Poster number 51194

Efficacy and Safety of MG-K10 in Adult Patients with Moderate-to-Severe Atopic Dermatitis: Results From The Phase 2 Study

Jinhua Xu[1], Litao Zhang[2], Yumei Li[3], Yunsheng Liang[4], Xiaoyan Chen[5], Yangfeng Ding[6], Yuling Shi[6], Jingyi Li[7], Aie Xu[8], Jinyan Wang[9], Heng Gu[10]

[1]Huashan Hospital Fudan University, Shanghai, China; [2]Tianjin Academy of Traditional Chinese Medicine Affiliated Hospital, Tianjing, China; [3]Affiliated Hospital of Jiangsu University, Zhenjiang, China; [4]Dermatology Hospital of Southern Medical University, Guangzhou, China; [5]Xianyang Hospital of Yan 'an University, Xianyang, China; [6]Shanghai skin disease Hospital, Shanghai, China; [7]West China Hospital, Sichuan University, Chengdu, China; [8]Hangzhou Third People's Hospital, Hangzhou, China; [9]NingBo No. Hospital, Ningbo, China; [10]Hospital for skin disease, Institute of Dermatology. Chinese Academy of Medical Sciences, Peking union medical college, Beijing, China;

Commercial support information
This study was supported and funded by Mabgeek Biotech.

Introduction, Objectives, Methods And Demographics

Introduction

- Atopic dermatitis (AD) is an inflammatory skin disease and characterized by overexpression of inflammatory Th2 cytokines, including IL-4 and IL-13.[1]
- MG-K10 is an innovative long-acting mAb that specifically binds to human IL-4Rα, and efficiently blocks the Th2 inflammatory signaling of IL-4 and IL-13. Following Fc mutation, MG-K10 allows long dosing interval owing to its extended half-life.
- Presented is the phase 2 clinical trial data of MG-K10 in moderate-to-severe AD with 16 weeks' treatment.

Objectives

To evaluate the preliminary efficacy, safety, PK,PD, and immunogenicity of multiple doses of MG-K10 in adult patients with moderate-to-severe AD.

Methods

This was a randomized, double-blind, placebo-controlled phase 2 study. Patients with moderate-to-severe AD were randomized 1:1:1:1 to subcutaneous dosing of MG-K10 150 mg every 4 weeks (Q4W) or 300 mg Q4W or 300 mg Q2W or placebo, all with two fold loading in first dose (Figure 1). Primary endpoints was EASI change from baseline at week 16. Other efficacy endpoints included EASI-75, EASI-90, IGA response(clear/almost clear [0/1] with ≥2-point improvement), pruritus NRS improvement, etc. Safety was assessed via AE and laboratory monitoring.

1. Han Y, Chen Y, Liu X, et al. Efficacy and safety of dupilumab for the treatment of adult atopic dermatitis: a meta-analysis of randomized clinical trials. J Allergy Clin Immunol, 2017, 140(3):888-891.

Demographics

- The 16-week primary efficacy endpoint analysis included 163 subjects in FAS.
- Baseline characteristics were as expected for patients with moderate-to-severe AD and were generally well balanced across groups (Table1).

Figure 1 Study Design

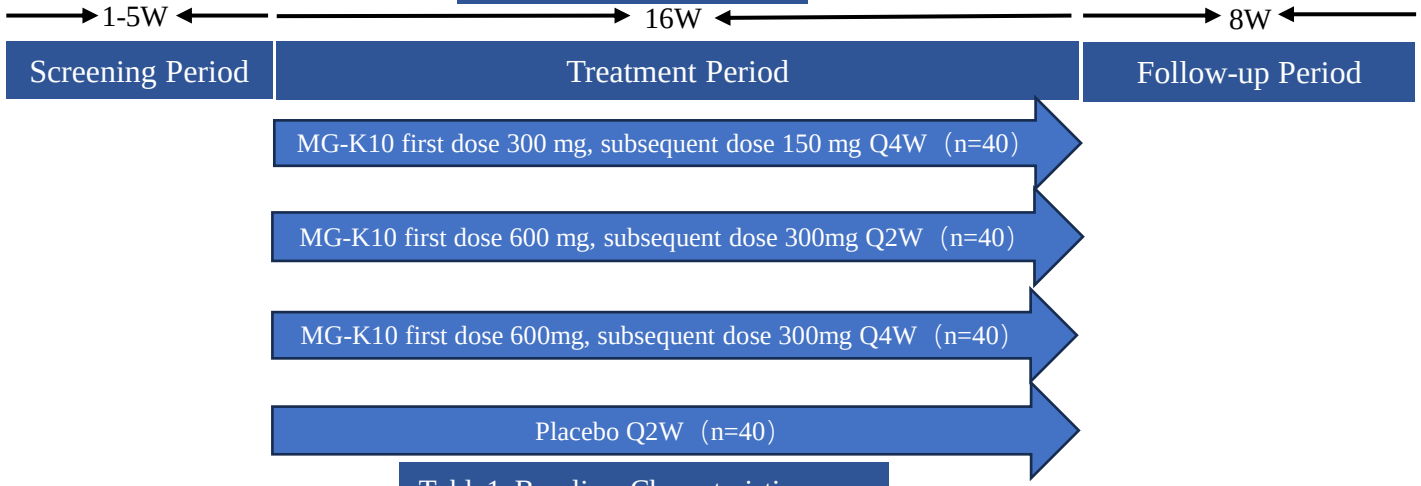


Table1 Baseline Characteristics

Characteristics	MG-K10 150mg Q4W (N=41)	MG-K10 300mg Q2W (N=41)	MG-K10 300mg Q4W (N=41)	Placebo (N=40)	Total (N=163)
Age--years*	45.8±17.26	47.4±16.27	42.2 ±15.97	44.9±15.37	45.1±16.19
Male (n/%)	28 (68.3)	34 (82.9)	26 (63.4)	22 (55.0)	110 (67.5)
Weight --kg*	69.5±14.95	70.4±11.88	68.6±±12.90	68.1±13.82	69.1±13.33
IGA Score of 3 (n/%)	26 (63.4)	27 (65.9)	26 (63.4)	26 (65.0)	105 (64.4)
IGA Score of 4 (n/%)	15 (36.6)	14 (34.1)	15 (36.6)	14 (35.0)	58 (35.6)
EASI Score*	24.3±9.59	24.2±7.98	24.0±8.78	22.8±7.67	23.8±8.49
BSA affected --%*	42.6±20.68	39.4±17.62	41.0±15.83	38.3±19.72	40.3±18.45
NRS Score*	6.5±2.12	6.8±2.20	6.6±1.95	6.0±1.63	6.5±2.00

*: Data are presented in Mean±SD

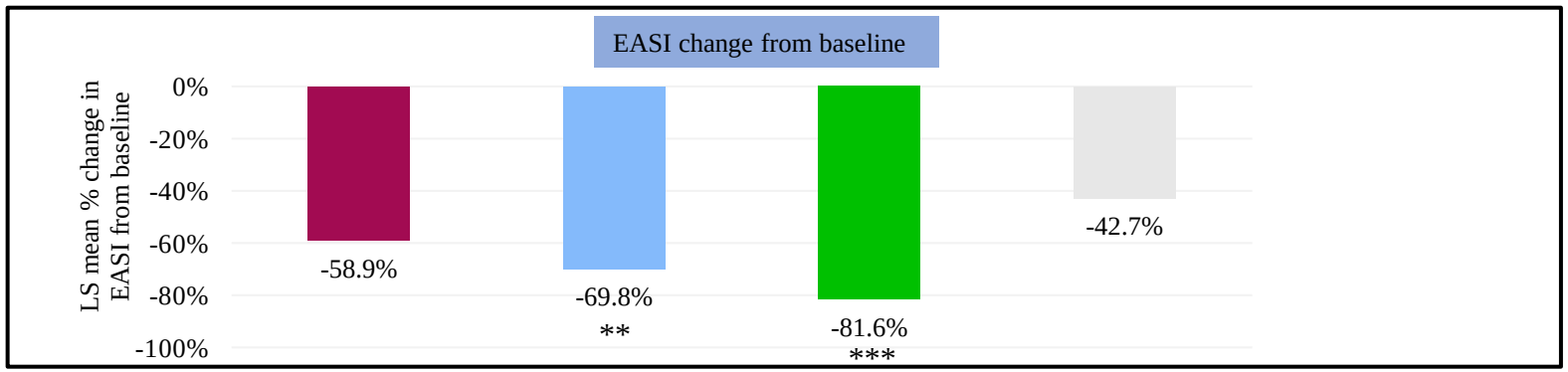
EASI: Eczema Area and Severity Index; IGA: Investigator's Global Assessment; BSA:Body Surface Area; NRS: Numerical Rating Scale; AE: Adverse Event; FAS: Full Analysis Set; PK: Pharmacokinetics; PD: Pharmacodynamics;

Results

Primary Endpoint

- At Week 16, patients receiving 150mg Q4W/300mg Q2W/300mg Q4W/placebo least squares mean percent change in EASI were -58.9%/-69.8%/ -81.6%/-42.7%, respectively (P=0.071/P=0.003/P<0.001 vs placebo) (Figure 2).

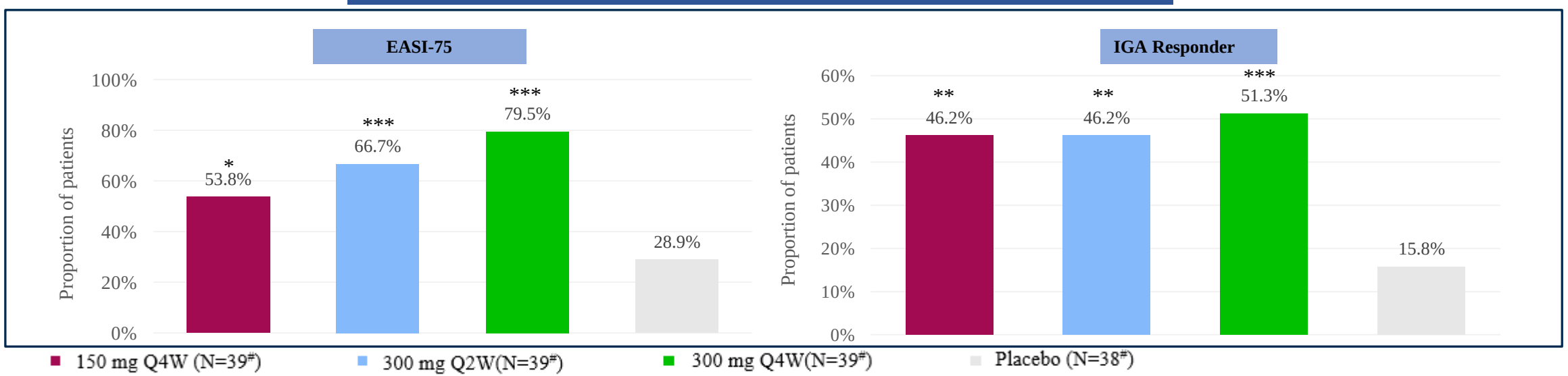
Figure 2 Least squares mean percentage change of EASI from baseline at week 16 [1]



Secondary Endpoint

- Compared with placebo, the proportion of patients who achieved EASI-75 and defined as IGA responder at week 16 was significantly higher across all MG-K10 treatment groups.

Figure 3 Proportions of patients who achieved EASI-75 (a) and IGA responder (b) at week 16



*P<0.05 vs Placebo， **P<0.01 vs Placebo， ***P<0.001 vs Placebo #Missing data was not imputed and was not included in the denominator when calculating proportions.

- [1]: ANCOVA analysis was performed with the primary efficacy endpoint of EASI score at baseline and group as factors, and adjusted for potential confounding variables such as IGA stratification at baseline.

Results (cont.)

- MG-K10 provided sustained and clinically meaningful improvements at both 300 mg Q2W and 300 mg Q4W in treating moderate-to-severe AD.
- Start from week 4, MG-K10 300 mg Q2W and 300 mg Q4W significantly improved NRS vs placebo.
- Improvements in all endpoints at week 16 were numerically greater with MG-K10 300 mg Q4W than 300 mg Q2W.

Figure 4 proportion of patients who achieved EASI-75 (a) and IGA responder (b) over time

Figure 5 LS mean percentage change in BSA (a) and weekly average of daily Peak Pruritus (b)

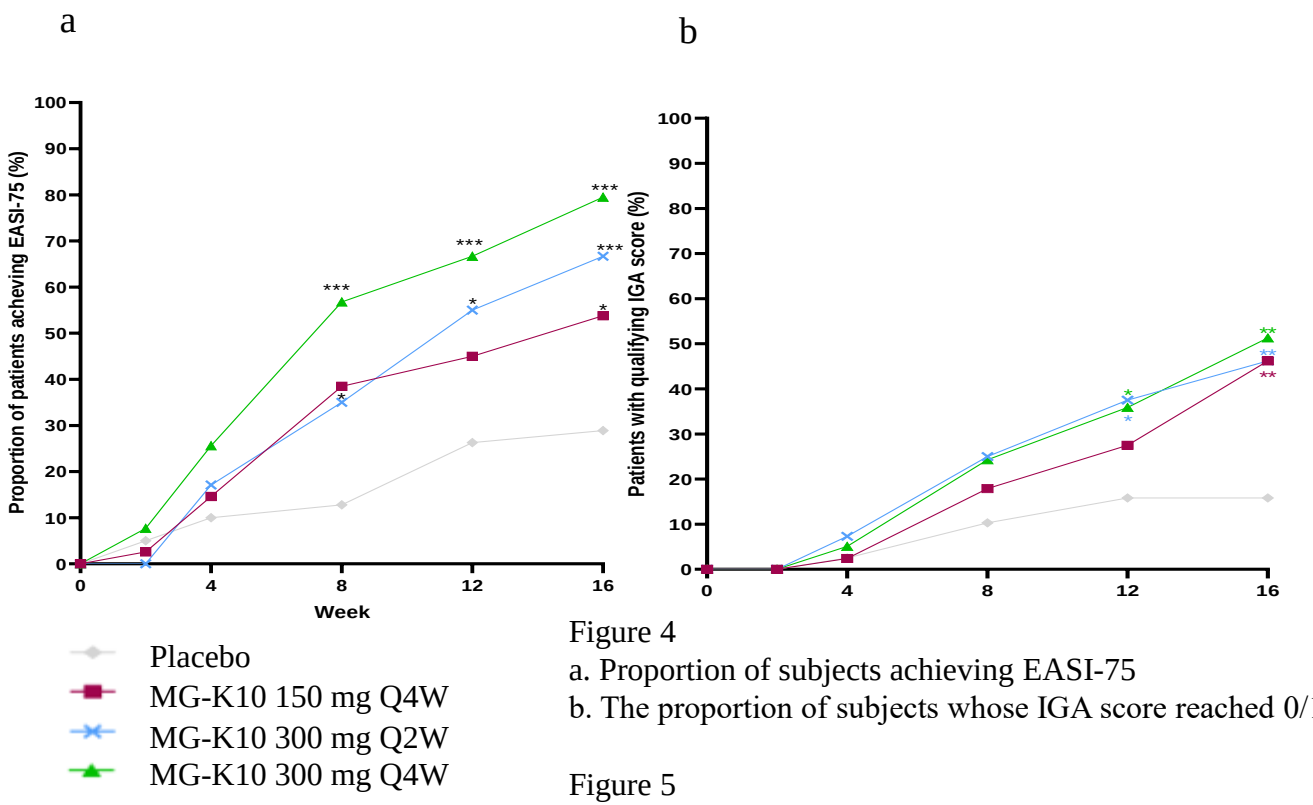


Figure 4
a. Proportion of subjects achieving EASI-75
b. The proportion of subjects whose IGA score reached 0/1 and a reduction of ≥2 points from baseline

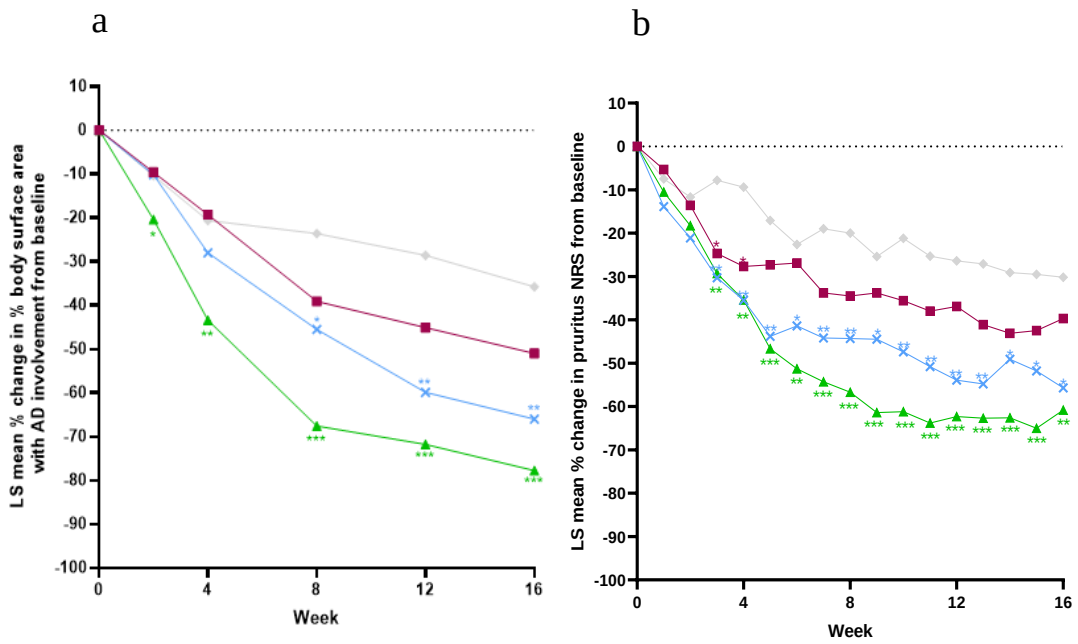


Figure 5
a. Change in BSA scores
b. Change in Average Weekly Pruritus Numerical-Rating Scale Score

Results (cont.), Conclusions

Safety Results

- MG-K10 was safe and well tolerated in this phase 2 trial.
- SAE and TEAE leading to drug discontinuations were rare, no AESI, no drug related SAE, or drug releated CTCAE Grade >=3 TEAEs.
- The incidence of adverse reactions that are of concern to the target (Conjunctivitis and related events, Eosinophilia) is low. No injection-site reactions or conjunctivitis were reported.

Table2 Adverse Events During the Study Treatment Period

TEAE	MG-K10 150mg Q4W n(%)	MG-K10 300mg Q2W n(%)	MG-K10 300mg Q4W n(%)	Placebo n(%)	Total n(%)
Any TEAEs	37 (90.2)	35 (85.4)	34 (82.9)	36 (90.0)	142 (87.1)
Drug Related TEAEs	9 (22.0)	13 (31.7)	15 (36.6)	9 (22.5)	46 (28.2)
Drug Related CTCAE Grade >=3 TEAEs	0	0	0	0	0
SAEs	1 (2.4)	0	1 (2.4)	1(2.5)	3 (1.8)
Drug Related SAEs	0	0	0	0	0
AESIs	0	0	0	0	0
TEAEs leading to drug interruption	3 (7.3)	3 (7.3)	2 (4.9)	1 (2.5)	9 (5.5)
TEAEs leading to drug discontinuation	1 (2.4)	0	1 (2.4)	0	2 (1.2)
TEAEs leading to study withdrawal	1 (2.4)	0	1 (2.4)	0	2 (1.2)
TEAEs leading to death	0	0	0	0	0

TEAE: Treatment-emergent adverse event;Defined as an AE that occurs or worsens after the first dose of study treatment;
TEAEs documented as “possibly related,” “probably related,” and “definitely related” to the study drug were considered drug related.
TEAEs that lack a relationship to the study drug are considered “related” to the study drug.

Conclusions

- Compared with the placebo, all MG-K10 groups demonstrated improvement in treating moderate-to-severe AD, and the improvement was most remarkable in 300 mg Q4W group.
- MG-K10 was safe and well tolerated.
- The Fc mutation enabled extended half life and robust efficacy response support less frequent dosing of MG-K10 versus other anti-IL-4Rα mAbs.