2nd EMA Workshop on Biosimilar Monoclonal Antibodies, 24 October 2011

Session 5.1: Pharmacovigilance

«What data/studies could be deferred to the post-authorisation phase?»

Innovator Industry Presentation

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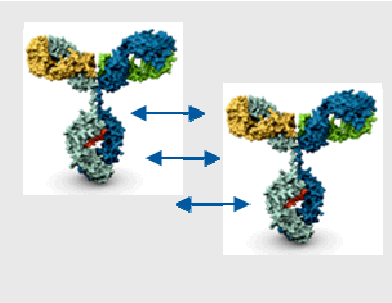
Good pharmacovigilance (PhV) of biosimilar monoclonal antibodies (mAbs): overview

- Reliable PhV data are key to understanding all biopharmaceutical products
- Same PhV standards must be applied to both originator and biosimilar mAbs
- Product/manufacturer identification is critical for mAb adverse event reporting within the framework of the established EU PhV system
- Post-marketing studies/data required for detection/evaluation of very rare AEs unlikely to be detected in abbreviated pre-approval clinical programs
- Risk Management Plan required to guide PhV activities (as for all biologics)



Molecular Similarity

Equivalent Clinical Results

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Unique product identification of each mAb

- Required for safety and PhV activities for each biological product
- Support product identification requirements in new EU PhV legislation:
  - Product name (proprietary and non-proprietary)
  - Manufacturer
  - Lot number
- To ensure patient safety and accurate labeling, AE reporting must identify responsible product: implementation of appropriate data capture necessary
- Support requirements to ensure product identification for purposes of tracking and traceability of safety findings

Biosimilars: Pharmacovigilance Requirements and Post-authorization Studies

Foundational principle: consistent with and based on reference product

- Biosimilars are highly similar, but not identical, to the reference product based on analytical comparability and abbreviated pre-clinical and clinical programs
- Pre-approval studies must be of adequate size & duration to establish sufficient comparability to meet biosimilarity criteria
- Post-approval studies are not a substitute for an adequate pre-approval program to address key safety findings
- Reference product will have years of post-marketing experience to establish and confirm its safety profile, and to inform PhV and post-authorisation programs for a biosimilar
- Consideration must be given to the potential for unique properties of the biosimilar molecule, on a case-by-case basis

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Biosimilars: Pharmacovigilance Requirements and Post-authorization Studies

Specific Considerations

- Target Effects
  - Principles of PhV relating to *target profile for biosimilar* should be same as for the reference product
  - PhV plan and RMP must take into account the safety experience and evolution of knowledge about the *target profile* developed during marketed use of the reference product
- Biosimilar Molecule
  - Complete evaluation of the biosimilar *molecule* may require additional assessments to identify potentially rare events, such as immunogenicity, hypersensitivity, or other unique findings (data dependent)
  - Where extrapolation to multiple indications is justified based on similar mechanisms of action and the totality of data, additional post-approval indication-specific safety data *may or may not** be required

*member organizations have somewhat differing views

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Risk Management Plans for Biosimilar MAbs

- As in general: the elements of the Plan are proportionate to the anticipated risk, taking into consideration of and further defining benefit-risk
- Should be based on:
  - identified risks and knowledge of reference product and product class, e.g. immunogenicity, including knowledge gained during marketed use of the originator, and/or mechanistic class (e.g. TNF inhibitors)
  - Intrinsic risks of clinical indications and patient populations (including extrapolated indications/patient populations)
  - pre-approval knowledge of biosimilar product and comparability data, e.g. immunogenicity assessments, results of pre-approval programme

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