Industry Day Theme # 2: Sustainable Medical Technologies

Assessment of analytical similarity of trastuzumab biosimilars: A case study

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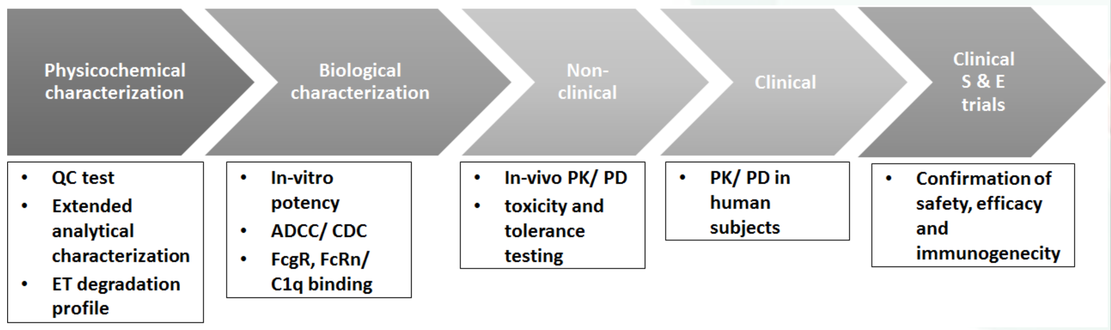
Abstract

Biosimilars are biological product that is similar in terms of quality, safety and efficacy to an already licensed reference product. The key step towards development of biosimilars is to establish analytical similarity with respect to the reference product for its regulatory approval. In the present work, an extensive array of orthogonal analytical tools have been used to demonstrate structural and functional similarity of trastuzumab biosimilars obtained from different manufacturers with their reference product to monitor the quality of approved biotherapeutics in the Indian marketplace. As an outcome, a robust evidence of analytical similarity was established and will help prevent a wrong drug candidate proceeding to advanced stages of clinical trials.

Introduction

- "Biosimilarity" means "the biological product is highly similar to the reference product with no clinically meaningful differences in terms of the safety, purity, and potency of the product".
- Regulatory agency expects the manufacturer to perform an extensive comparison with respect to quality, safety, and efficacy to demonstrate similarity between the biosimilar and reference product.

Workflow for Biosimilar development strategy for regulatory approval



Materials and Methods

- Structural and functional similarity assessment was established for five trastuzumab biosimilars (Biceltis from Emcure, Trasturel from Reliance, Canmab from Biocon, Vivitra from Zydus, Hertraz from Mylan) against the corresponding reference product Herclon from Roche
  - ✓ Demonstrate high similarity through an extensive physicochemical and *in vitro* biological comparability exercise
  - ✓ Understand the impact of any differences detected
  - ✓ Confirm similarity with regard to PK, safety and efficacy

State-of-the-art analytics (ICH Q5E guideline) to characterize biosimilars

Primary Structure	Higher Order Structure	Process related variants	Bioassays
• Intact mass • Reduced mass • Peptide mapping • Disulphide bridging	• Circular Dichroism • Fluorescence spectroscopy • FTIR • DSC	• RP-HPLC • SE-HPLC • CEX-HPLC • SDS-PAGE • DLS	• In-vitro binding • ADCC • CDC • SPR

Conclusions

Robust evidence of analytical similarity of Rituximab biosimilars with its reference through a comprehensive analytical similarity exercise

- ➢ Assessment made with multiple, complementary approaches/ tools providing in-depth structural and biological characteristics of the tested mAbs
- ➢ All biosimilars exhibited similar structural and biological properties vis-à-vis the innovator, indicating comparability of these medicines
- ➢ Few biosimilars exhibited differences in their glycoforms, charge isoform and biological properties

Industrial Significance

- ✓ Making medication affordable and accessible to all sections of society
- ✓ Shorter time to market than originator products
- ✓ Cost effective manufacturing with highly skilled, reasonably priced workforce
- ✓ Huge market and higher probability of Return on Investment (ROI)

Technology Readiness Level

Prospects for affordable, accessible, safe and efficacious life saving drugs

Results

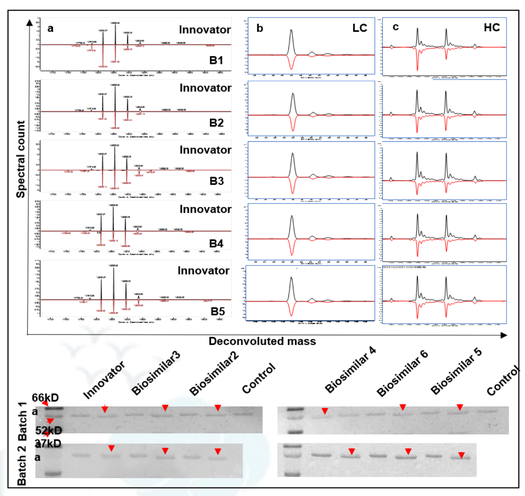


Figure 1: Intact and Reduced mass analysis of trastuzumab biosimilars

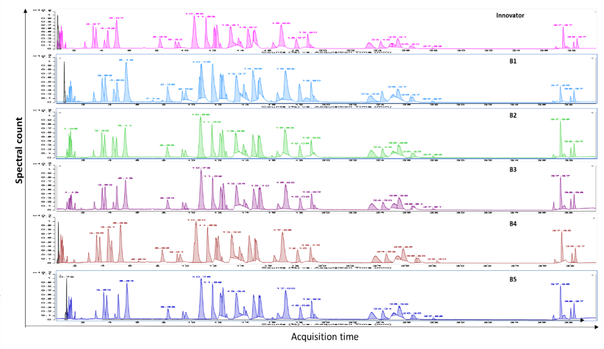


Figure 2: Peptide mapping analysis of trastuzumab biosimilars

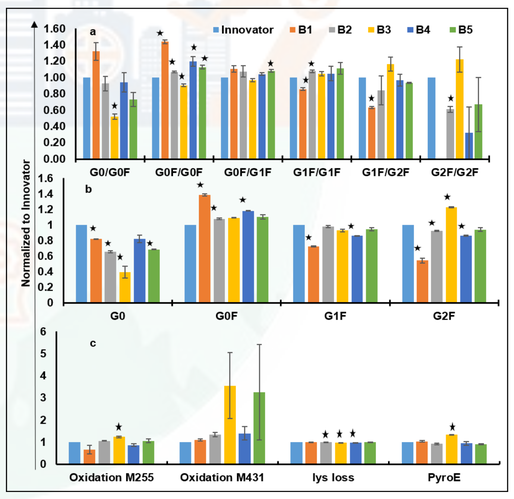


Figure 3: Glycoform analysis and PTMs of trastuzumab biosimilars for trastuzumab innovator and biosimilars using LC-MS

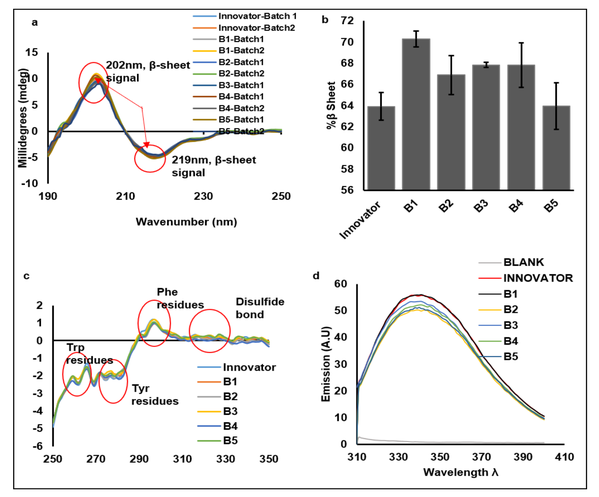


Figure 4: Higher Order Structure characterization of trastuzumab biosimilars

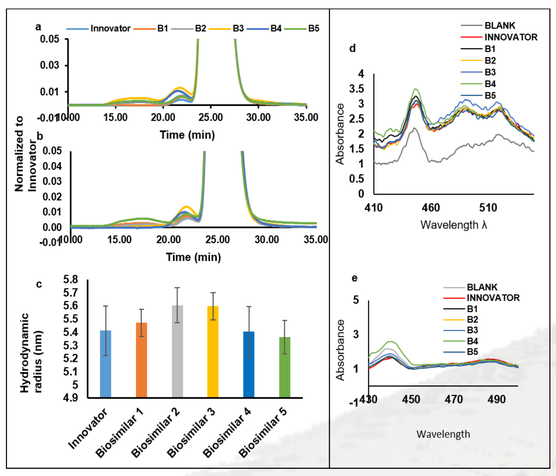


Figure 5: Size heterogeneity of trastuzumab biosimilars

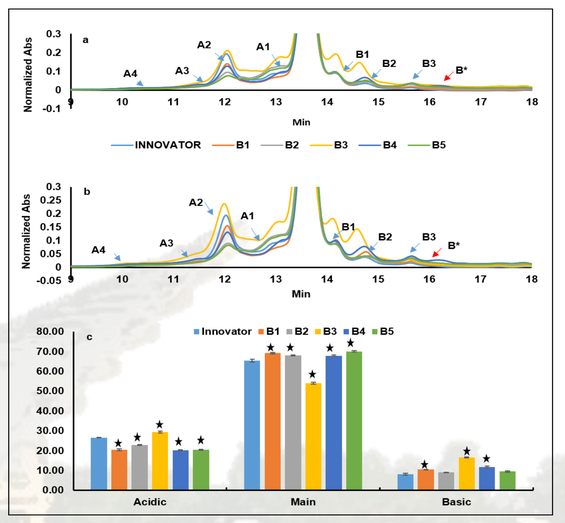


Figure 6: Charge variant analysis of trastuzumab biosimilars

References

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