ASC40，an oral once-daily fatty acid synthase (FASN) inhibitor, in patients with acne vulgaris: topline results from a phase 2 randomized, double-blind, placebo-controlled, multicenter trial

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Background

ASC40 is a potent (IC_{50} = 0.05μM) 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.

Methods

This phase 2 trial (NCT05104125) was a randomized, double-blind, placebo-controlled, multicenter study. 180 patients with moderate to severe acne vulgaris were randomized into three active treatment arms and one placebo control arm at the ratio of 1:1:1:1 to receive ASC40 (25, 50 or 75 mg tablet) or matching placebo tablet orally, once daily for 12-week treatment and 2-week follow-up. Efficacy and safety of 12-week treatment of ASC40 or placebo were assessed. The study design is shown in Figure 1.

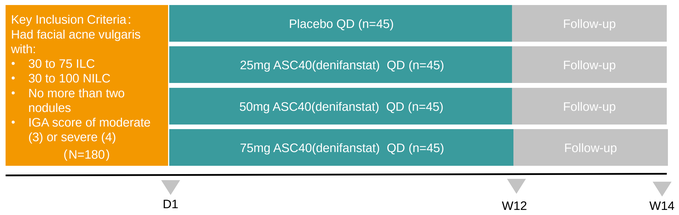


Figure 1.Study design of phase II clinical trial

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

Results

In total, 179 patients received at least one tablet of ASC40 or placebo and were included in the following analyses. One patient in 50 mg ASC40 arm did not take any study drug tablet, thus was excluded from the analyses. Demography and baseline characteristics data are presented in Table 1, which demonstrates a satisfactory balance among the different dose groups and the placebo group.

Results

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				
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				
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)
Total lesion count, mean (SD)	103.6(25.5)	101.1(22.5)	100.0(27.3)	105.0(22.9)
Non inflammatory lesion count, mean (SD)	58.9(21.5)	57.7(21.0)	58.2(23.8)	61.4(21.2)
Inflammatory lesion count, mean (SD)	44.7(13.5)	43.4(11.6)	41.8(9.7)	43.7(13.8)

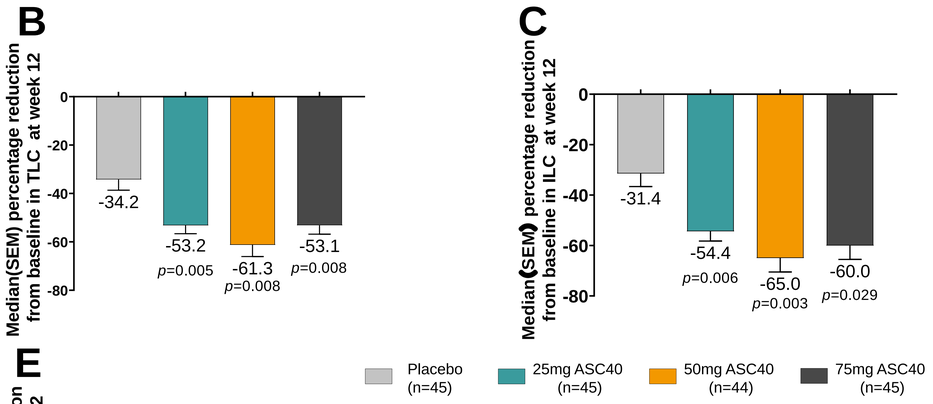
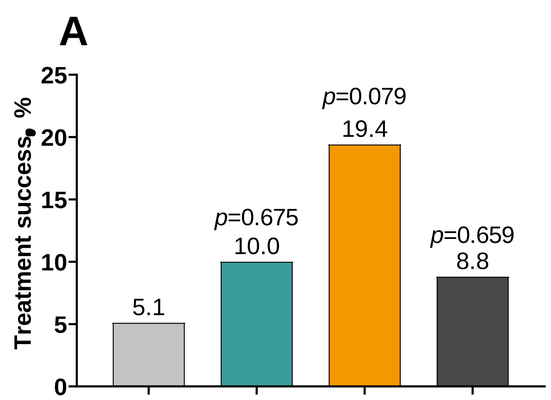


Figure 2：(A)Treatment success; (B) Median(SEM) percentage reduction from baseline in TLC at week 12; (C) Median(SEM) percentage reduction from baseline in ILC at week 12; (D) Median (SEM) absolute reduction from baseline in TLC at week 12; (E) Median (SEM) absolute reduction from baseline in ILC at week 12.

TLC: total lesion count; ILC: inflammatory lesion count; Treatment success: at least a 2-point reduction in Investigator's Global Assessment (IGA) from baseline and an IGA of 0 or 1 at week 12.

Figure 2. Efficacy results of 12-week treatment



Safety results of 12-week treatment

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).

Conclusions

- Topline results of this study showed that oral ASC40, once-daily, 12-week treatment was safe and well tolerated.
- ASC40 improved significantly in total lesion, inflammatory lesion, and IGA treatment success.
- Based on efficacy and safety assessment of this phase 2 study, the phase 3 clinical trial is warranted and will be initiated soon.