

Efficacy and Safety of Abdakibart, a Selective Anti-IL-1 β Agent for Treatment of Moderate to Severe Hidradenitis Suppurativa; Primary Results of the Placebo-Controlled Phase 2 LOTUS Trial

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Objective

- Compare the efficacy and safety of abdakibart, a humanized, IgG4 selective anti-interleukin-1 β (IL-1 β) immunoglobulin, to placebo in patients with moderate to severe hidradenitis suppurativa (HS)

Introduction

- HS is a chronic inflammatory skin disease of the pilosebaceous unit characterized by abscesses and inflammatory nodules (AN), and draining tunnels (DT)¹
- Three biologics (e.g., adalimumab, secukinumab, bimekizumab) are currently approved for the treatment of moderate to severe HS; however, response to treatment in HS is often suboptimal with high rates of loss of efficacy²⁻⁴
- IL-1 β has been demonstrated to be a key upstream inducer for tumor necrosis factor alpha (TNF- α) and Th17 cells in HS⁵
- We present the primary and major secondary efficacy and safety results from the global phase 2, double-blind, placebo-controlled LOTUS trial (NCT06603077)

Methods

Primary Study Endpoint

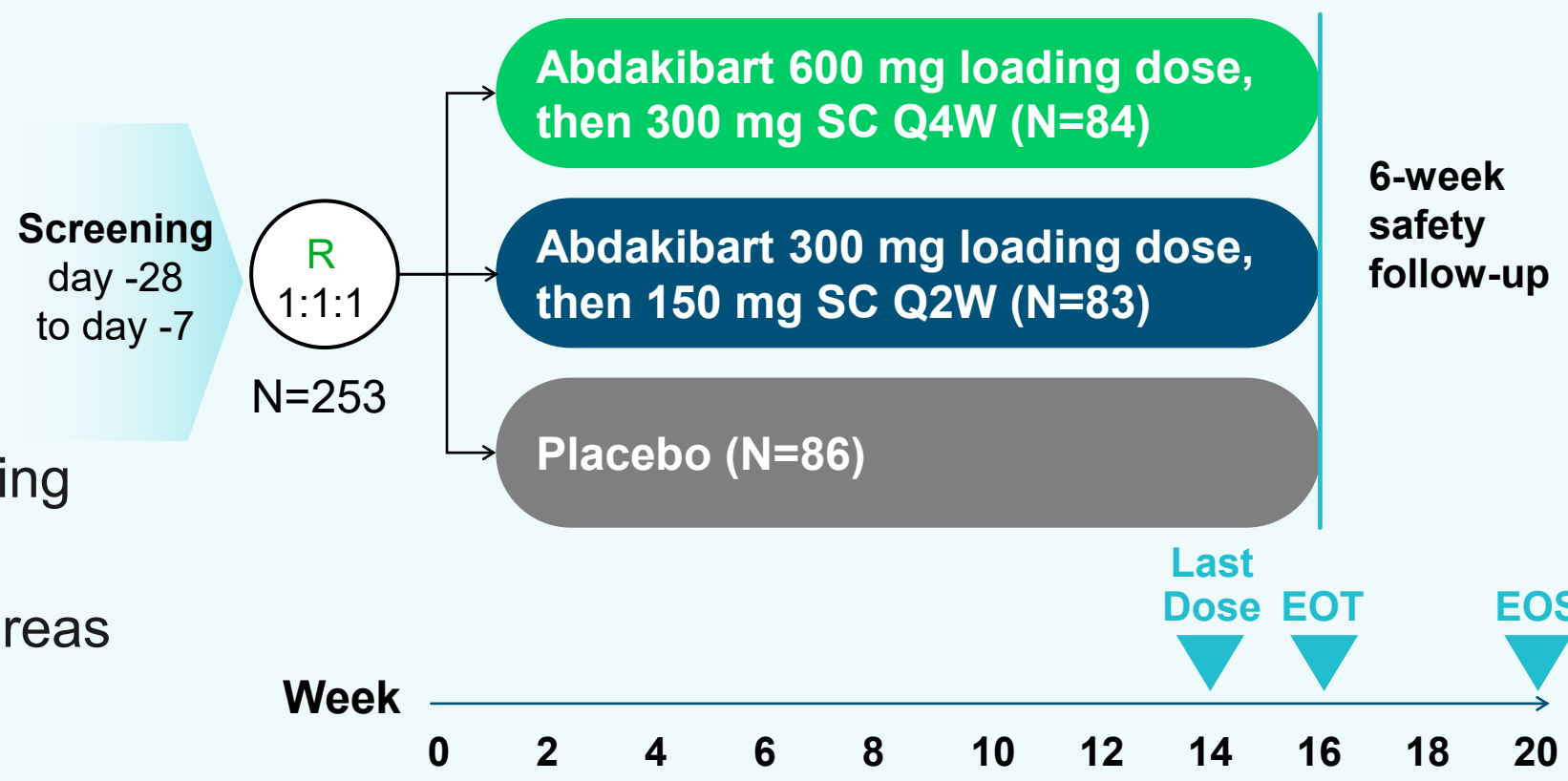
Percentage of patients achieving HiSCR75 at week 16

Key Inclusion Criteria

- Age ≥ 18 years
- HS symptoms for ≥ 6 months prior to screening
- Total AN count ≥ 5 at BL
- HS lesions present in ≥ 2 distinct anatomic areas
- ≥ 1 HS lesion that is Hurley stage II or III
- Biologic naïve or biologic experienced
- Stratified by Hurley stage and weight

AN, abscesses and inflammatory nodules; BL, baseline; EOS, end of study; EOT, end of treatment; HS, hidradenitis suppurativa; Q2W, every 2 weeks; Q4W, every 4 weeks; R, randomization; SC, subcutaneously.

- The primary endpoint was the percentage of patients achieving HiSCR75 at week 16
- HiSCR75 defined as $\geq 75\%$ reduction in total AN count with no increase in abscess count and no increase in DT count relative to baseline (BL)
- Secondary endpoints included percentage of patients achieving HiSCR50, percentage of patients achieving HiSCR90, and changes from BL in International Hidradenitis Suppurativa Severity Score System (IHS4), AN count, and DT count



- The primary endpoint analysis compared both abdakibart groups to placebo using a closed testing procedure which controlled overall Type 1 error at a 0.05 significance level (2-sided)
- Difference in responder rate and p -value were obtained using a Mantel-Haenszel test stratified by randomization stratification factors
 - Patients who received systemic rescue therapy before week 16, or discontinued study treatment due to an adverse event (AE) or lack of efficacy were treated as non-responders and patients with missing data were imputed as non-responders
- For continuous variables, least squares (LS) means were based on a mixed effects model for repeated measures with change from BL as the dependent variable; treatment group, visit, treatment-by-visit interaction, and randomization stratification factors as fixed effects; and BL score as a covariate

Results

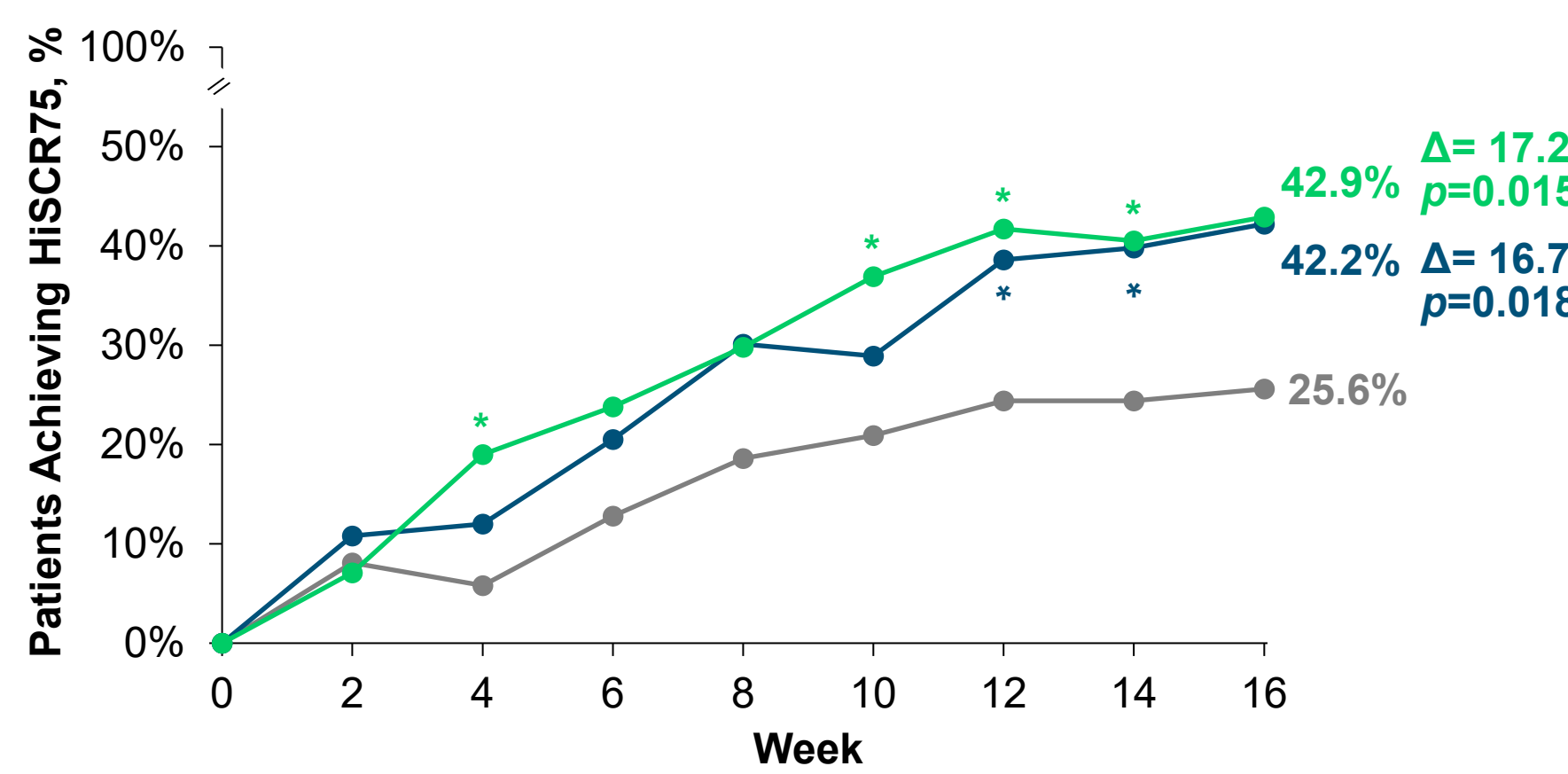
Demographics and Baseline Clinical Characteristics

Characteristic	Placebo (n=86)	Abdakibart 150 mg Q2W (n=83)	Abdakibart 300 mg Q4W (n=84)
Age, years, mean (SD)	37.7 (11.8)	38.4 (12.1)	39.0 (13.4)
Female, n (%)	45 (52.3)	55 (66.3)	53 (63.1)
White, n (%)	57 (66.3)	54 (65.1)	63 (75.0)
BMI, mean (SD), kg/m ²	33.9 (8.7)	36.4 (8.9)	34.9 (7.7)
Current smoker, n (%)	41 (47.7)	32 (38.6)	36 (42.9)
Duration of HS, years, mean (SD)	6.9 (6.3)	9.1 (8.1)	7.8 (9.5)
Hurley stage III, n (%)	34 (39.5)	32 (38.6)	34 (40.5)
Prior biologic use, n (%)	27 (31.4)	35 (42.2)	33 (39.3)
AN count, mean (SD)	13.8 (8.2)	13.5 (8.7)	14.0 (13.8)
DT count, mean (SD)	2.8 (3.4)	2.7 (2.9)	3.2 (3.7)
IHS4 score, mean (SD)	27.5 (19.0)	26.7 (19.1)	29.0 (21.3)

AN, abscess and inflammatory nodules; BMI, body mass index; DT, draining tunnels; HS, hidradenitis suppurativa; IHS4 International Hidradenitis Suppurativa Severity Score System; Q2W, every 2 weeks; Q4W, every 4 weeks; SD, standard deviation.

- A total of 253 patients were randomized; 86% completed study treatment
 - Seven patients discontinued due to lack of efficacy (placebo, n=2; abdakibart 150 mg Q2W, n=3; and abdakibart 300 mg Q4W, n=2) and 3 due to AEs (n=1, 2, and 0, respectively)
- BL characteristics were generally balanced, although the abdakibart groups had a longer mean duration of HS, and had higher percentages of women and of patients previously treated with an approved biologic

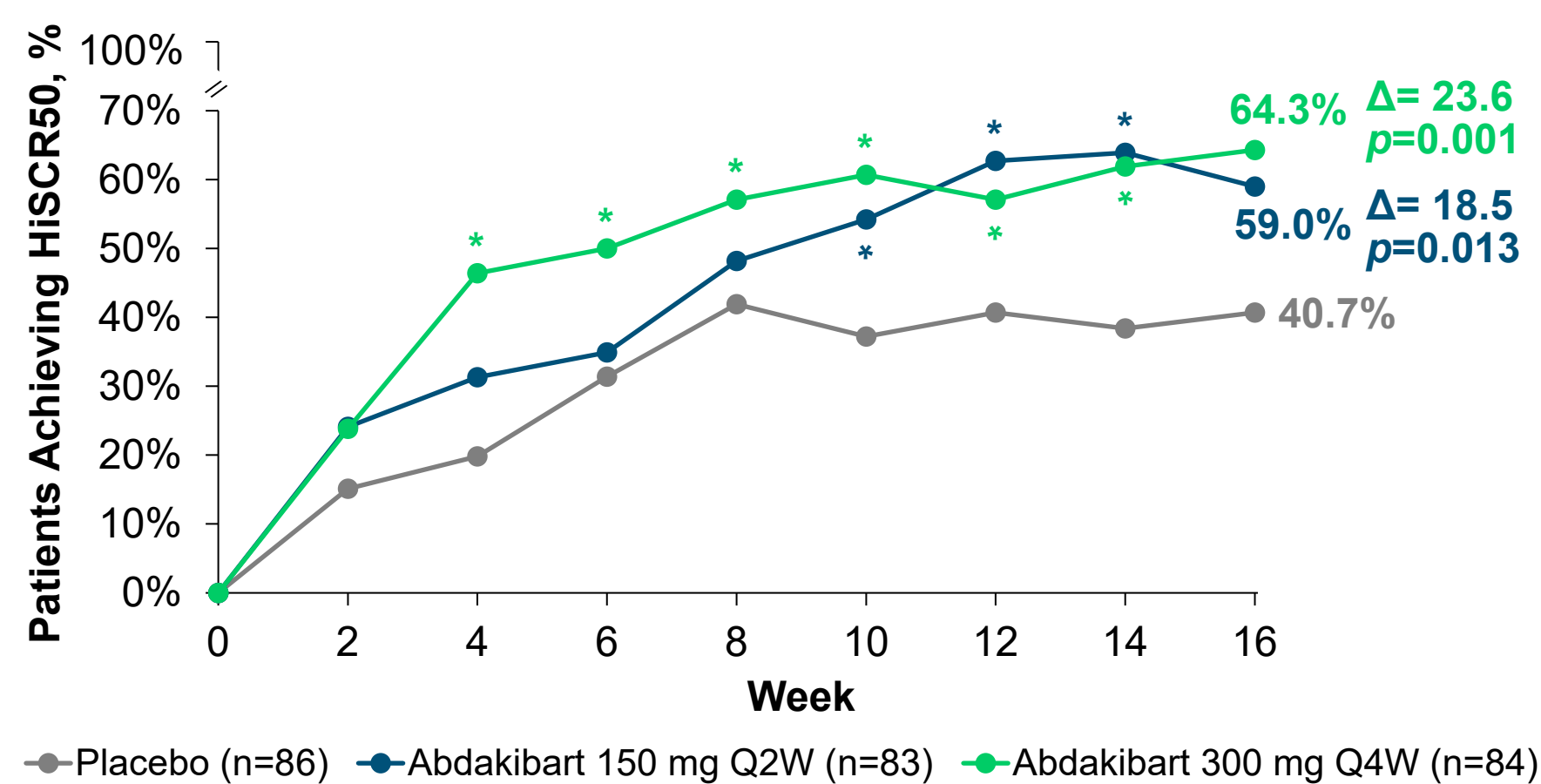
Primary Endpoint: Patients Achieving HiSCR75



*Nominal $p < 0.05$ vs placebo. Δ , difference vs placebo; HiSCR, Hidradenitis Suppurativa Clinical Response; Q2W, every 2 weeks; Q4W, every 4 weeks.

- At week 16, a statistically significantly greater percentage of patients in both abdakibart groups and the combined abdakibart group (not shown) achieved the primary endpoint of HiSCR75 vs placebo
- In addition, a greater percentage of patients in the 300 mg and combined abdakibart groups (not shown) vs placebo achieved HiSCR75 as early as week 4 (nominal $p < 0.05$)

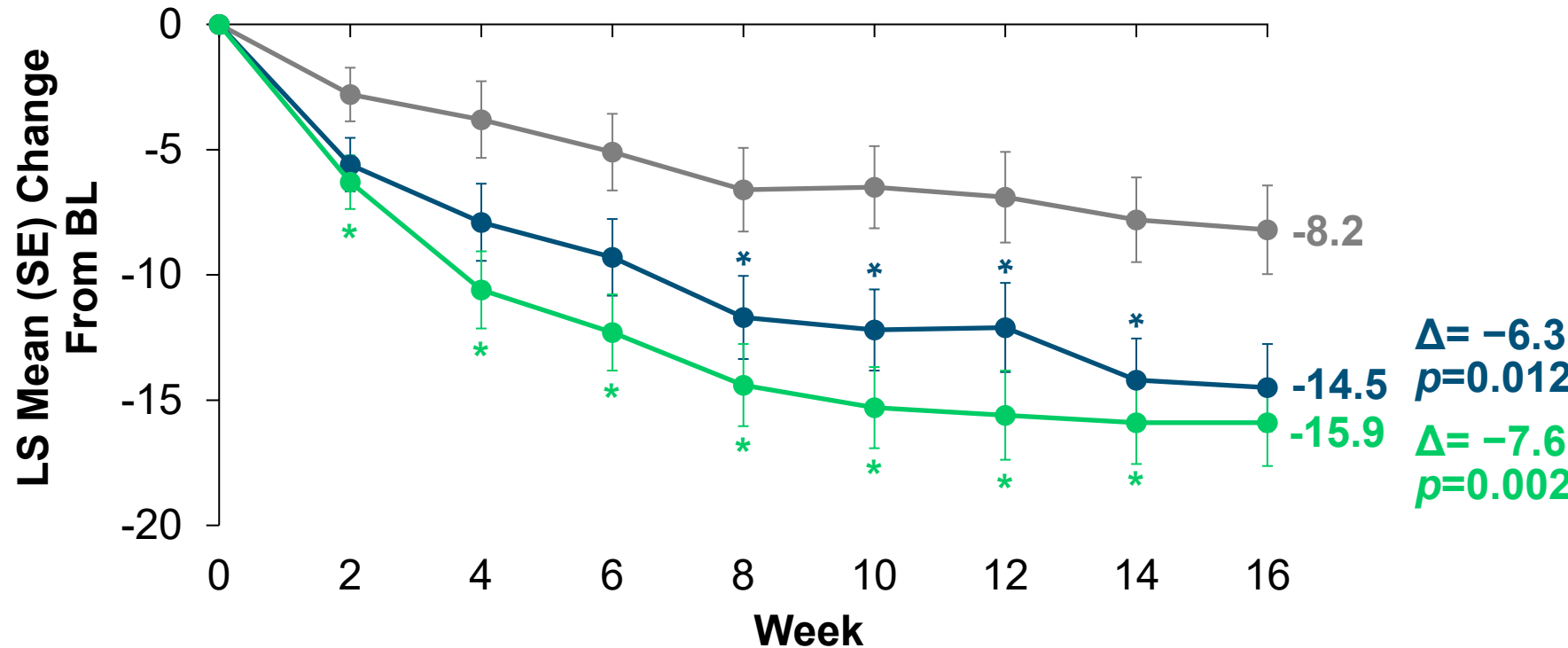
Patients Achieving HiSCR50



*Nominal $p < 0.05$ vs placebo. Δ , difference vs placebo; HiSCR, Hidradenitis Suppurativa Clinical Response; Q2W, every 2 weeks; Q4W, every 4 weeks.

- A greater percentage of patients in both abdakibart groups and the combined abdakibart group (not shown) vs placebo achieved HiSCR50 at week 16
- In addition, a greater percentage of patients in the 300 mg and combined abdakibart groups (not shown) vs placebo achieved HiSCR50 as early as week 4 (nominal $p < 0.05$)
- Numerically higher percentages of patients in both abdakibart groups vs placebo achieved HiSCR90 at week 16 (not shown)

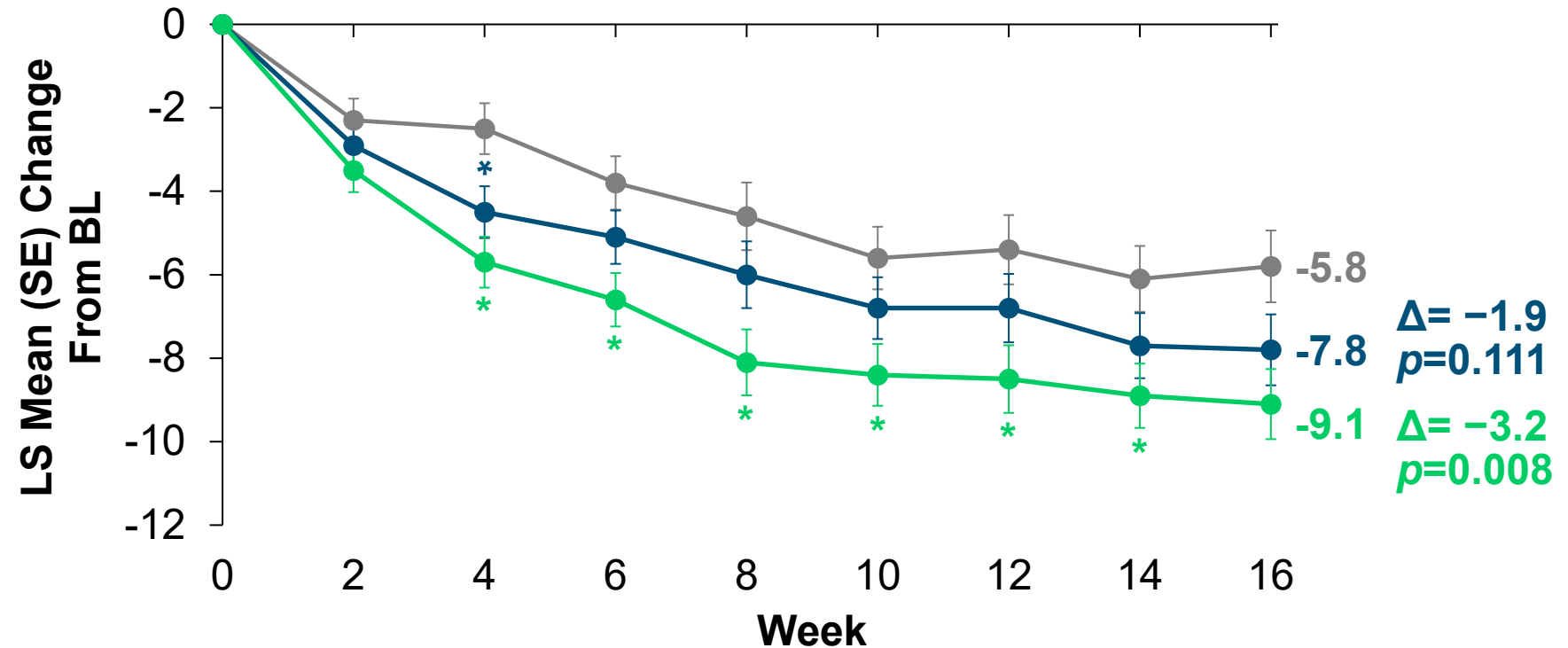
Change From Baseline in IHS4



*Nominal $p < 0.05$ vs placebo. Δ , difference vs placebo; BL, baseline; IHS4 International Hidradenitis Suppurativa Severity Score System; LS, least squares; Q2W, every 2 weeks; Q4W, every 4 weeks; SE, standard error.

- Improvement from BL in IHS4 scores was greater in both abdakibart groups versus placebo at week 16
- Improvements vs placebo (nominal $p < 0.05$) were observed as early as week 2 in the 300 mg abdakibart group

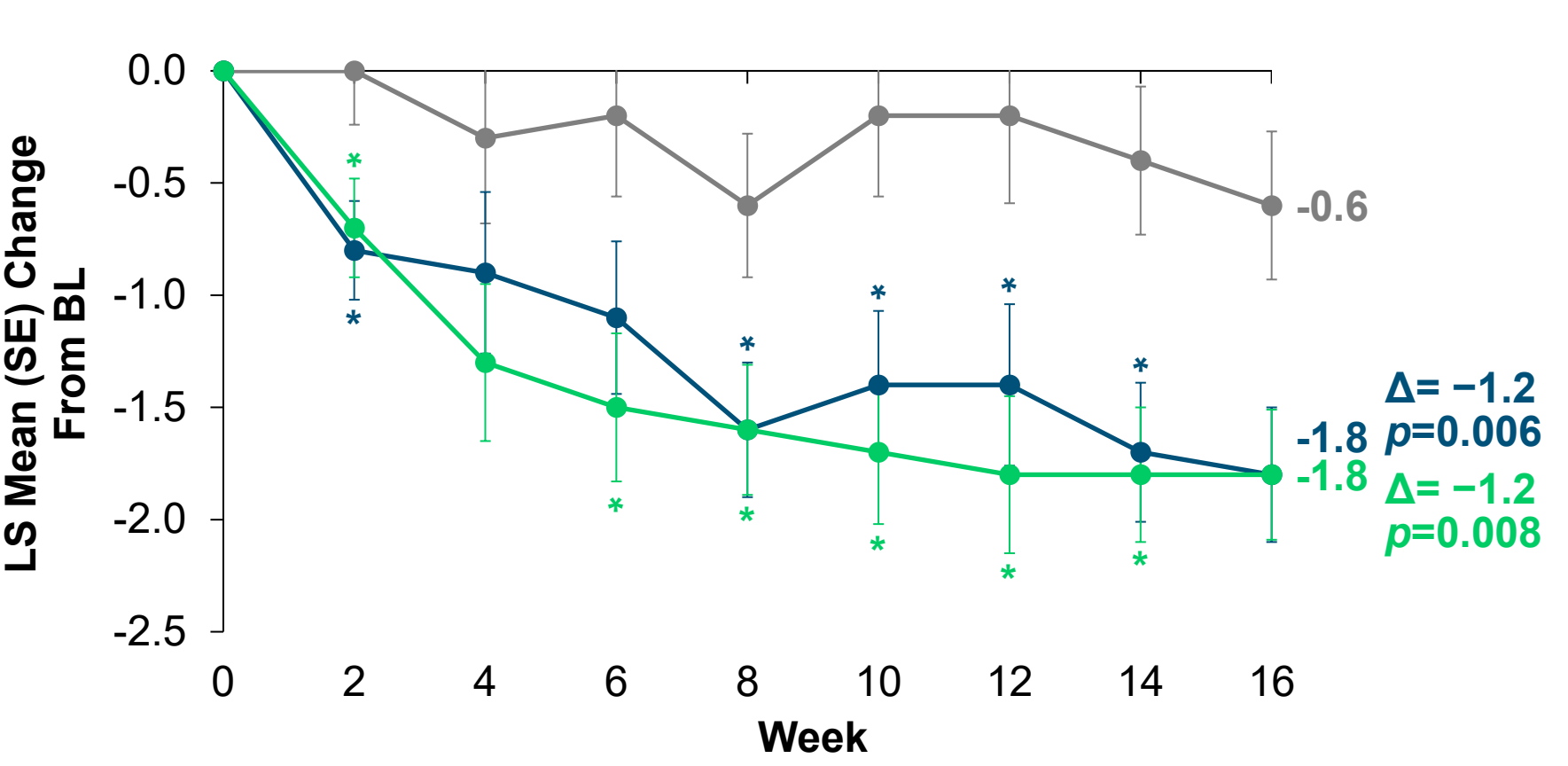
Change From Baseline in AN Count



*Nominal $p < 0.05$ vs placebo. Δ , difference vs placebo; AN, abscesses and inflammatory nodules; BL, baseline; LS, least squares; Q2W, every 2 weeks; Q4W, every 4 weeks; SE, standard error.

- Decreases from BL in AN counts at week 16 were greater for the 300 mg abdakibart group vs placebo
- Improvements vs placebo (nominal $p < 0.05$) were observed as early as week 4 in both abdakibart groups

Change From Baseline in DT Count



*Nominal $p < 0.05$ vs placebo. Δ , difference vs placebo; BL, baseline; DT, draining tunnels; LS, least squares; Q2W, every 2 weeks; Q4W, every 4 weeks; SE, standard error.

- The reduction from BL in DT count was greater for both abdakibart groups compared with placebo at week 16
- Improvements vs placebo (nominal $p < 0.05$) were observed as early as week 2 in both abdakibart groups

Conclusions

- In the LOTUS trial, both abdakibart doses demonstrated statistically significantly higher percentages of patients achieving HiSCR75 compared to placebo at week 16 in patients with moderate to severe HS
- Benefits were demonstrated in several secondary endpoints, with greater improvements relative to placebo observed as early as week 2
- No unexpected safety findings were observed with either dose of abdakibart

Treatment-Emergent Adverse Events

TEAE, n (%)	Placebo (n=86)	Abdakibart 150 Q2W (n=83)	Abdakibart 300 Q4W (n=83)
Any TEAE	46 (53.5)	43 (51.8)	46 (55.4)
Any serious TEAE	2 (2.3)	2 (2.4)	1 (1.2)
Any drug-related serious TEAE	0	0	0
Deaths	0	0	0
Any TEAE leading to study drug discontinuation	2 (2.3)	2 (2.4)	1 (1.2)
Most common TEAEs ^a			
Headache	7 (8.1)	7 (8.4)	11 (13.3)
Nasopharyngitis	5 (5.8)	7 (8.4)	1 (1.2)
Nausea	2 (2.3)	2 (2.4)	6 (7.2)
Upper respiratory tract infection	4 (4.7)	4 (4.8)	2 (2.4)
Influenza like illness	3 (3.5)	2 (2.4)	2 (2.4)
Migraine	1 (1.2)	1 (1.2)	3 (3.6)

^aTEAEs reported in ≥ 4 patients in the combined abdakibart groups. Q2W, every 2 weeks; Q4W, every 4 weeks; TEAE, treatment-emergent adverse event.

- Frequency of treatment emergent AEs (TEAEs) were similar between the abdakibart and placebo groups with no unexpected safety findings
- Injection site reaction was reported for 12 patients (placebo, 4 [4.7%]; abdakibart 150 mg Q2W, 3 [3.6%]; abdakibart 300 mg Q4W, 5 [6.0%])
- No AEs of neutropenia, malignancy, hypersensitivity reactions, or serious or opportunistic infections led to study discontinuation

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References: 1. Krueger JG, et al. *Br J Dermatol*. 2024;190:149-162. 2. Kimball AB, et al. *N Engl J Med*. 2016;375:422-434. 3. Kimball AB, et al. *Lancet*. 2023;401:747-761. 4. Ghatt S, et al. *JAMA Dermatol*. 2021;157:1279-1288. 5. Kim J, et al. *J Allergy Clin Immunol*. 2017;152:656-666.

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