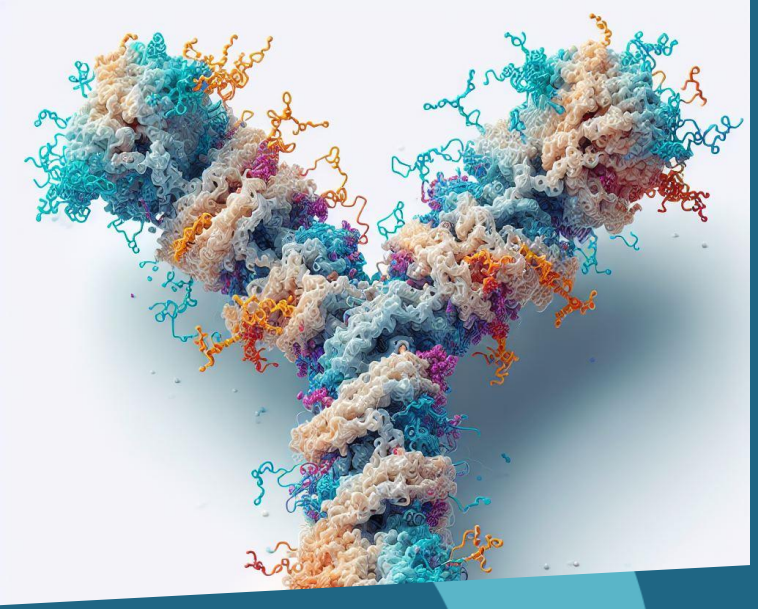

EuropaBio®

EMA WORKSHOP ON THE CHALLENGES IN DRUG DEVELOPMENT, REGULATION AND CLINICAL PRACTICE FOR IMMUNOGLOBULINS

"Perspectives on clinical development and clinical use of immunoglobulin medicines"

Vai Katkade - MD, PhD
Head of Global Medical Affairs – Pipeline
CSL Behring

Background to EMA workshop

5.3.2. Replacement therapy in secondary immunodeficiencies

Secondary immunodeficiencies (SID) in patients who suffer from severe or recurrent bacterial infections, ineffective antibiotic treatment and either proven specific antibody failure (PSAF)* or serum IgG level of <4 g/l.

* PSAF= failure to mount at least a 2-fold rise in IgG antibody titre to pneumococcal polysaccharide and polypeptide antigen vaccines.

If efficacy has been proven in primary immunodeficiency syndromes (see 5.3.1 no further studies are required to demonstrate efficacy in SIDs. Dosage regimens different from the standard dosages stated in the core SmPC should be supported by clinical data.

5.3.3. Chronic inflammatory demyelinating polyradiculoneuropathy as maintenance therapy (CIDP)

If the efficacy in primary immunodeficiency syndromes is established, then an extrapolation to maintenance therapy for CIDP after stabilisation with IVIg might be possible without the need to perform separate clinical trials in this indication, if adequately justified.

The dosage regimen should, however, be justified. If other dosage regimens than the ones provided in the guideline on core SmPC for human normal immunoglobulin for subcutaneous and intramuscular administration (SCIg/IMIg) are requested, they should be supported by relevant clinical data.

5.3.4. Hepatitis A prophylaxis

Clinical data are not required. The Monograph for Human normal immunoglobulin (0338) should be adhered to.

Workshop - Challenges in drug development, regulation and clinical practice for immunoglobulins

5th March 2025 (14 pm to 18 pm, CET)

Virtual meeting

Immuno-replacement and Immuno-modulation

IVIg & SCIg

Immuno-replacement

PID & SID

Immuno-modulation

Autoimmune diseases

Potential mechanisms of Ig in Immuno-modulation

Neutralisation via Fab	Anti-idiopathic neutralization of auto-antibodies
FcγR antagonism	Fcγ receptor blockade & modulation
Complement antagonism	Inhibition of complement activation & fragment scavenging
FcRn antagonsim	Ig saturation of FcRn accelerates destruction of pathogenic IgG specifically
Anti-inflammatory	Introduction of Tregs & immunomodulatory effects

Abbreviations: IVIg – Intravenous Immunoglobulin; PID – Primary Immune Deficiency; SCIg – Subcutaneous Immunoglobulin; SID – Secondary Immune Deficiency; FcγR: Fc gamma Receptor; FcRn – neonatal Fc Receptor, Tregs – regulatory T cells

SCIg for SID

Unmet needs remains in SID

Hematologic cancer & therapy reduces B-cells & antibodies, leading to SID and serious or recurrent infections

Infections are a major cause of mortality in patients with hematologic malignancies and SID from other causes

New approaches required

Infection prevention by IgRT is well documented

Supported by clinical guidelines and practice

Abbreviations: IgRT– Immunoglobulin Replacement Therapy

SCIg for Immuno-replacement therapy (PID/SID)

EMA SC/ IM Ig draft guideline

- One trial in PID indication allows PID and SID indication
- Harmonized with EMA IVIg guidelines (revised in 2018)

Rationale

- Evidence of efficacy and safety in PID indication can be extrapolated to SID indication
- SCIg therapy for SID is a medical need (in addition to important role played by IVIg)
- Assures patient availability of SCIg products

SCIg for Immuno-modulation (CIDP)

EMA SC/ IM Ig draft guideline

- One trial in PID indication as per guideline allows CIDP indication
- Not harmonized with EMA IVIg guidelines (as separate trial in ITP needed)

Rationale

- SCIg immunomodulation mechanism for CIDP ≠ IgRT mechanisms for PID; difference not fully understood
- Product modifications may lead to differences in efficacy
- Higher doses used in immunomodulatory conditions (CIDP) vs. PID; therefore, efficacy, safety and patient convenience cannot be extrapolated from PID trial data
- Unmet medical need for additional therapies in CIDP exist. Therapies should be evidence based (such as through product-specific RCTs)

Abbreviations: ITP - Immune Thrombocytopenic Purpura; RCT – Randomized Controlled Trial

SCIg/IMIg for hepatitis A prophylaxis

Hepatitis A prophylaxis indication granted for IMIg products with specified minimal anti-hepatits A titer of >100 IU/ml

Anti-hepatitis A titer in products depends on hepatitis A antibodies in plasma donor population

EuropaBio considerations:

1. Product availability and need for product declining due to effective vaccination
2. Ability of manufacturers able to meet EMA titre requirements
3. EMA's thinking on flexibility regarding titres and volumes would be helpful as guidance for manufacturers

03 Summary

5.3.2. Replacement therapy in SID

- If efficacy proven in PID (see section 5.3.1 of draft EMA guideline), no further studies required to demonstrate efficacy in SIDs.
- Dosage regimens different from standard dosages as per core SmPC should be supported by clinical data.

5.3.3. Chronic inflammatory demyelinating polyradiculoneuropathy as maintenance therapy (CIDP)

- If efficacy in PID is established, then extrapolation to maintenance therapy for CIDP after stabilization with IVIg might be possible without the need to perform separate clinical trials in this indication, if adequately justified.

5.3.4. Hepatitis A prophylaxis

- Clinical data not required.
- Ph. Eur. monograph for human normal immunoglobulin (0338) should be adhered to.

Thank you for your attention

Questions?
Comments?
vai.vatkade@cslbehring.com

About EuropaBio

For people and planet

- EuropaBio is Europe's largest biotechnology industry group, founded in 1996 to represent the interests of the biotechnology ecosystem across sectors.
- It has the vision to deliver a healthy, sustainable and competitive global Europe through biotechnology innovation applied across industrial sectors.
- It's mission is to build EU, national and global frameworks through which this critical technology is delivered across sectors, as the key opinion leader for Europe's biotechnology industrial ecosystem.

EuropaBio goals

- Biotechnology for Europe: To achieve the legislative, regulatory and economic frameworks that empower biotechnology to deliver benefit to citizens, plus growth and resilience for Europe.
- Biotechnology in view: To create visibility and recognition for the contribution of biotechnology and biomanufacturing within Europe's societal, environmental and economic ambitions.
- Biotechnology in action: To deliver intellectual property, skills, capacity and investment from Europe's innovation excellence.

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