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The IL-17A- and IL-17F-inhibiting Nanobody sonelokimab in patients with moderate-to-severe hidradenitis suppurativa (HS): Week 24 International Hidradenitis Suppurativa Severity Score System (IHS4) results from the Phase 2 MIRA trial

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Introduction & Objectives: Sonelokimab is a novel humanized Nanobody with a high affinity to IL-17A and IL-17F, which are important drivers of inflammation in HS. Being small in size (~40 kDa) and containing an albumin-binding domain, sonelokimab is designed to penetrate difficult-to-reach inflamed tissues and directly target sites of inflammation. In the Phase 2 MIRA trial, a significantly higher proportion of patients with moderate-to-severe HS achieved the primary endpoint of Hidradenitis Suppurativa Clinical Response 75 (HiSCR 75) with sonelokimab (120mg, 43.3%, $P<0.001$; 240mg, 34.8%, $P=0.007$) vs. placebo (14.7%) at Week (W) 12 (ITT-NRI). Further improvements were observed at Week 24.1 A key secondary endpoint was change from baseline in IHS4, a dynamic clinician-reported outcome measure that evaluates inflammatory nodules (1 point), abscesses (2 points), and draining tunnels (4 points). This endpoint was also met, with a significant improvement seen with sonelokimab (120mg, -19.3, $P<0.001$; 240mg, -14.5, $P=0.020$) vs. placebo (-7.9) at W12 (ITT, LSM, MMRM analysis). Here, we present W24 IHS4 results from the MIRA trial.

Materials & Methods: MIRA was a 24-week global, randomized, prospective, parallel-group, doubleblind, placebo-controlled Phase 2 trial (NCT05322473). Eligible patients were ≥ 18 years old with HS for ≥ 6 months, Hurley Stage II/III, total abscess and/or inflammatory nodule (AN) count ≥ 5 , and HS lesions in ≥ 2 distinct anatomical areas. At W12, patients receiving sonelokimab (120mg or 240mg) continued their allocated dose and patients receiving placebo were re-randomized 1:1 to sonelokimab 120mg or 240mg. Absolute and percent changes in IHS4 from baseline were assessed at W24. Disease severity was graded using IHS4 classifications of 'inactive or mild' (≤ 3), 'moderate' (4–10), or 'severe' (≥ 11). As a *post hoc* analysis, IHS4 was evaluated in a subgroup of patients with 'very severe' HS at baseline, defined as the upper tertile of patients with a 'severe'

disease severity grade (minimum baseline IHS4 score of 35). W24 data are reported as observed (discontinuation rate <10%).

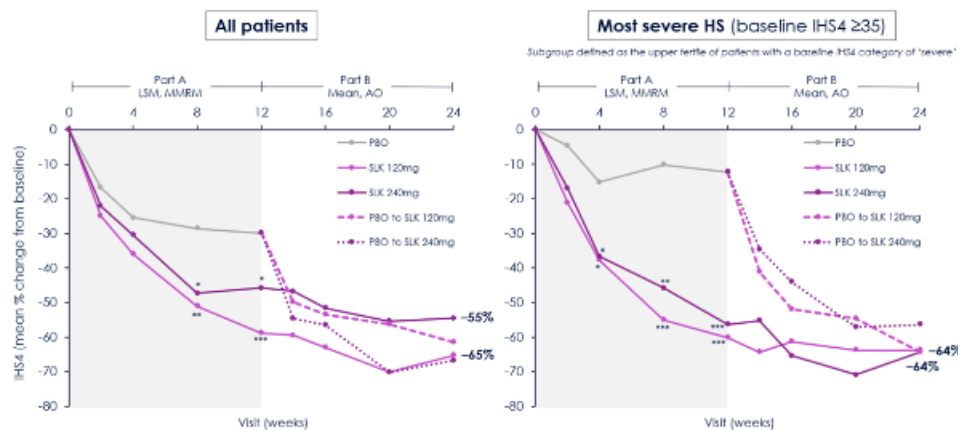
Results: At baseline, 67 and 66 patients were randomized to receive sonelokimab 120mg and 240mg, respectively. Mean IHS4 score at baseline was 30.9; all patients had a 'moderate' (15.0%) or 'severe' (85.0%) IHS4 severity grade. Improvements in IHS4 continued to be observed with sonelokimab at W24 (mean [%] change from baseline: 120mg, -22.3 [-65.2%]; 240mg, -15.9 [-54.5%]), and were consistent even in patients with the most severe disease at baseline (patients with baseline IHS4 ≥ 35 : 120mg, -63.8% [n=20]; 240mg, -64.3% [n=17]). Results in patients switching from placebo to sonelokimab were similar to those in patients randomized to sonelokimab at baseline (**Figure 1**). Finally, 47% of patients receiving sonelokimab 120mg achieved 'inactive or mild' disease (IHS4 ≤ 3) by W24 (**Figure 2**), including 24% with inactive disease (IHS4=0).

Conclusion: In the MIRA trial, the IL-17A- and IL-17F-inhibiting Nanobody sonelokimab demonstrated substantial improvements in IHS4 to W24, owing to efficacy across all three key inflammatory HS lesion types. These findings are consistent with previously reported high HiSCR 75 responses. The ongoing Phase 3 VELA 1 and 2 trials will further examine IHS4 outcomes with sonelokimab 120mg in patients with moderate-to-severe HS.

References:

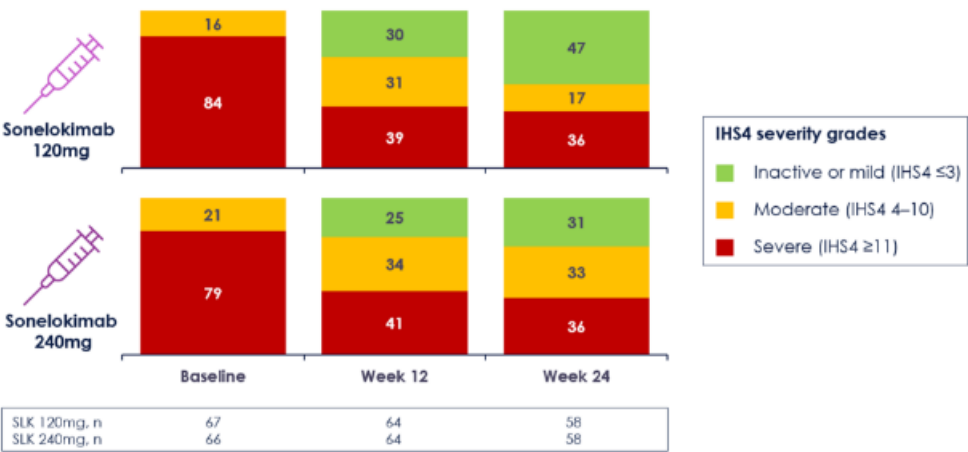
1. Kimball AB, *et al.* AAD 2024 (Abstract 56014).

Figure 1. Percent change from baseline in IHS4 score



*** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$; P -values are nominal. IHS4 data from Week 14 to Week 24 are as observed. IHS4 data from Week 0 to Week 12 are LSM % change from baseline with P -values analyzed using MMRM with treatment group, visit, Hurley Stage status, prior biologic use, associated baseline measurements, and visit by treatment as fixed effects and patient as a random effect. AO, as observed; IHS4, International Hidradenitis Suppurativa Severity Score System; LSM, least squares mean; MMRM, mixed model for repeated measures; PBO, placebo; SLK, sonelokimab.

Figure 2. Percent proportion of patients in each IHS4 severity grade



Data reported as observed.
IHS4, International Hidradenitis Suppurativa Severity Score System.