IMG-007, a non-depleting anti-OX40 monoclonal antibody, reduced skin lesion severity and serum inflammatory markers in adults with moderate-to-severe atopic dermatitis in a Phase 1b/2a study

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Introduction

- Anti-OX40/OX40L monoclonal antibodies (mAbs) have emerged as a promising class for the potential treatment of a spectrum of inflammatory and autoimmune diseases, including atopic dermatitis (AD).
- IMG-007 is a novel anti-OX40 mAb that blocks the OX40-OX40L signaling without depleting T cells due to silencing of antibody-dependent cellular cytotoxicity (ADCC) function.
- In Phase 1 single-dose studies in healthy adults, IMG-007 was well-tolerated, without any reported pyrexia or chills.
- IMG-007 also exhibited an extended half-life of 34.7 days at an anticipated therapeutic dose level, which would potentially enable less frequent dosing (e.g., once every 12 weeks, Q12W) for the treatment of AD.

Conclusion

- Treatment with IMG-007 for 4 weeks showed a rapid onset and durable clinical activity in adults with moderate-to-severe AD.
- IMG-007 has demonstrated marked and durable inhibition of serum Th1/2/17 biomarkers in adults with moderate-to-severe AD
- IMG-007 was safe and well tolerated without any reports of pyrexia or chills.
- The favorable tolerability profile coupled with an extended half-life would allow dose optimization including exploration of patient friendly extended dose intervals.
- IMG-007 represents a potentially differentiated OX40 antagonist for the treatment of AD.

Methods

Study Design

- This was a phase 1b/2a, open-label, single arm, multicenter study enrolling adult patients with moderate-to-severe AD, measured by eczema area and severity index (EASI) ≥16, investigator global assessment (IGA) ≥ 3, and body surface area (BSA) ≥10% at baseline.
- Eligible participants received up to three intravenous infusions of 300 mg IMG-007 over 4 weeks (Baseline, Week 2 and 4) and followed up for up to 24 weeks.
- Safety was assessed by the incidence of treatment-emergent adverse events; clinical activity was measured by the percentage change from baseline in the EASI and objective SCORing Atopic Dermatitis (O-SCORAD) scores.
- Serum samples were collected at baseline and post-treatment visits. Serun levels of Th1, Th2 and Th17 proteins were measured by Olink® Target 48 cytokine and Quantikine® ELISA kit.

Results

Baseline Demographics and Disease Characteristics

- A total of 13 patients were enrolled from 6 centers in the US and Canada. Baseline characteristics included a mean (standard deviation [SD]) age of 49.8 years (15.0) with 69.2% males, mean EASI of 29.5 (13.7), mean BSA of 52.0 (25.5), 61.5% patients had IGA=3 vs 38.5% with IGA=4.

Clinical Activity Results

- Treatment with IMG-007 resulted in a rapid and durable reduction in EASI (Figure 1) and SCORAD (Figure 2).
- EASI-75 response (≥ 75% reduction from baseline in EASI) was achieved by 54%, 54% and 46% of participants at week 16, 20 and 24, respectively (Figure 3).
- EASI-90 response (≥ 90% reduction in EASI) was achieved by 31% of participants at week 16, 20 and 24, respectively (Figure 3).
- Serum levels of Th1, Th2 and Th17 proteins at baseline were elevated, which were reduced to a range for healthy subjects at week 16 and 24 after IMG-007 treatment for four weeks (Figures 4,5).

Figure 1. Percent change from baseline in EASI score

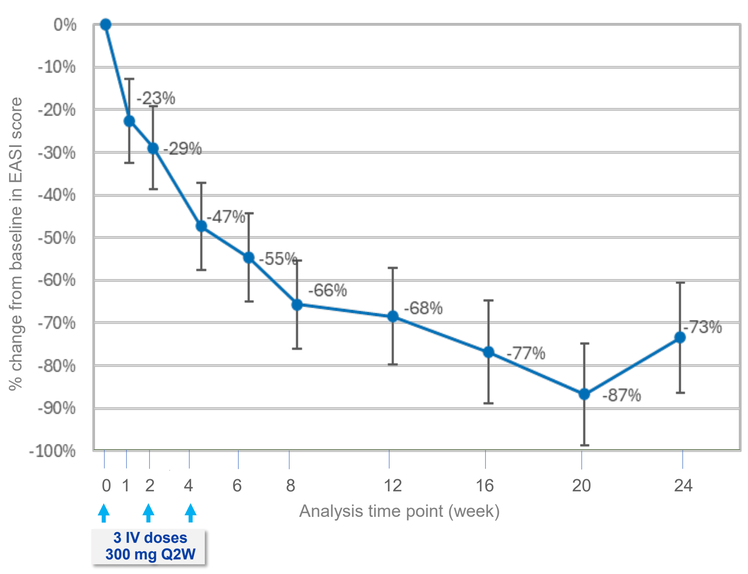


Figure 2. Percent (%) change from baseline in O-SCORAD score

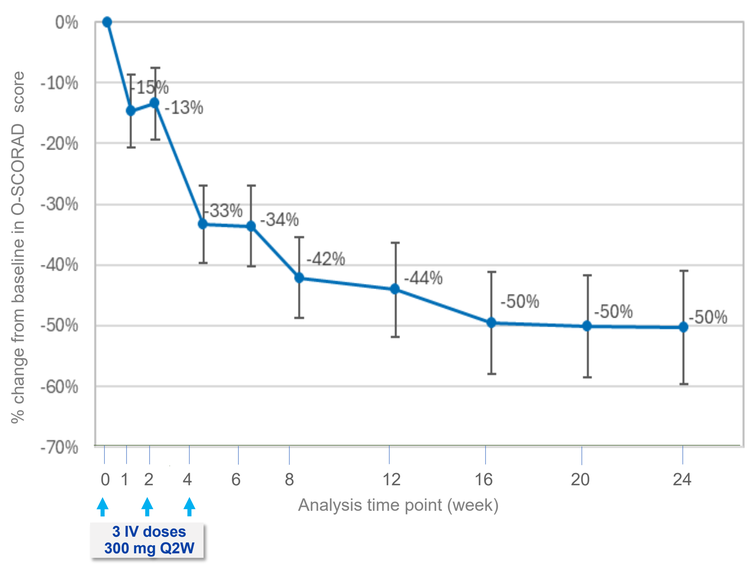
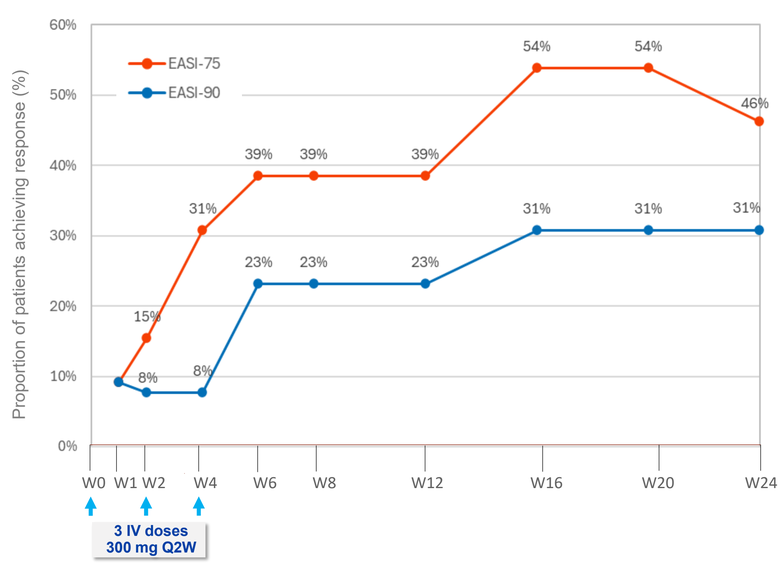
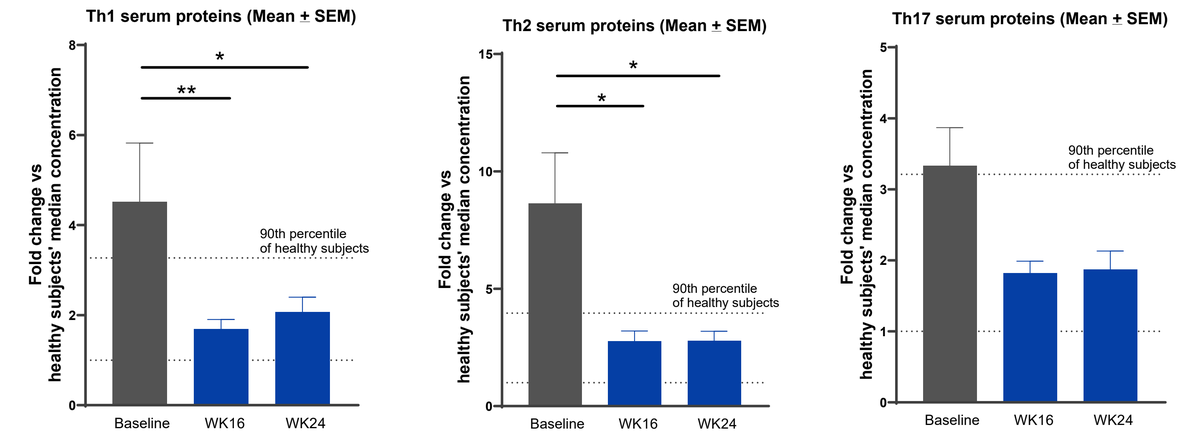


Figure 3. Proportion of patients achieving EASI-75 and EASI-90 response



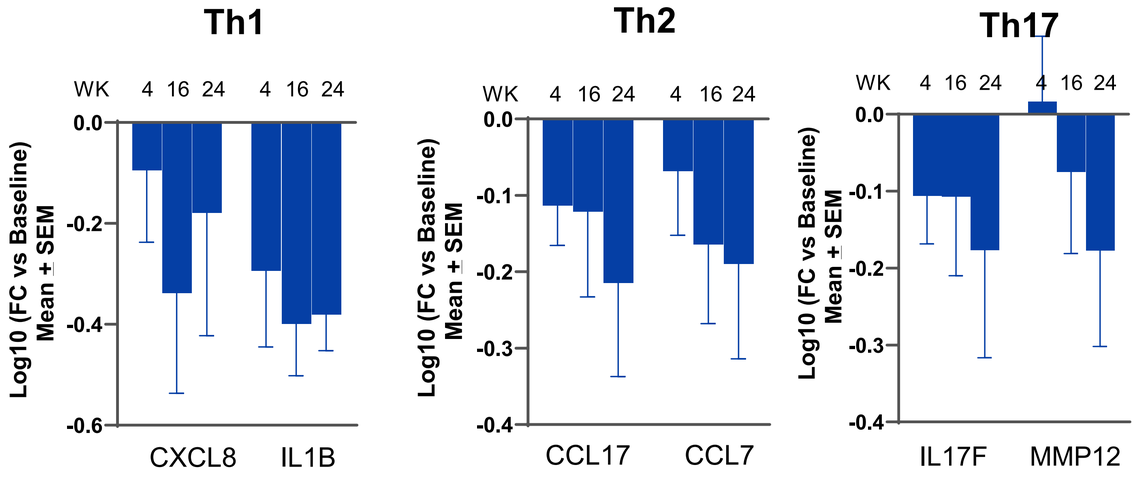
Full analysis set included all enrolled patients who received at least one dose of study treatment. N=13
For the percentage change from baseline in EASI and O-SCORAD scores, a mixed model repeated measure (MMRM) analysis was performed to compare the effect of IMG-007 at post baseline visits versus the baseline. Data after rescue therapy was set to missing
For binary endpoints, patients who received rescue therapies were counted as "non-responders". Last observation carried forward (LOCF) imputation was used for missing data, except for missing data that arises following study discontinuation with reason 'lack of efficacy' (none in the study). EASI-75: proportion of patients achieving ≥ 75% reduction from baseline in EASI, EASI-90: proportion of patients achieving ≥ 90% reduction from baseline in EASI

Figure 4. Fold change vs. healthy subjects' levels of Th1/2/17 serum markers at baseline, Week 16 and Week 24 post treatment of IMG-007



* p<0.05 for difference versus baseline, ** p<0.01 for difference versus baseline
N numbers at baseline, wk16, and 24 were 13, 6 and 6, respectively.
Post-systemic rescue treatment results were censored from the analysis.
Olink Target48 panel was used for detection of serum proteins including those related to signaling of Th1 (IL27, CXCL9, IL1B, IL18, CXCL10, IFNG, CCL3, CXCL8, CCL4, CXCL11), Th2 (CCL2, CCL8, IL4, CCL11, IL13, CCL13, CCL19,CCL7. CCL17 by ELISA) and Th17 (CXCL12, IL17F, MMP12, IL17C, IL17A, CSF2).
Classification of Th1/2/17 cytokines/chemokines was primarily based on Pavel A B, Guttman-Yassky E, Allergy 2021;76(1): 314-325
Median and 90th percentile levels of each protein in healthy subjects' serum were derived from validation data of Olink Target48 Cytokine panel and kit information of Human CCL17/TARC Quantikine ELISA.

Figure 5. Fold change vs. baseline of representative Th1/2/17 serum markers over time post treatment of IMG-007



FC: fold change, Log10 (FC vs Baseline): Log10 transform of fold change vs baseline
Ns at baseline, wk 1, 4, 16, and 24 were 13, 12, 11, 6 and 6, respectively
Post-systemic rescue treatment results were censored from the analysis
ELISA assay for CCL17 and OLINK T48 panels were used for quantification of serum protein levels
Classification of Th1/2/17 cytokines/chemokines was primarily based on Pavel A B, Guttman-Yassky E, Allergy 2021;76(1): 314-325

Safety Results

- There were no serious adverse events (SAEs), treatment-related AEs, or infusion-related reactions, such as pyrexia or chills.
- All AEs were mild or moderate, except in one participant who had erythrodermic AD at baseline and experienced a severe AD flare, which was deemed unrelated to treatment.

Disclosures:
1. Jonathan I. Silverberg is an adviser for ImageneBio, the study sponsor.
2. Yufang Lu is an employee of ImageneBio; Chongtian Guo and Yancong Shen were employees of ImageneBio when the study was conducted.
3. Aswin Nair was a statistical consultant for ImageneBio when the study was conducted.