**Introduction/Background:** Inflammatory T cell response is promoted by OX40, whose expression is increased in atopic dermatitis (AD). Targeting OX40 is a rational therapeutic strategy in treating AD. We hypothesized that an anti-OX40 monoclonal antibody (mAb) with a silenced antibody-dependent cell-mediated cytotoxicity (ADCC) function would have minimal antibody-dependent cell toxicities, thereby minimizing safety risks. IMG-007 is a novel nondepleting anti-OX40 mAb, bioengineered in its Fc region with a N297A mutation to abolish the ADCC function.

**Objectives:** To characterize the effects of a N297A mutation on the pharmacodynamic effect of IMG-007 in non-clinical studies.

**Methods:** The kinetics of IMG-007's binding to recombinant human Fcγ receptors was measured using surface plasmon resonance (SPR) Biacore 8K. The ADCC function was evaluated by measuring cytotoxicity to HEK293-OX40-Luc cells cocultured with primary human NK cells and antibody and quantified by flow cytometry. The cytokine release potential was assessed by incubating human peripheral blood mononuclear cells (PBMCs) with antibody under both solid and solution phases from 10 donors, followed with measurement of 10 cytokines in the culture supernatant using the Meso Scale Discovery (MSD) Proinflammatory Panel 1.

**Results:** IMG-007 exhibited a minimal binding affinity to Fcγ receptors, including FcγRs I, IIA, IIA (V176), IIB (F176), IIB and IIIB. At up to the highest concentration tested, IMG-007 did not induce any antibody induced cytotoxicity to the OX40+ HEK293-Luc cells. Furthermore, it did not induce the release of all 10 proinflammatory cytokines tested in human PBMCs under both solid and solution testing formats.

**Conclusions:** Silencing ADCC function in IMG-007 via bioengineering resulted in minimal binding to the Fcγ receptors and diminished cytotoxicity to OX40+ cells. IMG-007 represents a promising drug candidate for potentially treating AD.

**Keywords:** OX40, antibody, ADCC, cytokine release, cytotoxicity

**Disclosures:**
Chongtian Guo, Xiaotong Wu, Zi Lin, Yufang Lu - Inmagene Biopharmaceuticals - Employee - may hold stock options in the company