Preclinical characterization of IMG-007, a high-affinity, non-depleting anti-OX40 monoclonal antibody for the treatment of inflammatory and autoimmune disease

#1036

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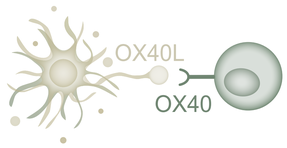
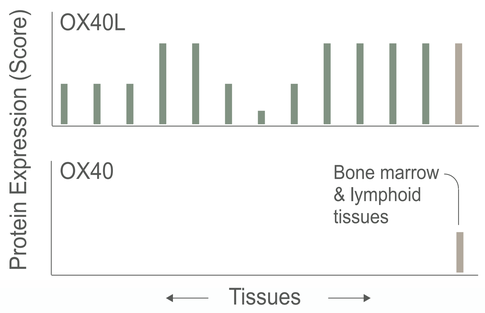
BACKGROUND

IMG-007 is an Fc-silenced (N297A) IgG1 antibody targeting OX40, designed to block OX40-OX40L costimulation while avoiding FcγR-mediated depletion. This enables upstream inhibition of T cell activation across multiple pathogenic pathways, limiting clonal expansion of effector and memory T cells while preserving T cell diversity, which may support a more favorable safety profile compared to Fc-competent, depleting anti-OX40 antibodies (1-3).

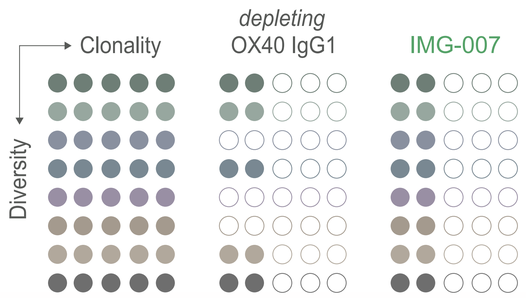


Targeting OX40, expressed on activated T cells, may provide a more specific approach than targeting the more broadly expressed OX40L, enabling modulation of T cell responses while avoiding broader immune suppression and potential sink effects associated with OX40L blockade.

Receptor targeting improves specificity*

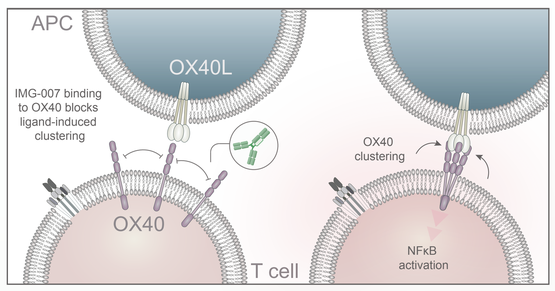


Non-depleting design preserves diversity

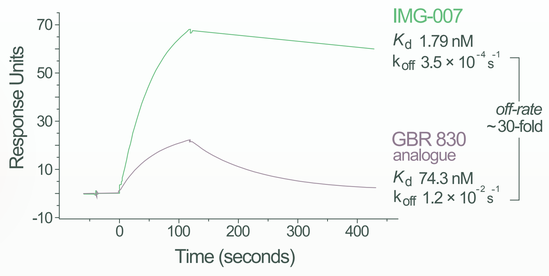


(*) Protein expression scores derived from Human Protein Atlas tissue microarray datasets across normal and cancer tissues. Expression scores reflect estimated semi-quantitative protein expression.

RESULTS

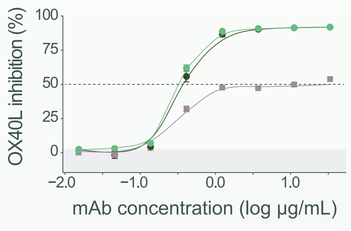


IMG-007 demonstrates ~40-fold higher affinity for OX40 vs comparator IgG1

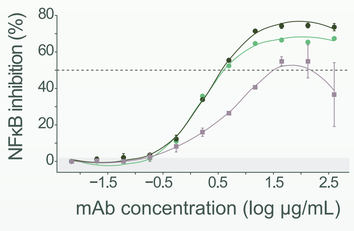


● IMG-007 ● Rocatinlimab analogue ■ GBR 830 analogue □ Background

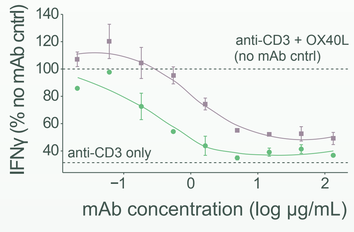
Inhibition of OX40-OX40L interaction (ELISA)



Inhibition of NFkB activation (reporter assay)



Inhibition of T cell-mediated IFNγ production



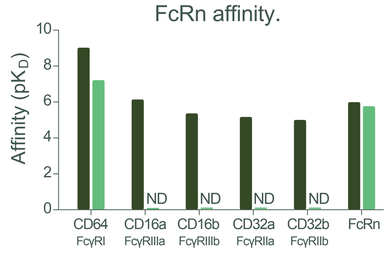
IMG-007 shows rocatinlimab-level OX40L inhibition without Fc-mediated effector function

Upper left: Schematic illustrating IMG-007 binding to OX40 and its proposed inhibition of ligand-induced receptor clustering and downstream NFκB signaling. **Upper right:** Representative SPR sensorgrams showing binding of IMG-007 and comparator IgG1 (GBR 830 analogue) to OX40 at a fixed concentration (100 nM) with antibody at 1 µg/mL. Kinetic parameters were derived from global fitting across a concentration series. **Lower left:** Inhibition of OX40–OX40L interaction in a plate-based assay using plate-bound OX40 and soluble OX40L. **Lower middle:** Inhibition of NFκB activation in OX40-transduced HEK293T cells. **Lower right:** Suppression of primary T cell–mediated IFNγ production following anti-CD3/OX40L stimulation.

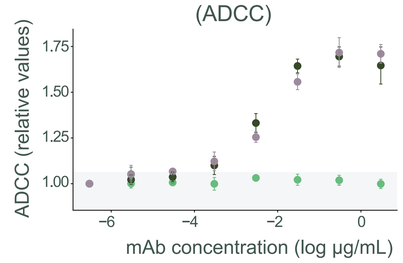
RESULTS

● IMG-007 ● IMG-007 Fc WT ■ GBR 830 analogue □ Background

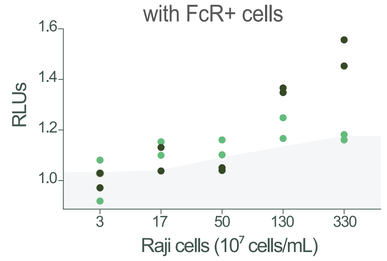
Minimal FcγR binding with preserved FcRn affinity.

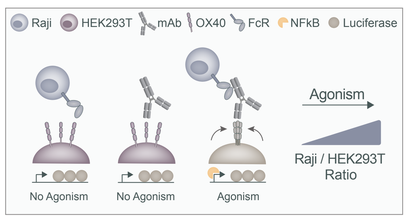


No NK cell-mediated cytotoxicity (ADCC)



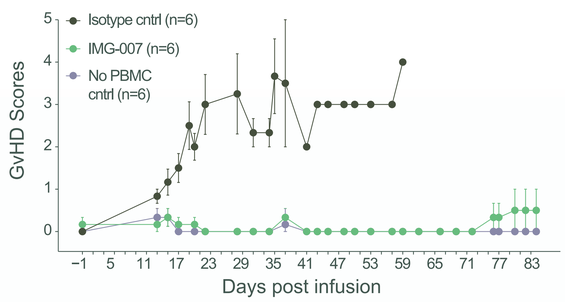
Minimal agonistic activity in culture with FcR+ cells



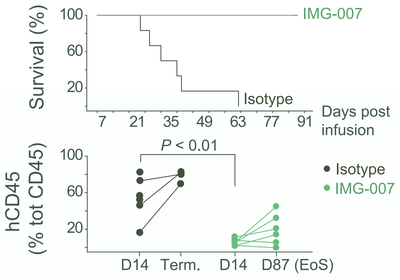


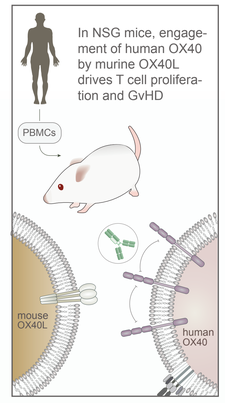
Fc silencing prevents depletion and limits agonism Binding of IMG-007 to FcRs was assessed by SPR, showing low or no binding to FcγRs while preserving FcRn affinity, consistent with maintained recycling and half-life. In functional assays, IMG-007 did not elicit ADCC in cultures of primary NK cells with OX40+ target cells. Agonistic activity was evaluated in co-cultures of FcγR+ Raji cells with OX40+ NFκB reporter cells, where IMG-007 showed minimal activity.

GvHD clinical score



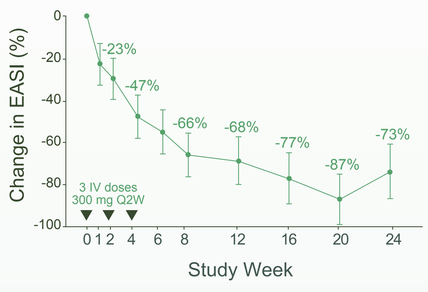
T cells expansion & survival

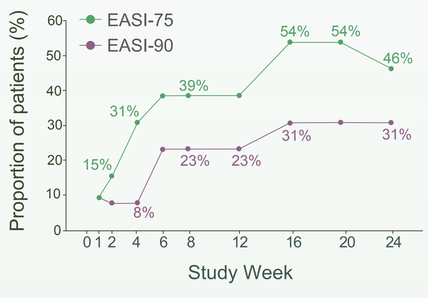




OX40 blockade reduces T cell expansion and GvHD. In a xGvHD model engrafted with hPBMCs, weekly IMG-007 injections prevented disease progression and expansion of donor CD45+ cells. This model is relevant for human OX40 biology, as murine OX40L engages OX40 on donor T cells, providing proof of inhibition of OX40-driven T cell responses in vivo.

CLINICAL





Phase 1b/2a proof-of-concept study in moderate-to-severe atopic dermatitis. Patients treated with three Q2W doses of IMG-007 achieved an 87% mean reduction in EASI at week 20; most reached ≥75% improvement, and nearly one-third achieved ≥90% by week 16. IMG-007 has demonstrated a consistent safety profile across all four studies conducted to date.

SUMMARY

- ✓ IMG-007 is a novel OX40-targeting antibody combining potent pathway inhibition with an Fc-silenced backbone
- ✓ Aglycosylation (N297A) confers silenced ADCC function and dominant antagonistic activity
- ✓ Preclinical studies demonstrated blockade of OX40L-mediated NF κB activation, cytokine production, and T cell proliferation
- ✓ The Fc-silenced design may support higher dosing and potentially a more favorable safety profile

Contact us about participating in our AD and AA trials.
← Scan to connect.

References: (1) Croft et al., Am J Clin Dermatol. (2024) OX40 in the pathogenesis of atopic dermatitis - a new therapeutic target; (2) Guttman-Yassky et al., Br J Dermatol. (2024) The role of OX40 ligand/OX40 axis signalling in atopic dermatitis; (3) Wang et al., Protein Cell (2018) IgG Fc engineering to modulate antibody effector functions **Disclosures** Jonatan Tuncel, Kurinji Pandiyan, Ben Porter-Brown, and Kristin Yarema are employees of ImageneBio and may hold equity interests. Chongtian Guo is an employee of Miragene, may hold equity interests, and is a former employee of the private company Inmagene, which conducted several of the studies presented. No other relevant financial relationships to disclose.

Presented at Society for Investigative Dermatology (SID) Annual Meeting: May 13-16, 2026; Chicago, IL, USA.