Hyper-sialylated IgG M254, an Innovative Therapeutic Candidate, Evaluated in Healthy Volunteers and Patients With Immune Thrombocytopenia Purpura: Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics

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BACKGROUND
Intravenous immunoglobulin (IVIg), a therapeutic blood product prepared from pooled plasma of 5000–50000 healthy donors, is the treatment of choice for several autoimmune disorders and inflammatory diseases. Although clinically useful, IVIg has several limitations including infusion-related adverse events and a prolonged infusion time (1–4 h) that results in significant patient discomfort. Hyper-sialylated IgG M254, a novel hyper-sialylated immunoglobulin G (IgG) investigational product derived from commercially available IVIg, is hypothesized to have greater potency than IVIg. Figure 1: M254 was designed based on scientific evidence demonstrating the importance of glycosylation on immunoglobulin function, especially the anti-inflammatory activity of IVIg, which has been shown to be dependent on Fc receptor. Preclinical data suggest that M254 has up to 10-fold enhancement of activity in vivo in several disease models. Therefore, the present 4-part first-in-human study is being conducted first in healthy volunteers and then in patients with ITP to evaluate the safety, tolerability, PK, and PD and platelet-response evaluation allows a model-based, informed dose selection for Part C. The present 4-part first-in-human study is being conducted first in healthy volunteers and then in patients with ITP to evaluate the safety, tolerability, PK, and PD and platelet-response evaluation allows a model-based, informed dose selection for Part C.

STUDY OBJECTIVE AND ENDPOINTS
A single ascending dose in healthy volunteers (N=25)
• Key inclusion criteria
  • Age at least 18 years or ≥ 16 years for young volunteers
  • willingness to give signed informed consent

• Key exclusion criteria
  • history of any drug allergy,
  • Diagnostic criteria consistent with ITP: microscopic or macroscopic blood
  • splenectomy) for ≥3 months
  • moderate or severe liver disease

• The majority of the treatment-emergent adverse events were mild, transient, and resolved spontaneously within 4 days.
• One subject in the 250 mg/kg M254 group had a transient moderate infusion reaction.

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• Safety
  • There were no severe or serious adverse events or deaths.
  • No subjects were withdrawn and none of the subjects dropped out during the course of the study.

• Pharmacokinetics
  • Upon single dosing with M254, the total IgG serum concentrations increased in the single dose groups and then in patients with ITP to evaluate the safety, tolerability, PK, and PD and platelet-response evaluation allows a model-based, informed dose selection for Part C.

• Summary of Related Treatment-Emergent Adverse Events by Preferred Terms

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• SUMMARY

IVIg is a novel hyper-sialylated IgG therapeutic candidate derived from commercially available IVIg, with potentially greater potency when compared with IVIg on an mg/kg basis. The present 4-part first-in-human study is being conducted first in healthy volunteers and then in patients with ITP to evaluate the safety, tolerability, PK and PD and platelet-response evaluation allows a model-based, informed dose selection for Part C. The present 4-part first-in-human study is being conducted first in healthy volunteers and then in patients with ITP to evaluate the safety, tolerability, PK and PD and platelet-response evaluation allows a model-based, informed dose selection for Part C. The present 4-part first-in-human study is being conducted first in healthy volunteers and then in patients with ITP to evaluate the safety, tolerability, PK and PD and platelet-response evaluation allows a model-based, informed dose selection for Part C. The present 4-part first-in-human study is being conducted first in healthy volunteers and then in patients with ITP to evaluate the safety, tolerability, PK and PD and platelet-response evaluation allows a model-based, informed dose selection for Part C.

• REFERENCES

1. van Iersel [Thijs] van Iersel, MD; Washburn N, Bronsema K, et al. LC-MS/MS quantification of M254, a hyper-sialylated anti-inflammatory agonist AND have albumin ≤35 g/L

2. van Iersel [Thijs] van Iersel, MD; Washburn N, Bronsema K, et al. LC-MS/MS quantification of M254, a hyper-sialylated anti-inflammatory agonist AND have albumin ≤35 g/L

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The study is currently ongoing in healthy volunteers with ITP in Part B.

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