of breast cancer in a managed-care population were calculated to be $2896 per member per month
  - Hospitalization accounted for the greatest share, followed by medications and surgical interventions
- Indirect costs of lost productivity (2007) were $12.2 billion, or $98,571 per patient per year
  - Includes direct medical, palliative/best supportive care, and lost productivity costs


HER2 Overexpression

- Approximately 20% to 25% of breast cancers overexpress HER2
- Historically, overexpression of this receptor was associated with an increased risk of disease recurrence and an overall worse prognosis
- Therapies that target HER2 have become important agents in the treatment of breast cancer and have altered the natural course of HER2 breast cancer

HER2 Drug Therapies

- Trastuzumab
  - Monoclonal antibody that binds the extracellular domain of HER2
- Pertuzumab
  - Monoclonal antibody that binds the extracellular dimerization domain of HER2
  - Usually used in combination with trastuzumab
- Ado-trastuzumab emtansine
  - An antibody drug conjugate composed of trastuzumab, a thioether linker and the microtubule agent DM1
- Lapatinib
  - Tyrosine kinase inhibitor against EGFR1 and HER2 that results in signaling pathways downstream of HER2

EGFR = epidermal growth factor receptor

Challenges for Managed Care

- Economic pressures
  - 37.7% of all healthcare spending in 2015 was spent on specialty drugs
    - The top 3 classes (inflammatory conditions, multiple sclerosis, and oncology) accounted for 56.3% of that spend
  - Anti-cancer therapies dominate the pipeline for new drugs
    - >800 drugs in development for cancer
    - 82 for breast cancer
  - 73% of cancer medicines in the pipeline have the potential to be personalized medicines


Examining the Clinical and Cost Implications of Current and Future Value-Based HER2+ Breast Cancer Care

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No Two Are Exactly Alike...

- Breast cancer is a heterogeneous disease
  - Biologic subtypes
  - Significantly different outcomes
- Classification of subtypes led to the development of personalized breast cancer therapy
- Personalized therapy for HER2+ breast cancer is one of the most important developments


Intrinsic Subtypes and Chemotherapy Sensitivity

<table>
<thead>
<tr>
<th>Method of Assessment</th>
<th>T-FAC (N=82)</th>
<th>AC-T (N=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene Expression Microarray</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>IHC Proxy</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Luminal A/B</td>
<td>45%</td>
<td>36%</td>
</tr>
<tr>
<td>Normal-like</td>
<td>45%</td>
<td>27%</td>
</tr>
<tr>
<td>HER2+/ER-</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Basal-like</td>
<td>0</td>
<td>NA</td>
</tr>
</tbody>
</table>

pCR to neoadjuvant anthracycline/taxane

pCR rate in invasive lobular cancer: 4.2%

mAbs = monoclonal antibody; TKI = tyrosine kinase inhibitor.

Mechanism of Action: Pertuzumab and Trastuzumab

Pertuzumab binds to a specific domain II and inhibits ligand-activated dimerization

Trastuzumab binds to subdomain IV and inhibits downstream signaling

The combined regimen of pertuzumab and trastuzumab offers the potential for a more comprehensive HER blockade

Mechanism of Action: Lapatinib Compared with Trastuzumab

Lapatinib inhibits Erb receptors and downstream signaling pathways, leading to cell proliferation and cell survival.

T-DM1 HER2-Targeted Antibody-Drug Conjugate

Intracellular emtansine release → inhibition of microtubule polymerization

T-DM1 = trastuzumab emtansine.

mAb = monoclonal antibody; TKI = tyrosine kinase inhibitor.


**Patient Selection for Neoadjuvant Chemotherapy**

<table>
<thead>
<tr>
<th>Morphology</th>
<th>Markers</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unicentric</td>
<td>ER-, HER2+</td>
<td>Good candidates</td>
</tr>
<tr>
<td>Unicentric</td>
<td>ER+ low-grade</td>
<td>Consider endocrine therapy</td>
</tr>
<tr>
<td>Multicentric EIC</td>
<td>Any</td>
<td>Requires mastectomy</td>
</tr>
</tbody>
</table>

**CAVEAT:** Patients with operable disease who desire mastectomy do not benefit from this approach.

**Patient- and Disease-related Factors that Influence Decision for Neoadjuvant Therapy**

- **Absolute**
  - Inflammatory cancer
  - Other T4 tumors
  - Fixed axillary nodes

- **Relative**
  - Large tumor in a small breast; patient desires breast-conserving therapy

**NOAH Study: Addition of Neoadjuvant Trastuzumab to Chemotherapy Improves Pathologic CR Rate and Clinical Outcomes**

<table>
<thead>
<tr>
<th>HER2-Positive</th>
<th>HER2-Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>With Trastuzumab (n=117)</td>
<td>Without Trastuzumab (n=118)</td>
</tr>
<tr>
<td>bpCR</td>
<td>50 (43%)</td>
</tr>
<tr>
<td>tpCR</td>
<td>45 (38%)</td>
</tr>
<tr>
<td>OR‡</td>
<td>102 (87%)</td>
</tr>
</tbody>
</table>

Note: Toxicity associated with the investigational arm of this study was acceptable and consistent with adverse events reported in other published reports with this agent. Data are n (%).

*For comparison of HER2-positive disease groups. †For comparison of HER2-negative disease without trastuzumab groups. ‡Complete partial clinical responses.

**NeoSphere Study Schema**

**NeoSphere: Efficacy Results by Breast and Lymph Nodal Status**

<table>
<thead>
<tr>
<th></th>
<th>TH (n=107)</th>
<th>THP (n=107)</th>
<th>HP (n=107)</th>
<th>TP (n=96)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCR in breast</td>
<td>29.0%</td>
<td>45.8%</td>
<td>16.8%</td>
<td>24.0%</td>
</tr>
<tr>
<td>pCR in breast and node negative at surgery</td>
<td>21.5%</td>
<td>39.3%</td>
<td>11.2%</td>
<td>17.7%</td>
</tr>
<tr>
<td>pCR in breast and node positive at surgery</td>
<td>7.5%</td>
<td>6.5%</td>
<td>5.6%</td>
<td>6.3%</td>
</tr>
</tbody>
</table>

The differences between the THP arm and other arms for pCR were statistically significant, with all the \( P \) values being < .05.

Note: All regimens administered intravenously (IV).

**NeoSphere Study Schema Diagram**

- TH q3w x 4 (n=107)
- THP q3w x 4 (n=107)
- HP q3w x 4 (n=107)
- TP q3w x 4 (n=96)
- Surgery
- H q3w x 13 + FEC q3w x 3
- H q3w x 13 + FEC q3w x 3
- H q3w x 13 + T q3w x 4 + FEC q3w x 3
- H q3w x 17 + T q3w x 4 + FEC q3w x 3

Note: All regimens administered intravenously (IV).

T = docetaxel; H = trastuzumab; P = pertuzumab; F = 5-fluorouracil; E = epirubicin; C = cyclophosphamide.

TRYPHAENA Study: Pathologic Complete Response by Hormone Receptor Status

FEC = 5-fluorouracil, epirubicin, cyclophosphamide (IV); T = docetaxel; H = trastuzumab; P = pertuzumab; TCH = T + carboplatin + H (IV).


NeoALTTO (BIG 01-06/EGF 106903) Study Design

Eligibility (N=450)
- Invasive operable HER2+ breast cancer
- T >2 cm
- LVEF ≥ 50%

Stratification
- T ≤ 5 cm vs >5 cm
- ER/PR-positive or -negative
- N 0-1 vs N ≥2
- Conservative surgery vs not

Targeted therapy
- L + T alone x 6 weeks (PO/IV) → L + T + P x 12 weeks (PO/IV/IV)*
- T alone x 6 weeks (IV) → T + P x 12 weeks (IV)*
- L alone x 6 weeks (PO) → L + P x 12 weeks (PO/IV)*

Adjuvant Therapy

Overall Survival with 2 Years vs 1 Year of Trastuzumab (All Patients)

<table>
<thead>
<tr>
<th></th>
<th>T (1 year) (n=1552)</th>
<th>T (2 years) (n=1553)</th>
<th>HR</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 years</td>
<td>96.5%</td>
<td>97.4%</td>
<td>1.05</td>
<td>.63</td>
</tr>
<tr>
<td>5 years</td>
<td>91.4%</td>
<td>92.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 years</td>
<td>87.6%</td>
<td>86.4%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HR = hazard ratio.

Phase 3 HERA Study Design

Eligibility (N=5102)
- Locally determined HER2-positive invasive early BC
- Treated with surgery +/- (neo)adjuvant chemotherapy +/- RT
- Centrally confirmed IHC 3+ or FISH+ LVEF ≥55%

Overall response:
- Observation* (n=1098)
- Trastuzumab 1 year 8 mg/kg q3wk (n=1553)
- Trastuzumab 2 years 8 mg/kg q3wk IV (n=1553)

*55 patients (12%) crossed over to trastuzumab after disclosure of first results in 2005.
HERA = Breast International Group [BIG] 01-01 trial; BC = breast cancer; FISH = fluorescence in situ hybridization.

NeoALLTO Study Efficacy: pCR and tpCR

<table>
<thead>
<tr>
<th>Response</th>
<th>L (N=154)</th>
<th>T (N=149)</th>
<th>L + T (N=152)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCR (no invasive cancer in the breast)</td>
<td>24.7%</td>
<td>29.5%</td>
<td>51.3%</td>
</tr>
<tr>
<td>P value:</td>
<td>.34 (L vs T); .0001 (L + T vs T)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tpCR (no invasive cancer in the breast or LNs)*</td>
<td>20.0%</td>
<td>27.6%</td>
<td>46.8%</td>
</tr>
<tr>
<td>P value:</td>
<td>.13 (L vs T); .001 (L + T vs T)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes: Toxicity associated with the investigational arm of this study was acceptable and consistent with adverse events reported in other published reports with this agent. Lapatinib has not been approved for neoadjuvant therapy in HER2-positive breast cancer.
*Excludes 15 patients with non-evaluable nodal status.
L = lapatinib; T = trastuzumab; LN = lymph node.
Metastatic

**CLEOPATRA: Trastuzumab + Docetaxel + Pertuzumab or Placebo**

Study dosing every 3 weeks
- Pertuzumab/Placebo: 840 mg IV loading dose, 420 mg maintenance
- Trastuzumab: 8 mg/kg IV loading dose, 6 mg/kg maintenance
- Docetaxel: 75 mg/m² IV, escalating to 100 mg/m² if tolerated

MBC = metastatic breast cancer.


808 patients with centrally confirmed HER2+ MBC

RA: 1:1

≥ 6 cycles of docetaxel recommended
- Trastuzumab + pertuzumab
- Until progressive disease

≥ 6 cycles of docetaxel recommended
- Trastuzumab + placebo
- Until progressive disease

**CLEOPATRA: Disease-free and Overall Survival in First-line HER2+ MBC**

**A. Independently Assessed Progression-free Survival**

**B. Overall Survival**

CI = confidence interval.


**CLEOPATRA: Updated Survival Results**

**EMILIA Study Design**

LABC = locally advanced breast cancer; MBC = metastatic breast cancer.


**Trastuzumab and Lapatinib: Overall Survival**


LABC or MBC (N=980)
- Prior taxane and trastuzumab
- Progression on metastatic treatment or within 6 months of adjuvant treatment

T-DM1 3.6 mg/kg q3w IV

Capcitabine 1000 mg/m² PO bid, days 1-14, q3w + Lapatinib 1250 mg/d PO qd

EMILIA Study Design

**HER2-positive LABC or MBC**
- Prior taxane and trastuzumab
- Progression on metastatic treatment or within 6 months of adjuvant treatment
EMILIA: Progression-free Survival as Assessed by an Independent Review Committee

EMILIA: Second Interim Analysis of Overall Survival

Milestones in the Management of HER2-positive MBC

Cost-Effectiveness

Quality-Adjusted Life-Years

When Is a Treatment Cost-Effective?

*Therapy provides 1 QALY
  - Prolongs life for 1 additional year for patient in perfect health

*Therapy provides 10 QALYs
  - 10 extra years of life for patient in perfect health
  - 20 extra years of life at a quality of life half that for patient in perfect health

QALY = quality-adjusted life-year; QoL = quality of life.

Trastuzumab

• Assumption: Associated with 52% reduction in disease recurrence and 33% reduction in risk of death

• Over a lifetime, cost per QALY: $27,800 (range, $18,000-$39,000)


Pertuzumab

Cost for Progressing State

Utility for Progressing State

Utility for Stable State

Cost for Pertuzumab

Cost for TH
EV: $784,746 per QALY

$500,000

$600,000

$1,000,000


Lapatinib

Efficacy of Lapatinib (15 years, 3 years)

Discount Rate (0%, 6%)

Cost of Lapatinib (-30%, +20%)

Utility of Current Health (1.002, 0.864)

Utility of Relapse (0.456, 0.964)

Cost of Relapse Treatment (-20%, +20%)

Cost of Palliative Care (-20%, +20%)

L+C

Cost of Relapse Treatment

Cost of Palliative Care

Biosimilars: Cost Containment?

Biosimilars vs Biologics

• Biologics are complex proteins with high MW

• Although highly targeted, they are costly, limiting access across the globe

• Many biologics are losing patent protection soon; biosimilars have the potential to significantly improve access to expensive agents

• Definition of biosimilarity

  – The biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components

  – There are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency*

*Scientific Considerations in Demonstrating Biosimilarity to a Reference Product. Guidance for Industry. US Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). 2015. page 3. (Section 768(b)(3) of the Affordable Care Act, adding section 351(i)(2) of the PHS Act.)

Biosimilars vs Generics

Heritage Study Design:
Confirmatory Double-Blind International Study

Part 1: Combined Treatment/PK Analysis
- MYL-1401O Loading dose 8 mg/kg
- Maintenance dose 6 mg/kg Q3W
- Trastuzumab Loading dose 8 mg/kg
- Maintenance dose until disease progression
- Docetaxel 75 mg/m² Q3W cycles
- Doxorubicin 60 mg/m² Q3W cycles

Part 2: Single Treatment
- MYL-1401O Maintenance dose until disease progression
- Trastuzumab Maintenance dose until disease progression

Screening: The day after trastuzumab infusion
Cycle 1, Day 1: Up to 28 Days Cycles 2-8*
Cycles 2-8:
- Docetaxel 75 mg/m² Q3W cycles
- Paclitaxel 80 mg/m² weekly 30 min after trastuzumab infusion
- Maintenance dose 6 mg/kg Q3W

Progression-Free Survival at Week 24

<table>
<thead>
<tr>
<th>Subject status</th>
<th>MYL-1401O + Taxane</th>
<th>Trastuzumab + Taxane</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>230</td>
<td>228</td>
</tr>
<tr>
<td>Events, n (%)</td>
<td>41 (17.8)</td>
<td>49 (21.1)</td>
</tr>
<tr>
<td>Log-rank test: P value</td>
<td>.303</td>
<td></td>
</tr>
</tbody>
</table>

Cox proportional hazard
Unstratified HR (95% CI)
- No. of subjects: 230, 228
- HR (95% CI): 0.83 (0.529, 1.218)
- P value: .303

Stratified HR (95% CI)
- No. of subjects: 220, 220
- HR (95% CI): 0.75 (0.488, 1.143)
- P value: .179

Conclusions

• Efficacy equivalence between MYL-1401O or trastuzumab in combination with taxanes as first-line therapy for HER2+ MBC at 24 weeks was statistically confirmed with similar safety, immunogenicity, and pharmacokinetics

• MYL-1401O has the potential to meet the need for an affordable treatment option for patients with HER2+ cancers
  - 5000 patients treated in India (small difference in formulation)
  - All pharmacovigilence data submitted to EMEA

• This is one of the first trials with biosimilars in oncology to demonstrate similar efficacy, safety, and immunogenicity against the reference product

• Ongoing trials with other biosimilars should further improve access

EMEA = European Medicines Agency

NCCN Guidelines

Adjuvant

- AC-TH
- AC-TP
- ddAC-TH
- TCH
- TCHP

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**Recurrent/Metastatic**

- First line
  - THP (docetaxel)
  - THP (paclitaxel)

- Other agents
  - T-DM1
  - TCH (paclitaxel weekly or Q3 weeks)
  - TH (paclitaxel or docetaxel)
  - Vinorelbine/Trastuzumab
  - Capecitabine/Trastuzumab

- Trastuzumab exposed
  - Lapatinib/capecitabine
  - Trastuzumab/capecitabine
  - Trastuzumab/lapatinib

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**Conclusions**

- Era of targeted therapy
  - Anti-HER2 therapy model

- Different approaches for
  - Neoadjuvant
  - Adjuvant
  - Metastatic

- Varying cost-effectiveness

- NCCN Guidelines → Wide berth for clinical judgment with eye toward cost

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**Challenges for Managed Care (cont)**

- Expanded indications for FDA-approved drugs
  - Increased frequency of administration
  - Longer duration of therapy

- Off-label use of biologics
  - Need for more definitive criteria for evaluation
  - Where is the evidence/data?
  - Legal/ethical questions

- Maintenance (?) use of biologics

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**Pharmacotherapy Management: Managed-Care Concerns**

- Challenges
  - Coverage issues
  - Benefit language
  - Utilization controls
  - Decision making
  - Newer models of care

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**Coverage Issues**

- Oral drugs covered under pharmacy benefit but access to drugs covered under medical benefit are subject to P&T review

- Supportive medications (eg, anti-nausea drugs, corticosteroids) coverage determined by route of administration

- Medicare Part B vs Part D determination further blurs the boundaries of coverage

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FDA = US Food and Drug Administration.
Value: Define the Value from Organizations Representing Healthcare Interests

<table>
<thead>
<tr>
<th>Organization</th>
<th>Value Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmaceutical Research and Manufacturers Association</td>
<td>The value of new and better medicine stems not only from the improved treatment of disease but also from a reduction in other healthcare costs, increased productivity, and better quality of life.</td>
</tr>
<tr>
<td>European Observatory on Health Systems and Policies</td>
<td>Value includes patient preferences, quality, equity, efficiency, and product acceptability among a wide range of stakeholders.</td>
</tr>
<tr>
<td>National Institute for Health and Clinical Excellence</td>
<td>The value of a treatment is based on scientific value judgments, including clinical evaluation and economic evaluation, and social value judgments, including considerations of effectiveness and efficiency.</td>
</tr>
<tr>
<td>Pharmacy Benefits Advisory Committee</td>
<td>The economic value of a drug takes into account its comparative cost-effectiveness, its comparative health gains, its affordability, the financial implications for the government budget, the severity of the condition treated, the presence of effective alternatives, the drugs’ ability to target those likely to benefit most, and its ability to address government health priorities.</td>
</tr>
</tbody>
</table>

Value Assessment: NCCN Guidelines: Evidence Blocks™

- Preferred regimen of TCH + pertuzumab for neoadjuvant HER2+ breast cancer

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>5</td>
</tr>
<tr>
<td>Safety</td>
<td>1</td>
</tr>
<tr>
<td>Quality of evidence</td>
<td>4</td>
</tr>
<tr>
<td>Consistency of evidence</td>
<td>2</td>
</tr>
<tr>
<td>Affordability</td>
<td>3</td>
</tr>
</tbody>
</table>

Value Domains: Value Domains and Metrics Identified by Key Opinion Leaders in Cancer Financing and Delivery

<table>
<thead>
<tr>
<th>Domains to Consider</th>
<th>Metrics for Assessing Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of life</td>
<td>Utilities</td>
</tr>
<tr>
<td>Quality of life</td>
<td>QALYs</td>
</tr>
<tr>
<td>Health status</td>
<td>Cost/QALYs</td>
</tr>
<tr>
<td>Cost</td>
<td>Quality</td>
</tr>
<tr>
<td>Quality of care</td>
<td>Efficiency</td>
</tr>
<tr>
<td>Equity</td>
<td>Effectiveness</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>Necessity</td>
</tr>
<tr>
<td>Compassion</td>
<td>Reasonableness</td>
</tr>
<tr>
<td>Opportunity</td>
<td>Affordability</td>
</tr>
</tbody>
</table>

**Patient Domains**

- Access to care
- Quality of care
- Compassion
- Respect
- Opportunity for treatment benefit
- Choice
- Hope
- Innovation and future discovery

**New Approaches to Oncology Care**

- Improving system barriers to patient-level data
  - Reducing reimbursement hurdles
- Rewarding improved quality by leveraging technology
  - Improved imaging
  - Genetic testing
  - Biomarkers
  - Targeted therapy

**Biologics**

- There is a wide range of biologic products
  - Vaccines
  - Blood and blood components
  - Gene therapy
  - Recombinant therapeutic proteins
- Biologics are composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues
- Biologics are isolated from a variety of natural sources
  - Human
  - Animal
  - Microorganisms

**Biosimilars**

- Pathway to approval created by the Affordable Care Act in 2010
  - Part of the law known as the Biosimilar Price Competition and Innovation Act
  - Product may be demonstrated to be 'biosimilar' if data show that the product is "highly similar" to an already approved biologic product
- Defined as a "Biological product that is approved based on a showing that it is highly similar to an FDA-approved biological product, known as a reference product, and has no meaningful differences in terms of safety and effectiveness from the reference product"
- Only minor differences in clinically inactive components are allowable

**Biosimilars (cont)**

- Highly similar to the US licensed reference biologic product notwithstanding minor differences in clinically inactive components
- No clinically meaningful differences from the reference product in terms of safety, purity, and potency

**Interchangeable**

- Biosimilar to the US licensed reference product
- Expected to produce the same clinical result to the reference product in any given patient
- If a product is indicated for multiple administrations, then the product must be able to be alternated with the reference product without any loss of efficacy or change in risk of adverse events
- May be substituted at the pharmacy level without the intervention of a healthcare provider
Biosimilars: Current Landscape

- Cost savings can be extrapolated from the European experience
- Since 2006, 13 biosimilars have been approved for use in Europe
- In 2010, cost discounts associated with biosimilars in Europe ranged from 10% to 35%
  - In comparison, generic small-molecule agents provide upward of 90% cost savings
  - Dose equivalency also plays a role
  - If a larger dose is needed to illicit the same therapeutic response, savings may be negated
- The current US climate
  - Zarxio®: Costs 15% less than the reference drug (filgrastim-sndz)
  - Granix®: Priced similarly to its reference product (tbo-filgrastim)


Outstanding Questions

- Pathway to biosimilars is still a work in progress
- The cost to conduct studies and to achieve interchangeability may be prohibitive
- How comfortable will physicians be prescribing biosimilar agents?
- How will managed-care organizations manage these agents?

AMCP. Academy of Managed Care Pharmacy. www.amcp.org.

Questions?

Conclusion

- Managed-care organizations can contribute to improved outcomes and reduced costs by increasing the understanding of current therapies, recognizing the potential benefit of future therapies, and developing an understanding of biosimilars and their future place in therapy