EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Immunogenicity of biologicals: a pharmacovigilance perspective

Workshop on immunogenicity assessment of biotechnology-derived therapeutic proteins

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An agency of the European Union

Recent examples of challenges from a pharmacovigilance perspective

Is this a formulation issue, and should an immunogenic aetiology be suspected?

Thrombotic Microangiopathy Associated with Interferon Beta

TO THE EDITOR: Interferon beta is a widely prescribed recombinant-protein therapy with a well-established favorable safety profile.[1] Here, we describe an unexpectedly high number of cases of thrombotic microangiopathy associated with severe or malignant hypertension in four patients with multiple sclerosis who were receiving therapy with recombinant interferon beta

NEJM 2014: 1270-1
Case series

Is there a difference in immunogenicity between *second* and *third* generation FVIII?

Factor VIII Products and Inhibitor Development in Severe Hemophilia A

	Third-Generation Full-Length (N=157)	Second-Generation Full-Length (N=183)
Inhibitor development — no. (%)		
Clinically relevant	41 (28.2)	64 (37.7)
High-titer	25 (17.9)	40 (25.2)

NEJM 2013: 231-9
Findings from EU haemophilia registries

Guideline on good pharmacovigilance practices (GVP)

Product- or Population-Specific Consideration II: Biological medicinal products

- GVP module on pharmacovigilance requirements for biologicals under development (public consultation ended 29 February 2016)

- Objectives of GVP PII:
  - To explain specific issues and challenges associated with PhV of biologicals
  - To provide guidance on addressing these challenges
  - To describe the roles and responsibilities of various stakeholders within EU network

- GVP PII *supplements* (and does not replace) other GVP modules or guidelines

Overview of specific guidance related to immunogenicity in GVP PII

- Routine pharmacovigilance activities should include, among others:
  - Introduction of measures to ensure traceability of batches and products
  - Signal detection on batch- and product-level
  - Define and monitor clinical endpoints relevant to the potential risk of immunogenicity
- Any further strategies for evaluating immunogenicity should be proposed in RMP
  - Determination of optimal strategy requires multidisciplinary approach, taking into account the nature of any potential immunogenicity observed pre-approval
- Risk analysis for significance of post-approval manufacturing changes in RMP

Disclaimer: orientations presented on this slide may change following public consultation