



Targeting the Neonatal Fc Receptor for the Treatment of Moderate-to-Severe Active Graves' Ophthalmopathy

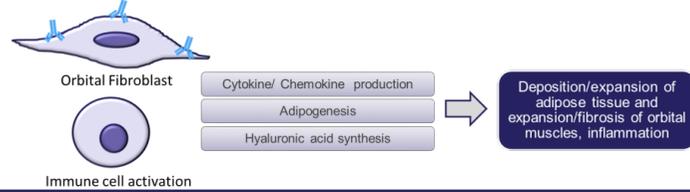
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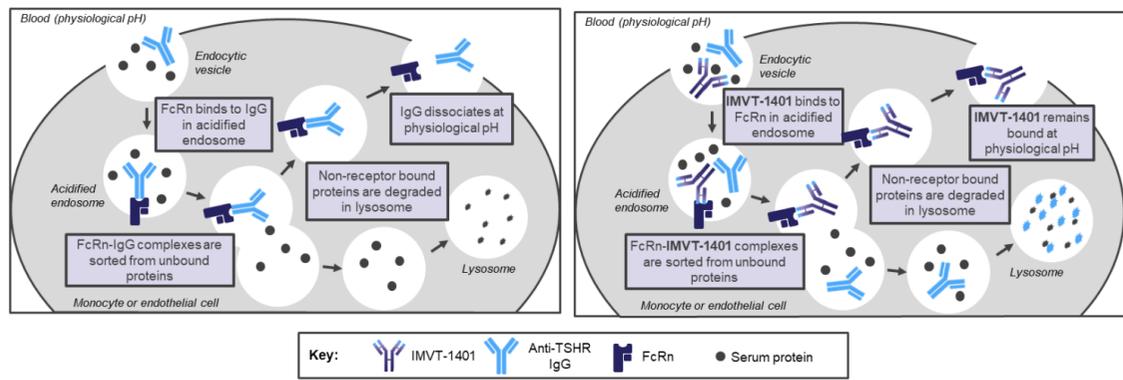
Introduction

- Graves' Ophthalmopathy (GO), or thyroid eye disease, is an autoimmune disease mediated by pathogenic IgG (pIgG) that targets the thyroid-stimulating hormone receptor (TSHR) and triggers adipogenesis and hyaluronic acid production in orbital fibroblasts resulting in tissue expansion and inflammation in the extra-ocular space
- Anti-TSHR antibody serum levels have been shown to be directly associated with GO clinical features with high anti-TSHR titers associated with a greater risk of severe disease course and poor outcome

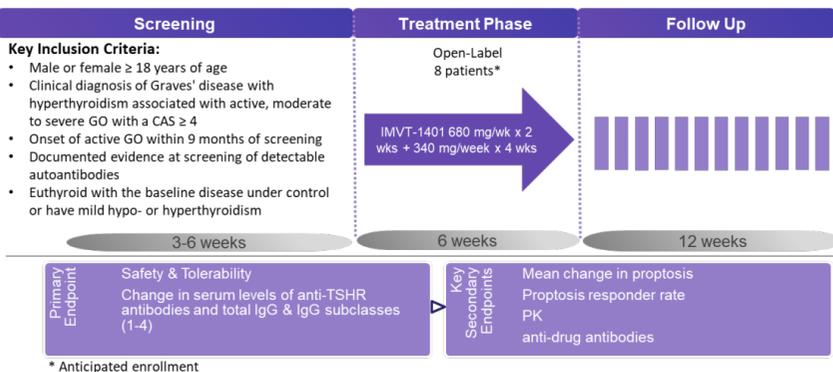


IMVT-1401: Description & Mechanism of Action

- IMVT-1401 (previously described as RVT-1401), a fully human monoclonal antibody, enables the rapid catabolism of IgG by inhibiting its binding to FcRn
- IMVT-1401 is being developed as a subcutaneous injection for the treatment of GO and other autoimmune disorders



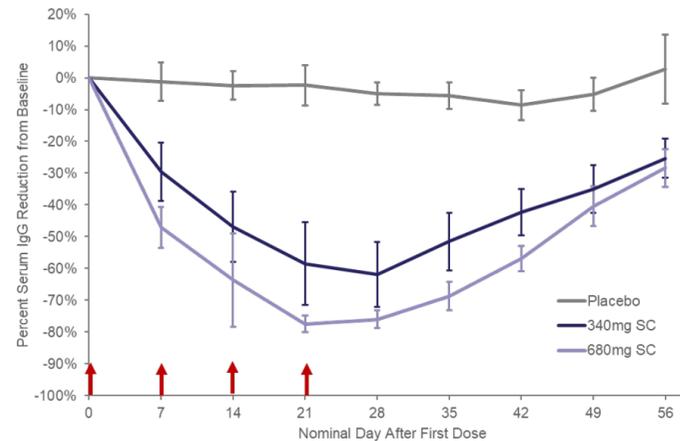
Trial Design of ASCEND-GO 1, a Phase 2a study in Graves' Ophthalmopathy



Study RVT-1401-1002, is a multicenter, open-label trial evaluating an induction dosing regimen followed by a maintenance regimen of subcutaneously injected IMVT-1401.

ClinicalTrials.gov Identifier: NCT03922321

Rapid and Sustained IgG Reduction in Healthy Volunteers Following Subcutaneous IMVT-1401 Treatment

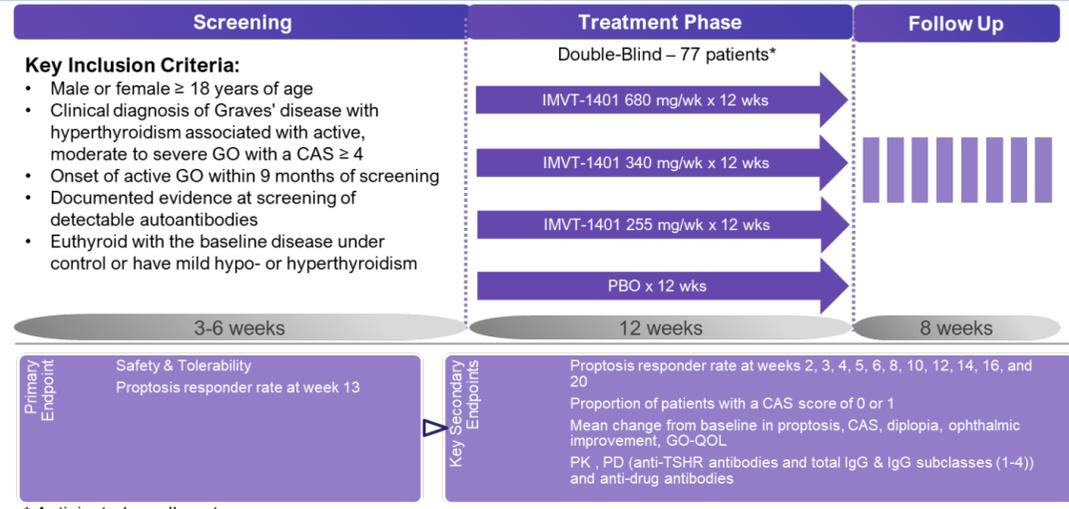


In the multiple ascending dose portion of the RVT-1401-1001 healthy volunteer study, subcutaneous injection with IMVT-1401 led to a dose-dependent reduction in IgG of up to 78%

The nadir IgG reduction in the 680 mg cohort was observed prior to the 4th dose suggesting the maximum reduction had been achieved after 3 doses

Five weeks after the last dose, mean IgG concentration had increased to within 30% of the baseline value

Trial Design of ASCEND-GO 2, a Phase 2b Study in Graves' Ophthalmopathy



Study RVT-1401-2001, is a multicenter, double-blind, placebo-controlled trial evaluating 3 active doses of subcutaneously injected IMVT-1401. ClinicalTrials.gov Identifier: NCT03938545

Conclusion

- IMVT-1401 is a novel, fully human monoclonal inhibitor of FcRn
- IMVT-1401 rapidly reduced total IgG following the first subcutaneous (SC) injection and demonstrated sustained IgG reduction in healthy volunteers
- IMVT-1401 is the first anti-FcRn antibody to be investigated in patients with Graves' Ophthalmopathy
- By reducing the level of autoantibodies, IMVT-1401 is hypothesized to be an effective treatment for patients with GO using a convenient SC injection for dose administration
- Results from these studies will be used to demonstrate proof of concept for IMVT-1401 in GO and determine the optimal dosing regimen to be used in Phase 3

Disclosures & References

Kahaly GJ, Wüster C, Olivo PD, Diana T. High Titers of Thyrotropin Receptor Antibodies Are Associated With Orbitopathy in Patients With Graves Disease. J Clin Endocrinol Metab. 2019 Jul 1;104(7):2561-2568.
 Kotwal A1, Stan M. Thyrotropin Receptor Antibodies-An Overview. Ophthalmic Plast Reconstr Surg. 2018 Jul/Aug;34(4S Suppl 1):S20-S27.
 Bartalena L1, Baldeschi L2, Boboridis K3, Eckstein A4, Kahaly GJ5, Marcocci C6, Perros P7, Salvi M8, Wiersinga WM9; European Group on Graves' Orbitopathy (EUGOGO). The 2016 European Thyroid Association/European Group on Graves' Orbitopathy Guidelines for the Management of Graves' Orbitopathy. Eur Thyroid J. 2016 Mar;5(1):9-26.
 RF, JC, and CC have equity interest in Immunovant Sciences Ltd, Inc, are employees of and receive personal compensation from Immunovant, Inc (or were at the time of abstract submission).