Biosimilars: Emerging Trends in Therapeutic Oncology

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President, Association of Community Cancer Centers
Financial Disclosure

I have had the following relevant financial interests in the past 12 months:

1. Sandoz
2. Amgen
Objectives

1. Define biosimilars and interchangeability designation
2. Assess current outcomes and data with therapeutic oncologic biosimilars
3. Assess and prepare for potential operational challenges when implementing biosimilars in oncology
Questions- Which one is the biosimilar?
Biosimilars

- Biologic product: Large, complex molecules that may be produced through biotechnology in a living system and are used to diagnose, prevent, treat, or cure diseases and medical conditions.

- Reference product: biologic product, already approved by FDA, against which a proposed biosimilar product is compared. A reference product is approved based on a full complement of safety and effectiveness data.

- Biosimilar: biologic product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product.
# Small Molecules vs. Biologics

<table>
<thead>
<tr>
<th></th>
<th>Small Molecule Drugs</th>
<th>Biologics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size (MW)</strong></td>
<td>Small (&lt;1,000 Daltons)</td>
<td>Large (&gt;10,000 Daltons)</td>
</tr>
<tr>
<td><strong>Source</strong></td>
<td>Chemical synthesis</td>
<td>Cultures of living cells</td>
</tr>
<tr>
<td><strong>Structure</strong></td>
<td>Simple, well defined, independent of manufacturing process</td>
<td>Complex (heterogeneous), defined by the exact manufacturing process</td>
</tr>
<tr>
<td><strong>Characterization</strong></td>
<td>Easy to characterize</td>
<td>Cannot be characterized completely</td>
</tr>
<tr>
<td><strong>Immunogenicity</strong></td>
<td>Mostly non-immunogenic</td>
<td>Immunogenic</td>
</tr>
</tbody>
</table>

### Example

- **Atorvastatin**
  - MW = 558.64
  - ![Atorvastatin Structure](Image1)

- **Trastuzumab**
  - MW = 185,000
  - ![Trastuzumab Structure](Image2)

Changes in Cost of Biologic Oncology Agents Over Time

- Trastuzumab increased 78% over 10 years\cite{1}
- Cost of biologics\cite{2}
  - 2005: 32% of $9.5B, Medicare Part B
  - 2014: 62% of $18.5B, Medicare Part B

Top 10 Drugs by Expenditures in Clinic: 2017

<table>
<thead>
<tr>
<th>Drug</th>
<th>2017 Expenditures ($ Thousands)</th>
<th>% Change from 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab</td>
<td>3,743,397</td>
<td>8.0</td>
</tr>
<tr>
<td>Pegfilgrastim</td>
<td>3,199,813</td>
<td>1.8</td>
</tr>
<tr>
<td>Rituximab</td>
<td>2,802,604</td>
<td>3.8</td>
</tr>
<tr>
<td>Nivolumab</td>
<td>2,533,504</td>
<td>21.8</td>
</tr>
<tr>
<td>Bevacizumab</td>
<td>2,348,893</td>
<td>-3.3</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>2,266,471</td>
<td>7.8</td>
</tr>
<tr>
<td>Epoetin alfa</td>
<td>1,839,876</td>
<td>1.6</td>
</tr>
<tr>
<td>Denosumab</td>
<td>1,823,997</td>
<td>13.3</td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>1,787,354</td>
<td>219.0</td>
</tr>
<tr>
<td>Ranibizumab</td>
<td>1,457,852</td>
<td>4.1</td>
</tr>
</tbody>
</table>

Trends in Biosimilars

- Total G-CSF product expenditures ↓ by 10.9% likely due to biosimilars
- Filgrastim-sndz 24.9% & tbo-filgrastim 18.8% of 4th quarter expenditures

Disrupting Pharmaceutical Biologic Ecosystem

Biologics are estimated to account for ~50% of US prescription drug expenditure in 2018

Biologics Price Competition and Innovation Act of 2009

Increased competition with biologic medications

Decreased prices, increased access, & increased innovation

Biologics/biosimilars have inherent heterogeneity, and slight differences in structure and clinically inactive components are expected.
Biosimilars Represent Paradigm Shift in Product Development

Reference Biologic\(^1\)

- Postmarketing Surveillance
- Phase III Clinical
- Phase II Clinical
- Phase I Clinical
- Preclinical
- Molecular Characterization

Biosimilar\(^2\)

- Postmarketing Surveillance
- Clinical
- Immunogenicity
- PK/PD
- Preclinical
- Molecular Characterization

Biosimilar Development & Extrapolation

Development of innovator product includes extensive preclinical and clinical studies for all indications versus development of biosimilar includes stepwise approach to demonstrating biosimilarity to reference product based on analytical studies, animal studies, and clinical studies.

Demonstrating analytical & functional similarity b/w biosimilar candidate and its reference product can reduce the number and scope of subsequent clinical trials.

If a biosimilar meets the requirements for biosimilarity, **extrapolation of data** may allow for approval of **additional indications** for which the reference product is indicated w/o other dedicated clinical studies.

Extrapolation: FDA Guidance

- **Scientific justification** for extrapolation should consider:
  - MOA in each condition
    - Target/receptor(s) for product relevant activity/function
    - Binding, dose/concentration response, and pattern of molecular signaling when product engages with target/receptor(s)
    - Relationships b/w target/receptor interactions and product structure
    - Target/receptor location and expression
  - PK, PD, and biodistribution of product in different populations
  - Immunogenicity of product in different patient populations
  - Differences in expected toxicities for each condition & patient population
  - “any other factor that may affect the safety or efficacy of the product in each condition of use and patient population for which licensure is sought”

Extrapolation: Summary

Extrapolation of indication must be scientifically justified and based on the **totality of the evidence** from the comparability exercise with reference product.

When seeking extrapolation indications, pivotal clinical studies to assess efficacy and safety (including immunogenicity) should be conducted in the most sensitive patient population, using endpoints that can detect clinically meaningful differences.

Goal of clinical program is not to re-establish patient benefit but to confirm similarity established by the structural and functional characterization.

Biosimilars 2020
The Year of the Biosimilar
## Bevacizumab-aawwb (MVASI)

<table>
<thead>
<tr>
<th>Objective Endpoint</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analytical &amp; Functional Assessment</strong></td>
<td></td>
</tr>
</tbody>
</table>
| VEGF binding affinity & inhibition of activity          | • Comparable equilibrium binding to VEGF as reference products bevacizumab  
• Displayed similar potency in inhibition of proliferation in HUVEC and inhibition of VEGFR2 receptor tyrosine kinase autophosphorylation |
| Comparative binding to FcRn and FcyRIIIa                | • Similar in vitro binding to FcRn to originator bevacizumab  
• In vitro binding to FcyRIIIa was moderately higher for biosimilar vs originator, difference not statistically significant  
• Bev-aawwb and bev have been shown to lack ADCC activity |
| Antitumor activity in xenograft models                  | • Displayed similar tumor growth inhibition in colon and epidermoid xenograft models  
• Inhibited VEGF-induced vascular permeability in mouse skin vascularity |
| Toxicology                                              | • Similar toxicokinetick parameters in animals studies                  |

Bevacizumab (MVASI)

### Objective Endpoint | Outcome
--- | ---
**Phase 1 Trial in Health Subjects**

**Primary endpoint:** $\text{AUC}_{\text{inf}}, \text{C}_{\text{max}}$
- Similar serum concentration-time profiles
- Peak concentrations were observed 1.5 -3 hr after of infusion

**Secondary endpoint:** Safety
- Most Aes were mold to moderate, no AES, SAEs, or deaths led to study discontinuation
- AEs possibly or probably related to study drug occurred in 27.3%, 17.1%, and 22.4% of patients who received Bev-awwb, Bev US, & Bev EU
- No clinically relevant changes in laboratory tests, ECG, vital signs, or physical examinations

## Bevacizumab-awwb vs Bevacizumab in Normal Volunteers: Pharmacokinetics

<table>
<thead>
<tr>
<th>Agent</th>
<th>Mean $C_{\text{max}}$ $\mu$g/mL (n)</th>
<th>Mean AUC$_{\text{last}}$ $\mu$g h/mL (n)</th>
<th>Mean AUC$_{\text{inf}}$ $\mu$g h/mL (n)</th>
<th>Median $t_{\text{max}}$ (h) (n) (range)</th>
<th>Mean $t_{1/2}$ (days) (n) (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bev-awwb</td>
<td>87.2 (67)</td>
<td>28,200 (62)</td>
<td>29,400 (66)</td>
<td>1.50 (67) (1.47-24.0)</td>
<td>17.77 (66) (3.68)</td>
</tr>
<tr>
<td>Bev (US)</td>
<td>89.1 (66)</td>
<td>28,500 (62)</td>
<td>29,600 (66)</td>
<td>1.50 (66) (1.48-24.0)</td>
<td>17.5 (66) (3.39)</td>
</tr>
<tr>
<td>Bev (EU)</td>
<td>84.7 (64)</td>
<td>29,400 (64)</td>
<td>30,600 (66)</td>
<td>3.94 (64) (1.47-8.00)</td>
<td>18.5 (66) (3.28)</td>
</tr>
</tbody>
</table>

Phase III Trial: Bevacizumab-awwb vs Bevacizumab in Advanced NSCLC

Patients with advanced NSCLC (N = 642)

<table>
<thead>
<tr>
<th>Agent</th>
<th>ORR, %</th>
<th>Median DoR, Mos</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab-awwb (n = 324)</td>
<td>39</td>
<td>5.8</td>
</tr>
<tr>
<td>Bevacizumab (n = 314)</td>
<td>41.7</td>
<td>5.6</td>
</tr>
</tbody>
</table>

Bevacizumab-awwb 15 mg/kg IV + Carboplatin/paclitaxel Q3W x 18 wks (n = 328)

Bevacizumab 15 mg/kg IV + Carboplatin/paclitaxel Q3W x 18 wks (n = 314)

- AE Grade ≥ 3
  - Bevacizumab-awwb: 42.9
  - Bevacizumab: 44.3

- SAE
  - Bevacizumab-awwb: 26.2
  - Bevacizumab: 23.0

- Fatal AE
  - Bevacizumab-awwb: 4.0
  - Bevacizumab: 3.6

FDA Advisory Committee document. ABP 215 – Bevacizumab biosimilar candidate.
Bevacizumab-awwb: Secondary endpoints

<table>
<thead>
<tr>
<th>Phase III trial in nonsquamous NSCLC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PFS</strong></td>
</tr>
<tr>
<td>• PFS was comparable in the Bev-awwb 60.1% vs bevacizumab 60.2%</td>
</tr>
<tr>
<td>• Estimated HR for Bev-awwb relative to bevacizumab was 1.03 (90% CI, 0.83, 1.29)</td>
</tr>
<tr>
<td><strong>OS</strong></td>
</tr>
<tr>
<td>• Fatal AEs occurred in 4.0% with Bev-awwb vs Bev 3.6%</td>
</tr>
<tr>
<td>• OS comparable Bev-awwb 86.7% vs Bev 88.3%</td>
</tr>
<tr>
<td><strong>Incidence of ADAs</strong></td>
</tr>
<tr>
<td>• Immunogenicity was similar, Bev-awwb 1.4% vs Bev 2.5%</td>
</tr>
<tr>
<td>• No patient developed neutralizing antibodies</td>
</tr>
</tbody>
</table>

ADA = Antidrug Antibody

Thatcher et al. 17<sup>th</sup> world conference on lung cancer. Vienna Austria Dec 4-7, ESMO conference 2018 Copenhage, Denkmark October.
Bevacizumab-awwb: Extrapolated Indications

- **Metastatic colorectal cancer**
  - First- or second-line treatment combined with IV 5-FU-based chemotherapy
  - Second-line treatment with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy after progression with first-line bevacizumab regimen
  - Not indicated for the adjuvant treatment of surgically resected colorectal cancer

- **Non-squamous NSCLC**
  - First-line treatment of unresectable, locally advanced, recurrent, or metastatic NSCLC in combination with carboplatin/paclitaxel

- **Glioblastoma**
  - Second-line treatment in progressive disease following prior therapy, based on improvement in ORR

- **Metastatic renal cell carcinoma**
  - In combination with interferon alfa

- **Cervical cancer**
  - In patients with recurrent, persistent, or metastatic disease, in combination with paclitaxel/cisplatin or paclitaxel/topotecan

Biosimilar Trastuzumab-dkst Monotherapy Versus Trastuzumab Monotherapy After Combination Therapy: Toxicity, Efficacy, and Immunogenicity From the Phase 3 Heritage Trial at 48 Weeks of Follow-up


1City Clinical Oncology Dispensary, Saint Petersburg, Russia; 2Mylan Inc, Canonsburg, PA, USA; 3Dnipropetrovsk State Medical Academy, Dnipropetrovsk, Ukraine; 4Regional Clinical Oncological Center, Kazan, Russia; 5Cardinal Santos Medical Center, Manila, Philippines; 6Siriraj Hospital, Bangkok, Thailand; 7Sumy State University, Sumy, Ukraine; 8King Chulalongkorn Memorial Hospital, Chulalongkorn University, Bangkok, Thailand; 9Curie Manavata Cancer Centre, Nasik, India; 10Department of Haematology, Oncology and Stem Cell Transplantation, University Medical Centre Freiburg and Faculty of Medicine, University of Freiburg, Freiburg, Germany; 11Corachan Genesis-Care Clinic, Barcelona, Spain; 12Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA; 13Biocor Research Limited, Bangalore, India; 14University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA
HERITAGE Study Design: Confirmatory Double-blind International Study

Designed per FDA and EMA guidelines to detect any potentially clinically meaningful differences between biosimilar and originator trastuzumab

Part 1: Double-blind combination treatment with taxanes

- **Trastuzumab-dkst (Ogivri™)**
  - Loading dose: 8 mg/kg IV
  - Dose: 6 mg/kg IV Q3W

- **Trastuzumab (Herceptin®)**
  - Loading dose: 8 mg/kg IV
  - Dose: 6 mg/kg IV Q3W

All patients received docetaxel 75 mg/m² Q3W or paclitaxel 80 mg/m² weekly; choice of taxane by institution

Part 2: Double-blind monotherapy

- **Trastuzumab-dkst until disease progression**
- **Trastuzumab until disease progression**

Cycle 1

Cycles 2-8

Week 24
(Primary PFS endpoint)

24-48 weeks

Week 48
(Primary PFS endpoint)

36 months or 240 deaths
(OS endpoint)

EMA, European Medicines Agency; FDA, Food and Drug Administration; IV, Intravenous; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization. *Continue 3-week cycles; if stable disease after 8 cycles, can continue combination treatment from part 1 at investigator’s discretion.

## Similar Efficacy Between Trastuzumab-dkst and Trastuzumab Observed Through 48 Weeks

**Progression-free survival**

<table>
<thead>
<tr>
<th>Trastuzumab-dkst</th>
<th>Trastuzumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (95% CI)</td>
<td>11.1 (8.81-11.20)</td>
</tr>
</tbody>
</table>

**Log-rank \( P \) value**

<table>
<thead>
<tr>
<th>Trastuzumab-dkst</th>
<th>Trastuzumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.842 + censored</td>
<td>0.131 + censored</td>
</tr>
</tbody>
</table>

**Stratified hazard ratio (95% CI)**

<table>
<thead>
<tr>
<th>Trastuzumab-dkst</th>
<th>Trastuzumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.95 (0.714-1.251)</td>
<td>0.61 (0.360-1.039)</td>
</tr>
</tbody>
</table>

**Overall survival**

<table>
<thead>
<tr>
<th>Trastuzumab-dkst</th>
<th>Trastuzumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>NE</td>
<td>NE</td>
</tr>
</tbody>
</table>

### Notes
- Stratified by assigned taxane, tumor progression, and tumor endocrine status.
- Assessments are ongoing and OS will be calculated after 240 deaths or 36 months.

NE, not estimable; OS, overall survival.
Similar Efficacy Between Trastuzumab-dkst and Trastuzumab Observed Through 48 Weeks

Progression-Free Survival

Overall Survival (immature)

Survival probability

Time, weeks

Log-rank $P=0.842$
+ Censored

Log-rank $P=0.131$
+ Censored

Presented by Hope Rugo at 2018 ASCO Annual Meeting
At week 24, 1.3% and 0% of patients demonstrated CR, and 68.3% and 64.0% demonstrated PR, with trastuzumab-dkst and trastuzumab, respectively.

At week 48,
- An additional 2 patients (1 per group) demonstrated CR and an additional 5 patients demonstrated PR in the trastuzumab-dkst group.
- The confirmed ORR is 70.0% and 66.7% with trastuzumab-dkst and trastuzumab, respectively.

CR, complete response; ORR, overall response rate; PFS, progression-free survival; PR, partial response.
Left Ventricular Ejection Fraction Was Comparable Between Trastuzumab-dkst and Trastuzumab Arms Through 48 Weeks

<table>
<thead>
<tr>
<th>New onset myocardial dysfunction through week 48</th>
<th>Trastuzumab-dkst N=247</th>
<th>Trastuzumab N=246</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF &lt;50% at least once postbaseline, n (%)</td>
<td>10 (4.0)</td>
<td>8 (3.3)</td>
</tr>
<tr>
<td>LVEF &lt;50% postbaseline and decrease &lt;10% points</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>LVEF &lt;50% postbaseline and decrease ≥10% points</td>
<td>9 (3.6)</td>
<td>7 (2.8)</td>
</tr>
</tbody>
</table>

- Overall mean and median LVEF over 48 weeks were similar in both groups
  - 5 patients (trastuzumab-dkst, n=3; trastuzumab, n=2) discontinued treatment because of a cardiac event
  - 16 patients (trastuzumab-dkst, n=10; trastuzumab, n=6) had LVEF values <50% at least once postbaseline that showed recovery to >50% during the study

LVEF, left ventricular ejection fraction.
HERITAGE Supports Trastuzumab-dkst as a Biosimilar to Trastuzumab in All Approved Indications

- In patients with HER2-positive MBC, HERITAGE demonstrated that
  - Trastuzumab-dkst, when administered in combination with a taxane, results in an equivalent ORR compared with originator trastuzumab
  - Trastuzumab-dkst was well tolerated as first-line therapy
  - Trastuzumab-dkst, as maintenance monotherapy after combination therapy with a taxane, results in similar PFS at 48 weeks to originator trastuzumab; OS survival is comparable but immature
  - No new safety issues were observed
  - In patients with HER2+ disease treated with a taxane and an HER2-targeted antibody in the first-line metastatic setting, ORR at week 24 was predictive of PFS at week 48
  - HERITAGE is ongoing and final OS will be assessed after 36 months or after 240 deaths, whichever occurs first
  - Based on current data, predicted to conclude by the end of 2018, with final OS available in 2019

HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.
<table>
<thead>
<tr>
<th>Agent</th>
<th>Study Design</th>
<th>Endpoints</th>
<th>Results</th>
<th>Researcher Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABP 980 (LILAC)</td>
<td>ABP 980 vs OriT (both + paclitaxel q3w x 4 cycles neoadjuvant, then w/out paclitaxel q3w to 1 yr adjuvant) on pCR in patients with HER2+ EBC (N=725; n = 696 in pCR evaluable pop.).</td>
<td>1st: RD, RR of pCR in breast tissue + axillary lymph nodes. 2nd: safety</td>
<td>pCR in ABP 980 vs OriT: 48.0% vs 40.5%; RD: 7.3%; RR: 1.19%. Grade ≥3 TEAEs: 14.8% vs 14.1%.</td>
<td>ABP 980 and OriT clinically equivalent in neoadjuvant setting for these patients.</td>
</tr>
<tr>
<td>PF-05280014</td>
<td>PF-05280014 vs T-EU (8 mg/kg→6 mg/kg q3w x 6 cycles w/docetaxel + carboplatin) in patients with HER2+ EBC (N=226), stratified by hormone receptor status, primary tumor size.</td>
<td>1st: steady state drug concentration C\text{trough}&gt;20 µg/mL at Cycle 5; 2nd: ORR, pCR</td>
<td>C\text{trough}&gt;20 µg/mL in PF-05280014 vs T-EU: 92.1% vs 93.3%. pCR, 47% vs 50%; ORR, 88.1% vs 82.0%.</td>
<td>PF-05280014 showed similarity to T-EU in safety and immunogenicity, and noninferiority in PK</td>
</tr>
<tr>
<td>PF-05280014</td>
<td>First-line PF-05280014 vs T-EU (first dose 4 mg/kg; then 2 mg/kg weekly until at least week 33 (both + paclitaxel) in patients with HER2+ MBC (N=707).</td>
<td>1st: ORR. 2nd: safety, tumor control, PK, immunogenicity</td>
<td>PF-05280014 vs T-EU: ORR = 0.940; Safety, PK, immunogenicity equivalent.</td>
<td>PF-05280014 similar to T-EU for efficacy, immunogenicity, safety, and PK.</td>
</tr>
<tr>
<td>SB3</td>
<td>SB3 vs OriT (8→6 mg/kg q3w x 8 cycles) + DOC and FEC (4 cycles) neoadjuvant in pts w/HER2+ EBC orLABC, LVEF ≥ 55% (N = 875)*, then 10 cycles adjuvant SB3 vs OriT.</td>
<td>1st: pCR in breast tumor. 2nd: safety, immunogenicity, EFS, OS</td>
<td>bpCR in SB3 vs OriT: 51.7% vs 42.0%.PK, safety, immunogenicity equivalent.</td>
<td>SB3 comparable to OriT for safety, PK, immunogenicity, and efficacy.</td>
</tr>
</tbody>
</table>

bpCR, breast pathologic complete response; EBC, early breast cancer; HER2, human epidermal growth factor receptor 2; LVEF, left ventricular ejection fraction; MBC, metastatic breast cancer; OriT, originator trastuzumab; pCR, pathologic complete response; PK, pharmacokinetics; T-EU, European Union-sourced reference trastuzumab.

WHICH Pill did you choose?

- Quality Payment Program (via MACRA), consisting of 2 tracks:
  - Merit-based Incentive Payment System (MIPS): Allows participating providers to earn a performance based payment adjustment, based on demonstrating providing high-quality and cost-efficient care. MIPS replaces the Physician Quality Reporting System (PQRS), value-based modifier, and Electronic Health Records Incentive Program (also called “meaningful use”), and adds a new category for Improvement Activities.
  - Advanced Alternative Payment Models (APMs): Specific programs that add incentive payments to provide high-quality and cost-efficient care. APMs can apply to a specific clinical condition, a care episode, or a population.
- Oncology Care Model (OCM), which utilizes appropriately aligned financial incentives to enable improved care coordination, appropriateness of care, and access to care for beneficiaries undergoing chemotherapy. The OCM encourages participating practices to improve care and lower costs through an episode-based payment model that financially incentivizes high-quality, coordinated care.83
Why the Long Face?

The first 2 biosimilars on the US market (for different reference products) had wholesale acquisition costs (WACs) discounted 15% from their reference products, with the discount increasing to nearly 20% for one of them.

However, the introduction of a rival biosimilar at a 35% discount resulted in one of the competitor biosimilars also increasing its discount from nearly 20% to an average sales price at 35%.

The Wholesale Acquisition Cost (WAC or “list price”) of both MVASI (trastuzumab-anns) and KANJINTI (trastuzumab-anns) will be 15% lower than their reference products. At launch, MVASI is priced 12% below the current Avastin Average Selling Price (ASP) and KANJINTI is priced 13% below the current Herceptin ASP.
New Space and New Faces

Bevacizumab
- Mvasi (Bevacizumab-awwb)
- Zirabev (bevacizumab-bvzr)

Rituximab
- Ruxience (rituximab-pvvr)
- Truxima (rituximab-abbs)

Trastuzumab
- Ogivri (trastuzumab-dkstmb)
- Herzuma (trastuzumab-pkrb)
- Ontruzant (trastuzumab-dttb)
- Trazimera (trastuzumab-qyyp)
- Kanjinti (trastuzumab-anns)
Considerations for evaluating biosimilars for formulary inclusion
Considerations for Biosimilar Formulary Inclusion

✓ Payors
✓ Formulary Decision
✓ Utilization through contracts
✓ Patient Assistance
✓ Reimbursement
✓ Education
✓ EMR Integration
✓ Pharmacovigilance
✓ State Board of Pharmacy Laws
### Considerations for P&T Committee Members
#### Evaluating Biosimilars for Formulary Inclusion

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<th><strong>Clinical Considerations</strong></th>
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<tbody>
<tr>
<td>• Indications</td>
</tr>
<tr>
<td>• Evaluation of efficacy and safety using available data</td>
</tr>
<tr>
<td>• Immunogenicity</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th><strong>Product Considerations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Nomenclature</td>
</tr>
<tr>
<td>• Manufacturing and supply chain considerations</td>
</tr>
<tr>
<td>• Packaging, labeling, and storage</td>
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<table>
<thead>
<tr>
<th><strong>Institutional Considerations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Substitutions and interchangeability</td>
</tr>
<tr>
<td>• Therapeutic interchange</td>
</tr>
<tr>
<td>• Transitions of care</td>
</tr>
<tr>
<td>• Pharmacovigilance</td>
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<tr>
<td>• Cost</td>
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<tr>
<td>• Reimbursement</td>
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<tr>
<td>• Provider and patient education</td>
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<tr>
<td>• Information technology</td>
</tr>
</tbody>
</table>
Guideline Recommendations

- Febrile neutropenia is defined as a single temperature $\geq 38.3^\circ$ C or $\geq 38^\circ$ C for over 1 hour.
- Neutropenia: $<500$ neutrophils/mcL or $<1000$ neutrophils/mcL and a predicted decline to $\leq 500$ neutrophils/mcL over the next 48 hours
- G-CSF refers to the following approved agents: filgrastim, filgrastim-sndz, tbo-filgrastim, and pegfilgrastim.
- Dose-limiting neutropenic event could be a nadir count or day of treatment count that could otherwise impact planned dose of chemotherapy.

Clinical Guideline Incorporating Biosimilars

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommendation</th>
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</thead>
<tbody>
<tr>
<td>G-CSF for prophylaxis of febrile neutropenia and maintenance of scheduled dose delivery</td>
<td>Filgrastim (Category 1); tbo-filgrastim (Category 1); filgrastim-sndz (Category 1); pegfilgrastim (Category 1)</td>
</tr>
<tr>
<td>MGFs for therapeutic use and maintenance of scheduled dose delivery</td>
<td>Filgrastim; filgrastim-sndz; sargramostim</td>
</tr>
</tbody>
</table>
| Mobilization of hematopoietic progenitor cells in autologous setting       | 1. Single-agent growth factor  
   • Filgrastim; filgrastim-sndz; tbo-filgrastim  
  2. Combination chemotherapy followed by MGF  
   • Filgrastim; filgrastim-sndz; tbo-filgrastim  
  3. Concurrent MGF  
   • Filgrastim/filgrastim-sndz + sargramostim  
  4. MGF + plerixafor  
   • Filgrastim; filgrastim-sndz; tbo-filgrastim |

G-CSF = granulocyte colony-stimulating factor; MGF = myeloid growth factor.
Questions