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Efficacy and safety of izokibep, a novel IL-17A inhibitor, in moderate-to-severe hidradenitis suppurativa: Week 12 results from a randomized, double-blind, placebo-controlled, multicenter, phase 3 study

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Introduction & Objectives:

Hidradenitis suppurativa (HS) is a chronic, painful, systemic inflammatory disease characterized by inflammatory nodules, skin abscesses, and draining tunnels, in which dysregulated interleukin (IL)-17A plays a key role. Izokibep (IZO) is a small protein therapeutic (18.6 kDa) designed to selectively inhibit IL-17A with high potency through tight binding affinity. We report the efficacy and safety of IZO at week (wk) 12 from a phase 3 study in patients with moderate-to-severe HS.

Materials & Methods:

Study 22107 (NCT05905783) included a 16-wk, randomized, placebo (PBO)-controlled treatment period. Eligible patients were 18 years of age or older and had 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 count ≥5; and an inadequate response, intolerance, or contraindication to oral antibiotics (use of a stable dose of oral antibiotics allowed in up to 30% of enrolled patients). Patients were randomized 1:1 to receive subcutaneous PBO every wk (QW) or IZO 160 mg QW. The primary study endpoint was HS Clinical Response (HiSCR)-75 at wk 12.

Results:

A total of 258 patients were randomized (PBO, n=129; IZO, 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. Baseline disease characteristics were generally balanced between groups. Efficacy outcomes are shown in **Table 1**. The primary endpoint of HiSCR75 at wk 12 was met; a higher percentage of patients receiving IZO vs PBO achieved HiSCR75 (33% vs 21%; P <0.05; **Figure 1**). Similarly, patients receiving IZO vs PBO achieved higher rates of HiSCR90 (25% vs 9%; P<0.001) and HiSCR100 (22% vs 8%; P<0.01). Among IZO-treated patients with a baseline pain numeric rating scale (NRS) ≥4, 33% achieved a ≥3-point reduction in pain NRS (vs 17% of PBO-treated patients). Greater improvements were seen with IZO vs PBO in Dermatology Life Quality Index (least squares mean [standard error] change from baseline, –4.9 [0.5] vs –2.7 [0.5]). Treatment-emergent adverse events (AEs) occurred in 79.1% and 52.7% of patients receiving IZO and PBO, respectively, through wk 12. The most common AEs (≥5%) among IZO-treated patients were injection-site reaction (65.1%), headache (10.1%),

nasopharyngitis (7.0%), diarrhea (5.4%), and fatigue (5.4%). Serious AEs were reported at low rates (IZO, 0.8%; PBO, 3.1%). No *Candida* infections, inflammatory bowel disease, or suicidal ideation were reported with IZO.

Conclusion:

In this phase 3 study, IZO 160 mg QW met the primary endpoint, with one-third of patients with moderate-to-severe HS achieving HiSCR75 at wk 12. Additionally, IZO-treated patients demonstrated early improvements at wk 12 across other key disease measurements, including HiSCR90, HiSCR100, pain, and quality of life. IZO treatment was well tolerated, with no new safety signals and a safety profile generally consistent with that of other IL-17A–selective inhibitors.

Table 1. Week 12 Efficacy Results

	Placebo QW (n=129)	Izokibep 160 mg QW (n=129)
HiSCR75	21%	33%†
HiSCR90	9%	25%†††
HiSCR100	8%	22%††
HiSCR50	37%	48%
DLQI, CFB, LSM (SE)	–2.7 (0.5)	–4.9 (0.5)**
AN count of 0, 1, or 2[a]	27%	50%**
≥3-point reduction in pain NRS[b]	17%	33%*
≥1 disease flare[c]	31%	29%

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 for reason of adverse event or lack of efficacy, with multiple imputation for all other patients with missing data. Statistical significance per the prespecified testing hierarchy: †P<0.05, ††P<0.01, †††P<0.001 vs placebo. Nominal P-value: *P<0.05, **P<0.01 vs placebo.

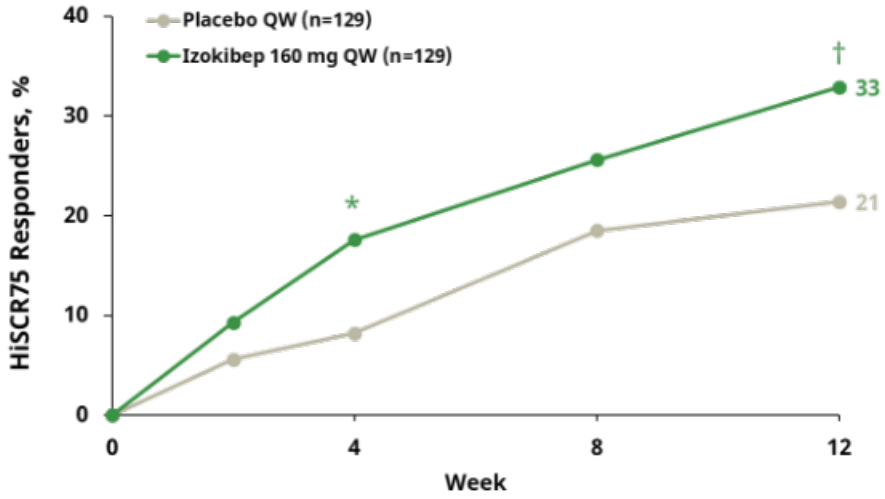
[a]In patients with baseline Hurley stage II (placebo, n=82; izokibep, n=78).

[b]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 for reason of adverse event or lack of efficacy and patients who received prohibited analgesic therapy for HS within 28 days of the visit, with multiple imputation for all other patients with missing data.

[c]Disease flare defined as ≥1 flare (≥25% increase in AN count with a minimum increase of 2 AN relative to baseline) at any time through week 12.

AN, abscess and inflammatory nodule; CFB, change from baseline; DLQI, Dermatology Life Quality Index; HS, hidradenitis suppurativa; HiSCR50/75/90/100, ≥50%/≥75%/≥90%/100% improvement in HS Clinical Response (≥50%/≥75%/≥90%/100% reduction from baseline in the total AN count, with no increase from baseline in abscess or draining fistula count); LSM, least squares mean; NRI, nonresponse imputation; NRS, numeric rating scale; QW, every week; SE, standard error.

Figure 1. HiSCR75 Through Week 12



The primary study endpoint was HiSCR75 at week 12. 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 for reason of adverse event or lack of efficacy, with multiple imputation for all other patients with missing data. Statistical significance per the prespecified testing hierarchy: †P<0.05 vs placebo. Nominal P value: *P<0.05 vs placebo.

AN, abscess and inflammatory nodule; HS, hidradenitis suppurativa; HiSCR75, ≥75% improvement in HS Clinical Response (≥75% reduction from baseline in the total AN count, with no increase from baseline in abscess or draining fistula count); NRI, nonresponse imputation; QW, every week.