RVT-1401, A Novel Anti-FcRn Monoclonal Antibody, Is Well Tolerated in Healthy Subjects and Reduces Plasma IgG Following Subcutaneous or Intravenous Administration
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Objective:
To characterize safety, pharmacokinetics, and pharmacodynamics of single and repeat doses of RVT-1401 administered via subcutaneous (SC) injection and intravenous (IV) infusion to healthy subjects.

Background:
Myasthenia Gravis (MG) is a chronic autoimmune neuromuscular disease thought to be directly caused by pathogenic IgG. RVT-1401 is a fully human monoclonal antibody being developed for the treatment of MG and other autoimmune disorders. RVT-1401 inhibits the binding of IgG to FcRn, resulting in rapid catabolism of IgG via lysosomal degradation.

Design/Methods: Healthy subjects were enrolled in randomized single and multiple ascending dose (SAD/MAD, respectively) cohorts. Initial cohorts received open-label single 0.1 mg/kg IV (n=4) or 0.5 mg/kg SC (n=3) doses. Subsequent cohorts were randomized to receive single SC or IV doses of RVT-1401 or placebo (6:2) ranging from 100 to 765 mg. Subjects in MAD cohorts received four weekly SC doses of RVT-1401 (340 mg or 680 mg) or placebo (8:2).

Results: Total IgG reduction increased with increasing doses, with a nadir at approximately 8-10 days after a single dose. An average reduction in total IgG of 47% was observed following single SC dose of 765 mg. Weekly SC injections of RVT-1401 further reduced total IgG over single dose administration, resulting in maximum reduction >75%. RVT-1401 exhibited non-linear pharmacokinetics across the dose range studied. Following SC administration of doses more than 200 mg, maximum serum concentrations were achieved within 1.5 to 4 days of administration. All adverse events (AEs) were mild to moderate in severity, with no subjects requiring premature discontinuation due to AEs.

Conclusions: RVT-1401 was well tolerated following both single and multiple doses in healthy subjects. RVT-1401 rapidly reduced total IgG and is the first anti-FcRn to demonstrate a sustained IgG reduction using only SC injection. These data demonstrate the potential of RVT-1401 to treat MG and other autoimmune diseases.