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Efficacy and safety of izokibep, a novel interleukin-17A inhibitor, in moderate to severe hidradenitis suppurativa: Week 16 results from a randomised, double-blind, placebo-controlled, multicentre, phase 3 study

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Introduction

Dysregulation of interleukin (IL)-17A plays a key role in hidradenitis suppurativa (HS) pathogenesis. Izokibep is an Affibody® molecule (small protein therapeutic; 18.6 kDa) designed to inhibit IL-17A with high potency through tight and selective binding.[1] In a phase 3 study of patients with moderate to severe HS, izokibep met its primary endpoint of improved HS Clinical Response (HiSCR)-75 vs placebo at week 12. Here, we report week 16 izokibep efficacy and safety results from the phase 3 study.

Materials and Methods

Study 22107 (NCT05905783) included a 16-week, randomised, placebo-controlled treatment period. Eligible patients were 18 years or older with a diagnosis of HS for ≥6 months, lesions present in ≥2 distinct anatomic areas (1 Hurley stage II/III), a total abscess and inflammatory nodule (AN) count ≥5, and an inadequate response, intolerance, or contraindication to oral antibiotics (use of a stable dose of oral antibiotics was allowed in up to 30% of patients). Patients were randomised 1:1 to receive subcutaneous placebo or izokibep 160 mg every week. Efficacy endpoints, including HiSCR75/90/100/50, pain, and quality of life, and safety were assessed at week 16. Response rates were determined using nonresponse imputation or multiple imputation (additional statistical analysis methods are detailed in the **Figure** footnote).

Results

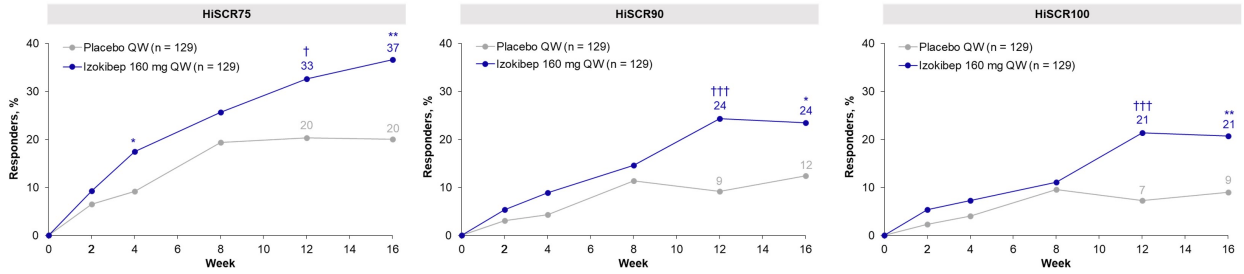
A total of 258 patients were randomised (placebo, n = 129; izokibep, n = 129). Overall, the mean (standard deviation [SD]) age was 37.3 (12.4) years, 69% of patients were female, and the mean (SD) disease duration was 10.2 (8.7) years. At baseline, mean (SD) AN count was 13.5 (13.3) for izokibep and 13.2 (11.5) for placebo. Baseline Hurley stage II/III was 60%/40% and 64%/36%. Other disease characteristics were similar between groups. Efficacy outcomes are shown in **Figure 1A**. At week 16, higher percentages of patients receiving izokibep vs placebo achieved HiSCR75 (37% vs 20%; **Figure 1B**), HiSCR90 (24% vs 12%), HiSCR100 (21% vs 9%), and HiSCR50 (50% vs 32%). Among patients with a baseline pain numeric rating scale (NRS) ≥4 treated with izokibep, 38% achieved a ≥3-point reduction in pain NRS (vs 17% of patients receiving placebo). Greater improvements were seen with izokibep vs placebo in Dermatology Life Quality Index (least squares mean [standard error] change from baseline, −4.4 [0.6] vs −2.9 [0.5]). Izokibep was generally well tolerated. Treatment-emergent adverse events (TEAEs) were reported in 83% and 59% of patients receiving izokibep and placebo, respectively, through week 16. TEAEs occurring in ≥5% of patients treated with izokibep were mostly mild or moderate in severity: injection-site reaction (67%; 1 severe event), headache (11%), nasopharyngitis (9%), diarrhoea (5%), fatigue (5%), and upper respiratory tract infection (5%). Low rates of serious TEAEs were reported (izokibep, 0.8%; placebo, 3.9%). There were no reports of *Candida* infection, inflammatory bowel disease, or suicidal ideation with izokibep.

Figure 1. Efficacy results

A.

	Placebo QW (n = 129)	Izokibep 160 mg QW (n = 129)
HiSCR75, %	20	37**
HiSCR90, %	12	24*
HiSCR100, %	9	21**
HiSCR50, %	32	50**
DLQI, CFB, LSM (SE)[a]	−2.9 (0.5)	−4.4 (0.6)*
AN count of 0, 1, or 2, %[b]	29	46*
≥3-point reduction in pain NRS, %[c]	17	38**
≥1 disease flare, %[d]	34	29

B.



A. Week 16 efficacy results. **B.** HiSCR75, HiSCR90, and HiSCR100 through week 16. Response rates were determined using NRI for patients who received antibiotic therapy that could affect HS and for patients with missing data who discontinued treatment due to an adverse event or lack of efficacy; multiple imputation was used for all other patients with missing data. Statistical significance per the prespecified testing hierarchy: †P<0.05; †††P<0.001 vs placebo. Nominal P-value: *P<0.05; **P<0.01 vs placebo.
[a]LSM using mixed model repeated measures including treatment, baseline DLQI, stratification factors, visit week, and treatment by visit week interaction as covariates. [b]In patients with baseline Hurley stage II (placebo, n = 82; izokibep, n = 78). [c]In patients with baseline pain NRS ≥4 (placebo, n = 79; izokibep, n = 73). Response rates were determined using NRI for patients with missing data who discontinued treatment due to an adverse event or lack of efficacy and patients who received prohibited analgesic therapy for HS within 28 days of the visit; multiple imputation was used for all other patients with missing data. [d]Disease flare was defined as ≥1 flare (a ≥25% increase in AN count with a minimum increase of 2 AN relative to baseline) at any time through week 16.
AN, abscess and inflammatory nodule; CFB, change from baseline; DLQI, Dermatology Life Quality Index; HiSCR50/75/90/100, a ≥50%/≥75%/≥90%/100% improvement in HS Clinical Response (a ≥50%/≥75%/≥90%/100% reduction from baseline in the total AN count, with no increase from baseline in abscess or draining fistula count); HS, hidradenitis suppurativa; LSM, least squares mean; NRI, nonresponse imputation; NRS, numeric rating scale; QW, every week; SE, standard error.

Conclusion

Early improvements previously reported with izokibep over placebo were sustained across key HS disease measures at week 16, with over one-third of patients achieving HiSCR75. No new safety signals were observed with izokibep.

References

1. Klint S, et al. *MAbs*. 2023; 15(1):2209920.