

Pre-clinical Toxicology Summary of Ilizomab

Introduction

This summary provides an overview of the preclinical toxicology evaluation of Ilizomab, a monoclonal antibody targeting [specific immune pathway], conducted in rodent and non-human primate models to assess its safety, pharmacokinetics, and potential toxicity profile.

Study Design

- **Species:** Rats and Cynomolgus monkeys
- **Duration:** 28-day and 90-day repeat-dose studies
- **Doses:** Low (1 mg/kg), Medium (5 mg/kg), High (15 mg/kg)
- **Endpoints Assessed:**
 - Clinical observations (body weight, food consumption, clinical signs)
 - Hematology, serum chemistry, and cytokine profiling
 - Organ pathology (gross and histopathology)

Key Findings

- **General Tolerability:**
 - Ilizomab was well tolerated at doses up to **15 mg/kg** in both species
 - No treatment-related mortality observed
- **Hematological Effects:**
 - Mild, dose-dependent decreases in lymphocyte counts at high doses, reversible after treatment cessation
- **Liver and Renal Toxicity:**
 - No significant liver enzyme elevations or renal dysfunction markers detected
- **Cytokine Modulation:**
 - Dose-dependent reduction in inflammatory cytokines (IL-6, TNF- α), consistent with proposed mechanism of action
- **Immunogenicity:**

- Low anti-drug antibody formation in non-human primates
- **Observed Side Effects:**
 - Mild to moderate **fatigue** was noted in some animals, resolving post-dosing
 - **Nausea** observed at higher doses but did not impact overall health outcomes
 - **Syncopalike episodes** recorded in isolated cases at **15 mg/kg**, transient and not dose-limiting

Conclusion

Ilizomab demonstrated a favorable safety profile in preclinical models, with no dose-limiting toxicities identified. Mild fatigue, nausea, and rare instances of syncope were observed but were not associated with long-term adverse effects. The findings support further clinical development in SLE patients, with careful monitoring of hematological parameters and potential side effects during clinical trials.