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Depth of the Efficacy Response to Lutikizumab Treatment in Moderate-to-Severe Hidradenitis Suppurativa (HS)

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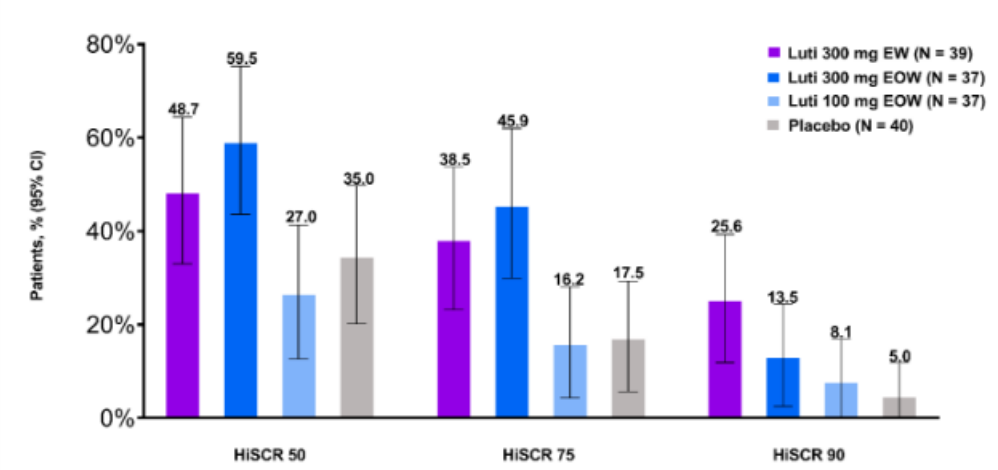
Introduction & Objectives: Hidradenitis suppurativa (HS) is an unpredictable progressive disease. Treatments that target the underlying cytokine-driven mechanisms of the disease are expected to have higher clinical efficacy benchmarks to address the unmet needs of patients. Lutikizumab (luti), a dual-variable-domain interleukin (IL) 1α/1β antagonist, has shown greater response rates over placebo in the achievement of HiSCR 50, HiSCR 75, and pain NRS 30 at week 16 in a phase 2b study in patients with hard-to-treat moderate-to-severe HS, who have failed anti-TNF therapy. Most patients (70.6%) had severe baseline Hurley Stage 3 disease. The objective of this analysis was to assess the depth of response of lutikizumab compared to placebo, evaluated by achievement of HiSCR 90 and the International Hidradenitis Suppurativa Severity Score System (IHS4) endpoints, IHS4-55/75/90.

Materials & Methods: In this phase 2b multicenter, randomized, double-blind, placebo-controlled trial (NCT05139602) Main Study, adult patients with a clinical diagnosis of HS, who failed anti-TNF treatment, were randomized at baseline in a 1:1:1:1 ratio to one of 4 treatment groups, each with a planned N = 40: lutikizumab 300 mg every week (luti 300 mg EW); lutikizumab 300 mg every other week (luti 300 mg EOW); lutikizumab 100 mg EOW (luti 100 mg EOW); placebo EW. The primary efficacy objective of the main study was to assess the achievement of HiSCR 50 after 16 weeks of treatment with each lutikizumab group compared to placebo. Additional efficacy assessments included achievement of HiSCR 75/90 and IHS4-55/75/90 at week 16. Statistical approaches included non-responder imputation incorporating multiple imputation (NRI-MI) to handle missing data for HiSCR 50/75/90, IHS4-55, and NRI for IHS4-75/90.

Results: A total of 153 patients (61.4% female; mean [SD] age 40.5 [12.4] years) were randomized across 54 sites, with most patients (70.6%) diagnosed with severe baseline Hurley Stage 3 disease. At week 16, 25.6%, 13.5%, and 8.1% of patients receiving luti 300 mg EW, 300 mg EOW and 100 mg EOW, respectively, achieved HiSCR 90, compared to 5.0% of patients receiving placebo (Figure 1). Furthermore, at week 16, IHS4-55, IHS4-75, and IHS4-90 was achieved by 48.7%, 28.2%, and 23.1% of patients receiving luti 300 mg EW, by 62.2%, 40.5%, and 21.6% of patients receiving luti 300 mg EOW, and by 27.0%, 13.5%, and 5.4% of patients receiving luti 100 mg EOW, compared to 32.5%, 20.0%, and 7.5% of patients receiving placebo, respectively (Figure 2). The IHS4-55/75/90 response rates were consistent with those reported for HiSCR 50/75/90.

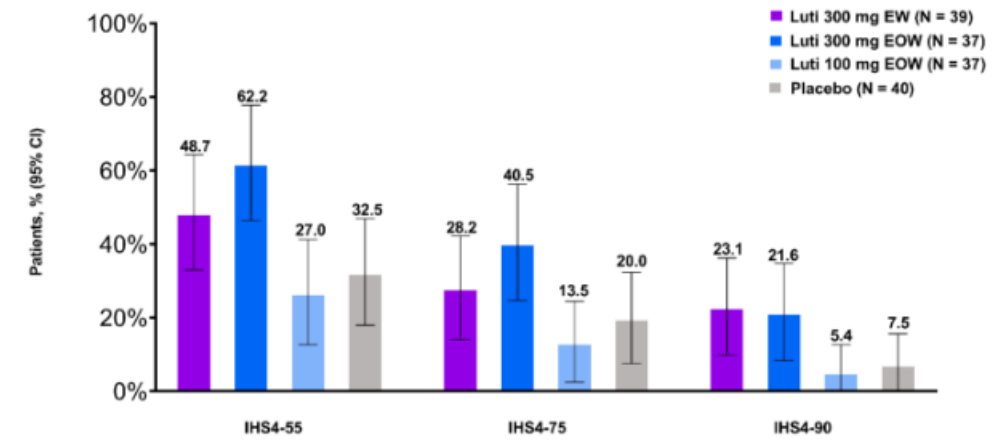
Conclusion: In a hard-to-treat patient population, treatment with luti 300 mg EW and luti 300 mg EOW provides efficacy responses at deep levels at week 16 compared to placebo, as demonstrated by HiSCR 75/90 response rates and IHS4-55/75/90 response rates. These results support further investigation of the clinical efficacy of lutikizumab as a potential treatment option for patients with moderate-to-severe HS.

Figure 1. Achievement of HiSCR 50/75/90 at Week 16 (NRI-MI)



EOW, every other week; EW, every week; HiSCR, hidradenitis suppurativa clinical response; Luti, lutikizumab; NRI-MI, non-responder imputation incorporating multiple imputation.
NRI-MI is used to handle missing data due to COVID-19.
HiSCR 50/75/90 are defined as at least a 50%, 75%, or 90% reduction from baseline, respectively, in the total abscess and inflammatory nodule (AN) count, with no increase in abscess count and no increase in draining fistula-count relative to baseline.

Figure 2. Achievement of IHS4-55/75/90* at Week 16



EOW, every other week; EW, every week; IHS4, International Hidradenitis Suppurativa Severity Score System; Luti, lutikizumab; NRI, non-responder imputation.
IHS4 55/75/90 are defined as at least a 55%, 75%, or 90% reduction from baseline in IHS4, respectively.
*NRI-MI is used to handle missing data for IHS4-55, and NRI is used for IHS4-75/90.