CEC06: Toxicity assessment in drug development

Chairs:

Stine Bartelt, Måløv, Denmark | N. N.

Presentations:

Challenging early target safety assessment strategies
Jens Schuemann, Novartis Institutes for BioMedical Research, Basel, Switzerland

Phototoxicity of small molecules -from initial assessment to in vivo studies
Allan Dahl Rasmussen, Lundbeck A/S, Valby, Denmark

Effects of an FGF21 analogue on the female reproductive system
Sophia GryMoesgaard, Novo Nordisk A/S, Måløv, Denmark

Reproductive Toxicology: impact on clinical trials/label
Michele Bouisset-Leonard, Novartis A/S, Basel, Switzerland

PEGylated coagulation factor IX: The road to regulatory approval
Hanne Offenberg, Novo Nordisk A/S, Måløv, Denmark

Abstract:

The CEC aim to share and discuss different challenges; such as early target safety assessment, study designs (including reproductive organ assessment), non-clinical findings, regulatory feedback, clinical trial implications, experienced by the industry with different compounds. This advanced level CEC presuppose that participants are familiar with the regulatory requirement for nonclinical toxicity assessment of a compound in drug development and willingness of active participation in group discussions. The setup will be as follows: A case will be presented and the course participants will be in groups discussing the issue and how to progress in such a situation. Following the discussion the presentor will reveal how the company managed this challenge. The first 2 sessions will focus on early target safety assesment and phototoxicity. The follwoiing 2 cases focus on effects of reproductive organs. Reproductive toxicology testing involves investigation of all stages of the male and female reproductive cycle and development. It occurs in parallel with the clinical development of a drug and could impact the design of the clinical trials (exclusion criteria, contraception measures...) and later on the label. This case study will provide an opportunity to better understand how unexpected challenges in reproductive toxicology could impact clinical trials and/or labeling. The last case is about learnings from the recent regulatory submission of Refixia® or N9-GP, a 40 kDa glycopegylated (PEG) recombinant coagulation factor IX intended for prophylaxis, on-demand treatment of bleeding and surgical procedures in haemophilia B of all ages. Toxicity studies of limited duration were initially performed in cynomolgus monkeys, however the monkeys developed neutralising cross reacting antibodies that affected exposure and resulted in acquired haemophilia. Regulators expressed concern related to the long term effects of PEGylation and potential adverse effects related to this. The session will focus on discussion of options to investigate long term effects of N9-GP and support the approval in all indications. We look forward to great scientific discussions, see you!