First FASN inhibitor ASC40 to treat acne vulgaris patients: final results from a Phase 2 trial

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DISCLOSURES

- The following authors have nothing to disclose: Leihong Xiang, Rixin Chen, Liming Wu, Ai'e Xu, Li He, Jinyan Wang, Yan Lu, Rong Xiao, Lunfei Liu, Yanyan Feng.
- Jinzi J. Wu is an employee and stockholder of Ascletis Pharma Inc.
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Background and methods

Methods

This phase 2 trial (NCT05104125) was a randomized, double-blind, placebo-controlled, multicenter study. 180 patients were 1:1:1:1 assigned to the ASC40 25\50\75mg or placebo QD for 12- week treatment and 2-week follow-up. Efficacy and safety of ASC40 vs placebo were assessed.

Background

ASC40(denifanstat) is a potent and selective small molecule inhibitor of fatty acid synthase (FASN). Mechanisms of action of ASC40 for acne treatment are novel: (1) direct inhibition of facial sebum production through inhibition of de novo lipogenesis (DNL) in sebocytes; and (2) inhibition of inflammation through decreasing cytokine secretion. Previous clinical studies showed that ASC40 treatment for 10 days reduced significantly facial sebum palmitic acid levels. Here we report the efficacy and safety results from a phase 2 study of ASC40 in patients with moderate to severe acne vulgaris after 12-week treatment. The study design is shown in Figure 1.

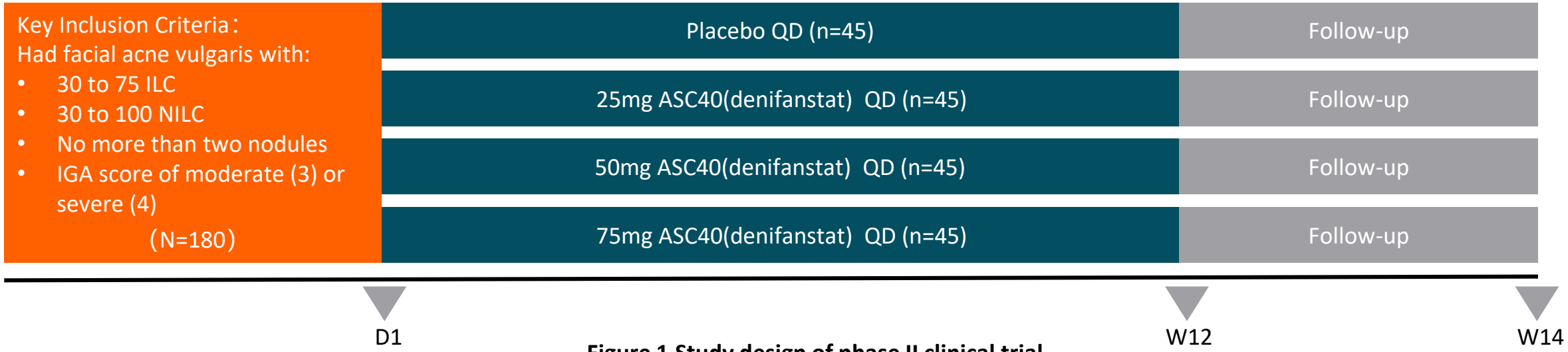


Figure 1.Study design of phase II clinical trial

ILC: inflammatory lesion count； NILC： noninflammatory lesion count； IGA： Investigator's Global Assessment

2024 AAD Annual Meeting, San Diego, March 8-12, Abstract ID 49342

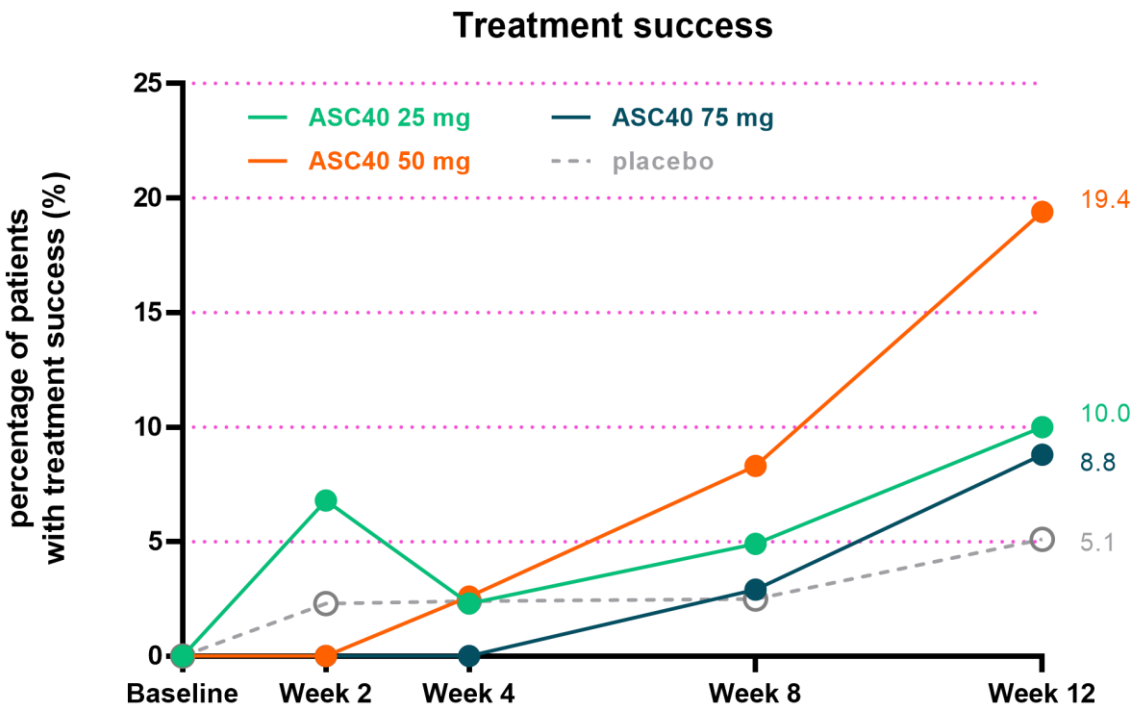
Results: baseline and treatment success

Table 1. Demography and baseline characteristics

Baseline characteristic	25 mg ASC40, oral, QD (n=45)	50 mg ASC40, oral, QD (n=44)	75 mg ASC40, oral, QD (n=45)	Placebo oral , QD (n=45)
Sex, n(%)				
Male	19(42.2)	16(36.4)	17(37.8)	20(44.4)
Female	26(57.8)	28(63.6)	28(62.2)	25(55.6)
Age, median (range), y	22.0(18-35)	22.0(18-34)	22.0(18-30)	23.0(18-39)
IGA score, n(%)				
3 (moderate)	29(64.4)	29(65.9)	34(75.6)	33(73.3)
4 (severe)	16(35.6)	15(34.1)	11(24.4)	12(26.7)
TLC, mean (SD)	103.6(25.5)	101.1(22.5)	100.0(27.3)	105.0(22.9)
NILC, mean (SD)	58.9(21.5)	57.7(21.0)	58.2(23.8)	61.4(21.2)
ILC, mean (SD)	44.7(13.5)	43.4(11.6)	41.8(9.7)	43.7(13.8)

TLC: Total lesion count; NILC: Non inflammatory lesion count; ILC:Inflammatory lesion count; IGA: Investigator's global assessment.

Figure 1. Proportion of patients with treatment success



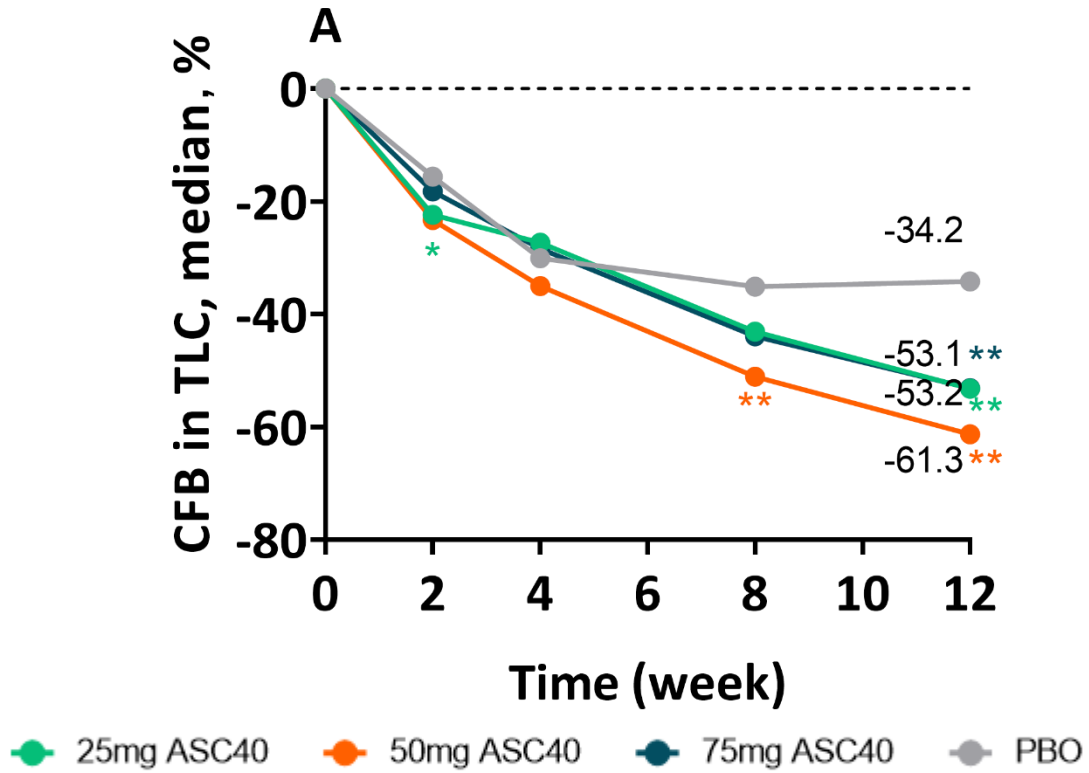
Treatment success: ≥2-point reduction in IGA from baseline and an IGA of 0 or 1. PBO: placebo.

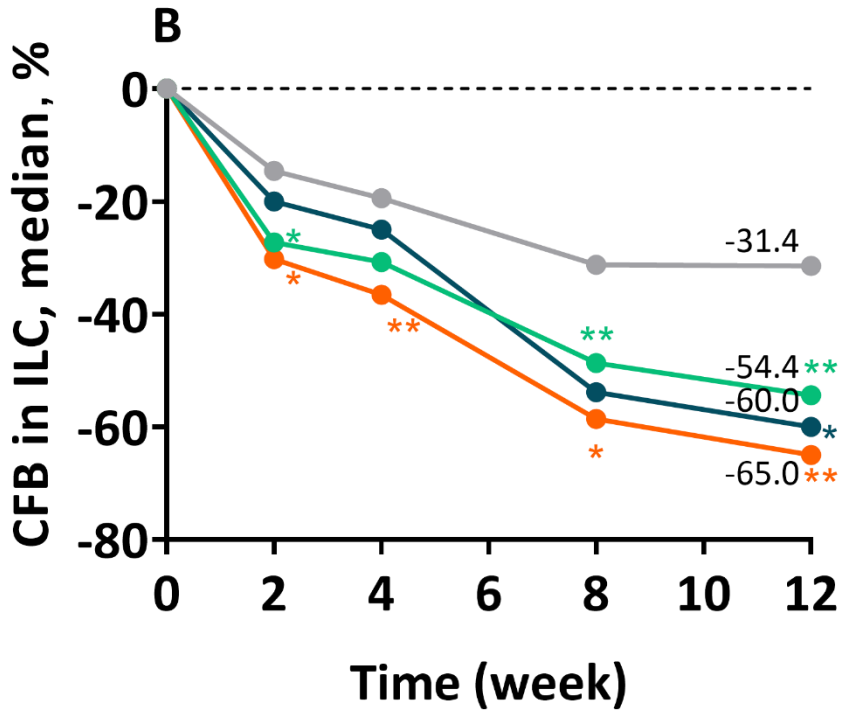
- **50 mg QD demonstrated the best efficacy: placebo-adjusted proportion of patients with treatment success and IGA reduction≥2 were 14.3% and 16.2%, respectively.**

2024 AAD Annual Meeting, San Diego, March 8-12, Abstract ID 49342

Results: change from baseline in lesion count

Figure 2. Efficacy results of 12-week treatment. **(A)** median percentage change from baseline in total lesion count. **(B)** median percentage change from baseline in inflammatory lesion count.





CFB： change from baseline; TLC: Total lesion count; ILC: Inflammatory lesion count; PBO: placebo. *: p<0.05 vs placebo; **: p<0.01 vs placebo

- **Placebo-adjusted median percentage (absolute) change from baseline in total lesion and inflammatory counts were -27.1% (-23.5) and -33.5% (-13), respectively (*p*=0.008 (0.030) and 0.003 (0.003)).**

2024 AAD Annual Meeting, San Diego, March 8-12, Abstract ID 49342

Safety and conclusion

Safety

The incidence rates of study drug related AEs were comparable among 25 mg (grade 1 = 28.9%; grade 2 = 20.0%), 50 mg (grade 1 = 36.4%; grade 2 = 11.4%), 75 mg (grade 1 = 44.4%; grade 2 = 17.8%) ASC40 and placebo (grade 1 = 35.6%; grade 2 = 13.3%). The most common study drug related AE was dry eyes whose incidence rates were similar among 25 mg (grade 1 =17.8%; grade 2 = 6.6%), 50 mg (grade 1 = 22.7%; grade 2 = 2.3%), 75 mg (grade 1 = 15.5%; grade 2 = 11.1%) ASC40 and placebo (grade 1 = 28.9%; grade 2 = 6.6%). There were no clinically significant findings in clinical laboratory, vital signs and electrocardiography. There were no ASC40 related grade 3 or 4 AEs and no ASC40 related serious AEs (SAEs).

Conclusion

Based on efficacy and safety data from this phase 2 trial, a phase 3 clinical trial of 50 mg QD ASC40 with 12-week treatment has been initiated.

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