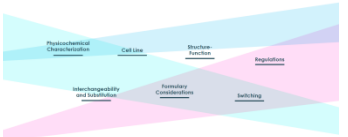

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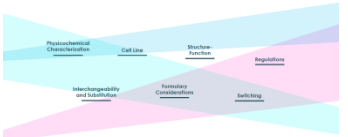
GaBI Scientific Meetings

First GCC Stakeholder Meeting on **Approval Process, Interchangeability/Substitution and Safety of Biosimilars**

20 November 2017, Holiday Inn Izdihar Riyadh, Saudi Arabia



Oncologist perspective – the use of biosimilar trastuzumab in breast cancer: clinical experience

Assistant Professor Meteb Al-Foheidi, MD, FRCPC

20 November 2017

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GENERICS AND BIOSIMILARS INITIATIVE
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The use of Biosimilar Trastuzumab in Breast Cancer: Clinical Experience

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Definition of Biosimilars

- Large proteins derived from living cell lines
- Highly similar to the reference biologic agent, but not identical
- No clinically meaningful differences in safety and efficacy between biosimilar and reference product
- Utilize the same mechanism(s) of action as reference product
- Have the same route of administration, dosage form, and strength

Bui LA, et al. *Drug Discover Today*. 2015;20:1-15.
Camacho LH, et al. *Cancer Med*. 2014;3:889-899.

Why the Need for Oncology Biosimilars?

- Anticancer agents accounted for $5.8 billion in drug expenditures in the United States in 2015[a]
  - 16.6% increase from 2014
  - 17.3% of all drug expenditures
- Biosimilars could temper cost of anticancer drugs
  - Savings likely not as great as with generics (estimated at 10% to 30% for biosimilars)[b]
- Increase access to anticancer agents in the United States and worldwide

a. Schumock GT, et al. *Am J Health-Syst Pharm*. 2016;73:1058-1075.
b. Federal Trade Commission website.

Biosimilars Are Not the Same as Generics

- Complex manufacturing process from living cells introduces heterogeneity in biosimilar product
  - Production process is often proprietary
- Highly similar to reference product but not identical
  - Exact copies of biologics are not possible with current technology
- Standard FDA approval pathway for generics is not appropriate for biosimilars owing to their greater complexity

Bui LA, et al. *Drug Discover Today*. 2015;20:1-15.

State of Biosimilar Oncology Development

- Supportive care therapies[a]
  - Filgrastim-sndz: first approved biosimilar in the US (2015)
  - Pegfilgrastim, epoetin alfa in development
- Monoclonal antibodies
  - Trastuzumab (phase 3, *HER2+* MBC)[b]
  - Rituximab (phase 3, follicular lymphoma)[c]
  - Bevacizumab (phase 3, advanced NSCLC)[d]

a. Rugo H, et al. *Cancer Treat Rev*. 2016;46:73-79; b. Clinicaltrials.gov; NCT02472964; c. Clinicaltrials.gov; NCT02260804; d. Clinicaltrials.gov; NCT01763645.

Oncology Biosimilar Clinical Studies: *Endpoints*

- No universal consensus on which endpoints to use or in what disease setting
- Should be appropriately sensitive to detect meaningful clinical differences between biosimilar candidate and reference product
- Long-term endpoints (eg, OS, PFS) not feasible or necessary for biosimilar oncology studies
  - Focus is on short-term endpoints
    - Overall response rate
    - pCR (eg, trastuzumab biosimilar in neoadjuvant breast cancer setting)

Rugo H, et al. *Cancer Treat Rev*. 2016;46:73-79.
European Medicines Agency.

Extrapolation of Indications

- Therapeutic oncology biosimilars can generally be extrapolated to other tumor types if biosimilarity is demonstrated in one
- Efficacy data from late-stage disease setting can support moving biosimilar to earlier stages
- A biosimilar cannot be approved for an indication not held by the reference product
  - Would need to follow 351(a) approval pathway for biologics

Camacho LH, et al. *Cancer Med*. 2014;3:889-899.

Interchangeability of Biosimilars

- FDA: switch between biosimilar and reference product with no adverse clinical consequences
- Currently, no definitive guidance on data required to demonstrate interchangeability
- Coverage of oncology biosimilars by insurance remains to be determined

Tkaczuk KH, Jacobs IA. *Semin Oncol*. 2014;41:S3-S12.

Therapeutic Oncology Biosimilars: *Trastuzumab*

- Multinational, randomized, double-blind, phase 3 trial (HERITAGE) presented at ASCO® 2016
  - 458 pts with *HER2*+ mbc randomized to taxane chemotherapy plus either trastuzumab or trastuzumab biosimilar (Myl-1401O)
  - Overall response at week 24 was 64% for trastuzumab vs 69.6% for Myl-1401O
  - Ratio of overall responses fell within predefined equivalence margin (1.09; 95% CI: 0.95, 1.24)
  - Serious AEs (primarily neutropenia) occurred at similar rates between the two arms

Rugo HS, et al. *J Clin Oncol*. 2016. Abstract LBA503.

Postmarketing Safety

- Potential for immunogenicity
- Clinical studies of biosimilars not large enough to detect rare adverse events
- Passive vs active surveillance
  - Passive: clinician reports an adverse event to a regulatory authority or the manufacturer
  - Active: prospectively looking for adverse events
- No major safety signals from European experience with biosimilars

Camacho LH, et al. *Cancer Med*. 2014;3:889-899; Rugo H, et al. *Cancer Treat Rev*. 2016;46:73-79; Academy of Managed Care Pharmacy website.

Summary and Conclusions

- A number of oncology biosimilars approved in the European Union
- Cost savings of about 30%
- No major safety signals from EU experience
- Therapeutic biosimilars are coming soon to the US market
- Hospital pharmacy and therapeutics committees will have a large role in determining how biosimilars are used within their institutions