

Presentation: D2T01.4

Efficacy and safety of abdakibart, a humanized high affinity and potency IgG4 anti-IL-1 β agent for treatment of moderate to severe hidradenitis suppurativa at week 16; IHS4 subgroup and lesion type ANdT results of the phase 2 placebo-controlled LOTUS Trial

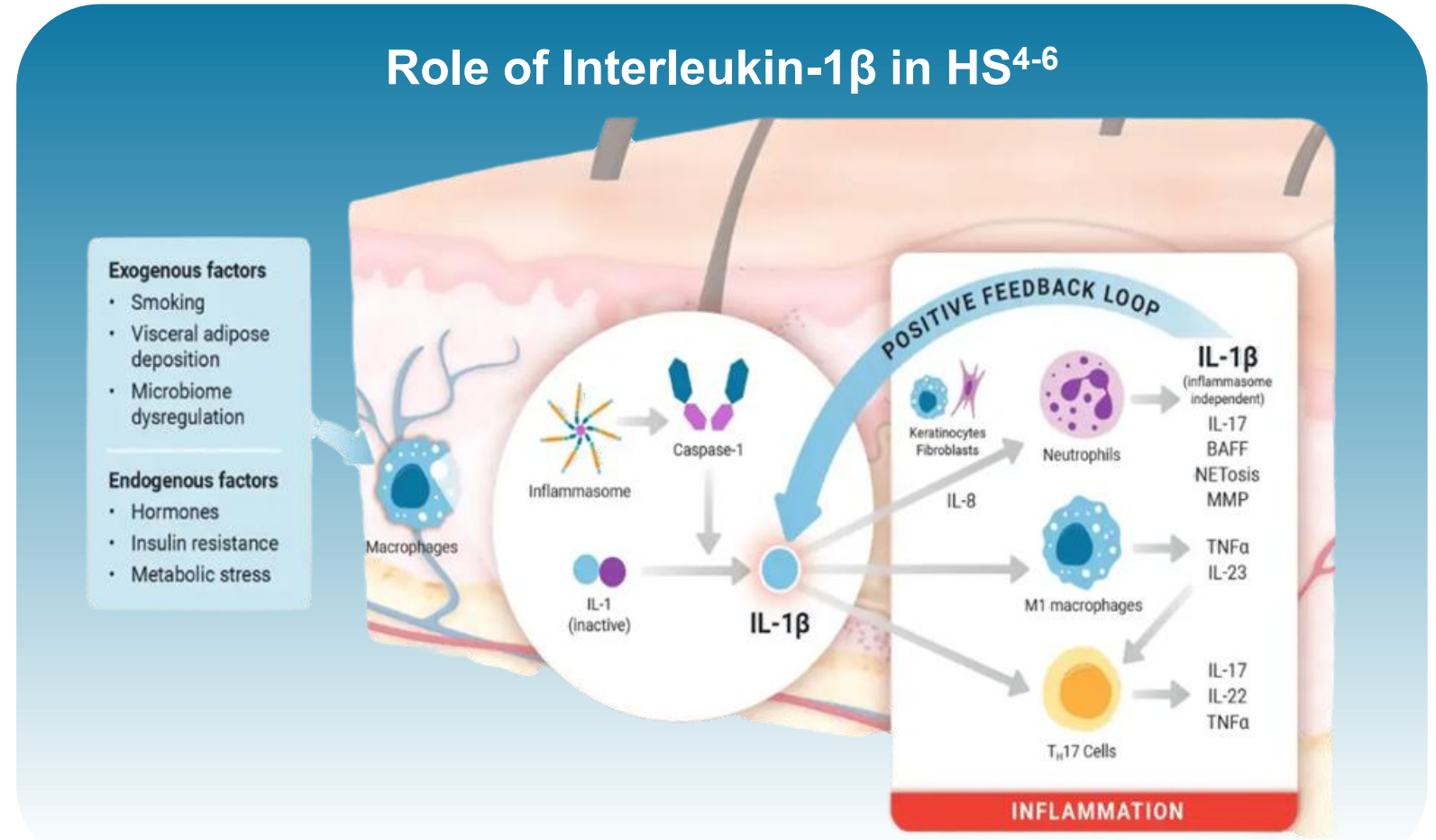
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- Investigator for AnaptysBio, Bayer, Bristol Myers Squibb, OASIS Pharmaceuticals, and Ventyx
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IL-1 β is a key mediator in the pathophysiology of HS

- Interleukin-1 beta (IL-1 β) is a pro-inflammatory cytokine¹
- IL-1 β plays a central role in the pathogenesis of a wide range of human diseases including HS²
- IL-1 β is the primary activator of Th-17 cells in HS³
- IL-1 β gene expression is up to 100x increased in HS lesions compared to skin in healthy controls⁴



Abdakibart, a humanized IgG monoclonal antibody inhibits IL-1 β

Abdakibart Characteristics¹

- Abdakibart selectively inhibits IL-1 β ¹
- Bermekimab, an IL-1 α specific mAb, performed no better than placebo in a phase 2 study with adalimumab comparator arm²
- Despite approval of anti-TNF α and anti-IL17A/F biologics, response to treatment in HS is often suboptimal with high rates of loss of efficacy³⁻⁵



Potential to translate to higher efficacy	IL-1 β	Specificity
	<3 Kd (pM)	IL-1 β binding affinity
	73%	Subcutaneous bioavailability
Potential for less frequent dosing	19 days	Half-life
	Q2W & Q4W	Dosing evaluated in HS study

The LOTUS trial, a phase 2, double-blind, placebo-controlled study, compared the efficacy and safety of abdakibart to placebo in patients with moderate to severe HS

LOTUS: Efficacy and Safety of Abdakibart (AVTX-009) Treatment in Participants With Moderate-to-Severe Hidradenitis Suppurativa (NCT06603077)

Primary Study Endpoint

Percentage of participants achieving HiSCR75 at 16 weeks

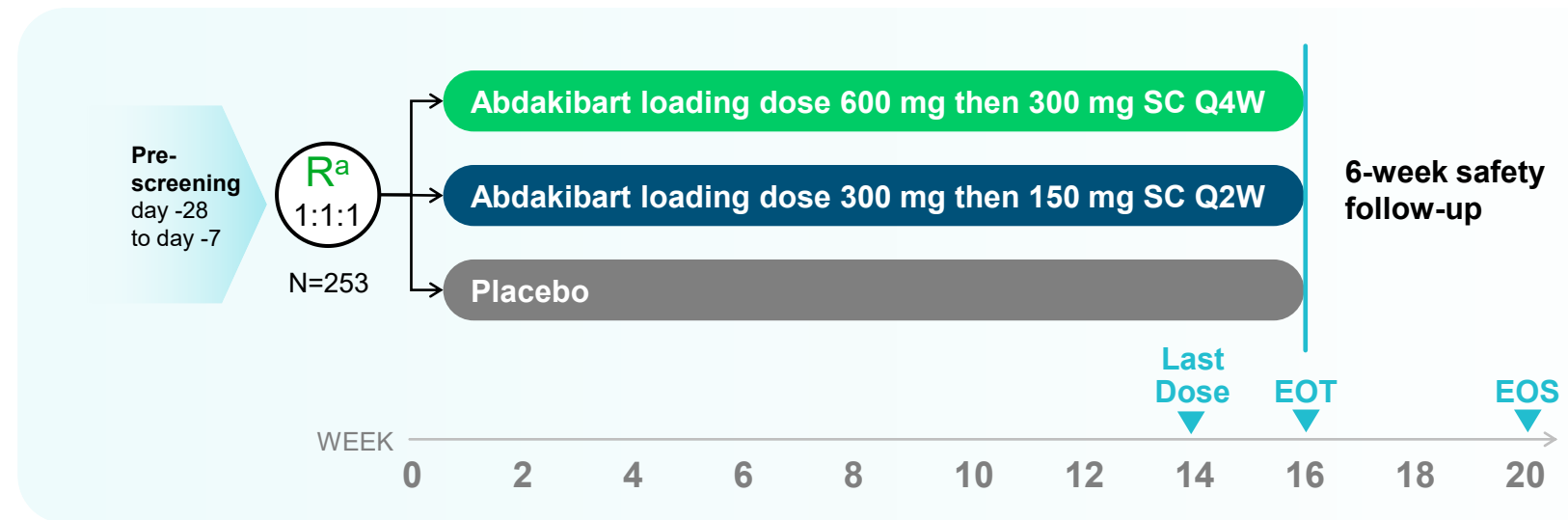
- Both abdakibart groups individually compared to placebo using a closed testing procedure which controlled overall Type 1 error at a 0.05 significance level (2-sided)

Key Secondary Endpoints

- HiSCR50/90 response
- Mean change from baseline in IHS4, AN count, dT count

Key Inclusion Criteria

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



Primary and key secondary endpoints are presented in Poster E2275. Here, we present additional endpoints related to lesion burden.

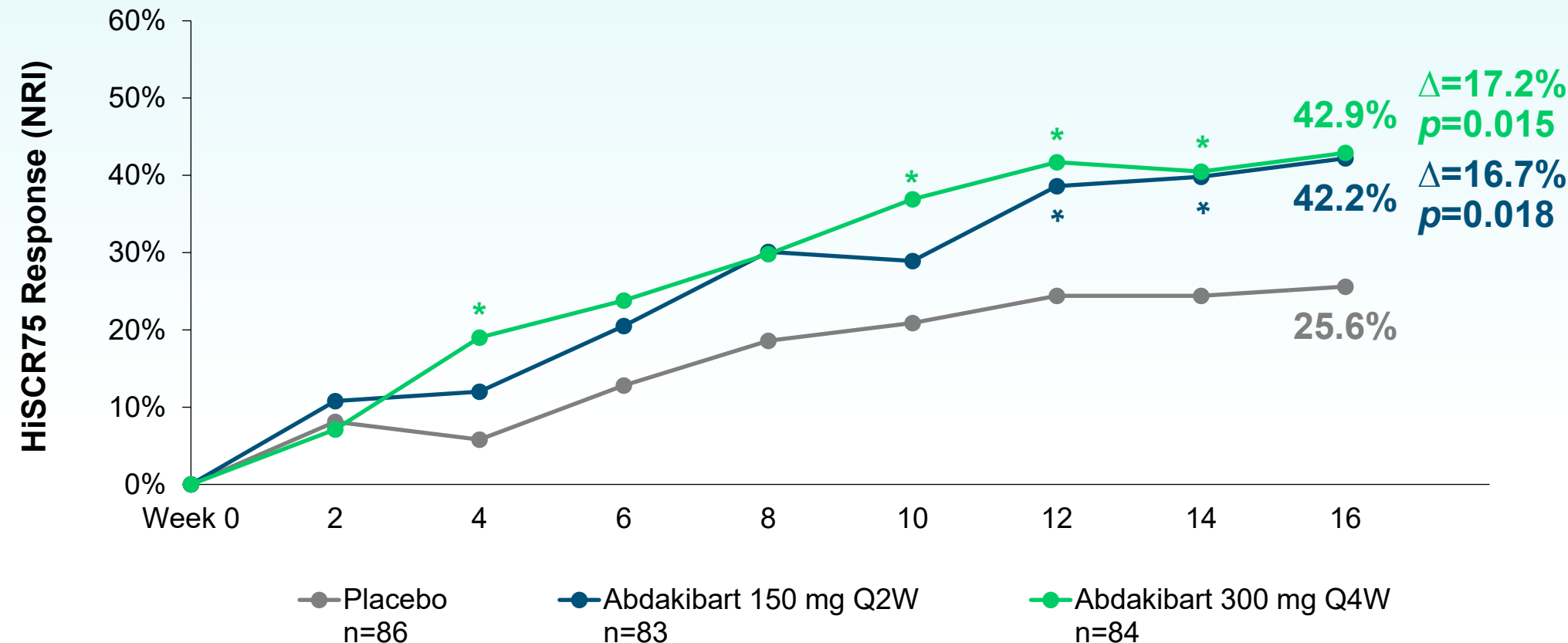
Demographic and baseline characteristics

	Placebo	Abdakibart		
	n=86	150 mg Q2W n=83	300 mg Q4W n=84	Combined n=167
Age , years, mean (SD)	37.7 (11.8)	38.4 (12.1)	39.0 (13.4)	38.7 (12.7)
Gender, female , %	52.3	66.3	63.1	64.7
Race, white , %	66.3	65.1	75.0	70.1
BMI , kg/m ² , mean (SD)	33.9 (8.7)	36.4 (8.9)	34.9 (7.7)	35.7 (8.3)
Current smoker , %	47.7	38.6	42.9	40.7
Duration of HS diagnosis , years, mean (SD)	6.9 (6.3)	9.1 (8.1)	7.8 (9.5)	8.4 (8.8)
Hurley stage III , %	40.7	42.2	44.0	43.1
IHS4 score , mean (SD)	27.5 (19.0)	26.7 (19.1)	29.0 (21.3)	27.9 (20.2)
Abscess count , mean (SD)	2.6 (3.6)	2.3 (3.2)	2.2 (3.0)	2.2 (3.1)
AN count , mean (SD)	13.8 (8.2)	13.5 (8.7)	14.0 (13.8)	13.8 (11.5)
dT count , mean (SD)	2.8 (3.4)	2.7 (2.9)	3.2 (3.7)	3.0 (3.3)
dT count >1 , %	47.7	61.4	59.5	60.5
ANdT count , mean (SD)	16.6 (9.5)	16.2 (10.3)	17.2 (14.4)	16.7 (12.5)
Prior biologics use ,* %	31.4	42.2	39.3	40.7
Concomitant oral antibiotic for HS , %	5.8	7.2	4.8	6.0

*Prior treatment with any biologic for the treatment of HS.

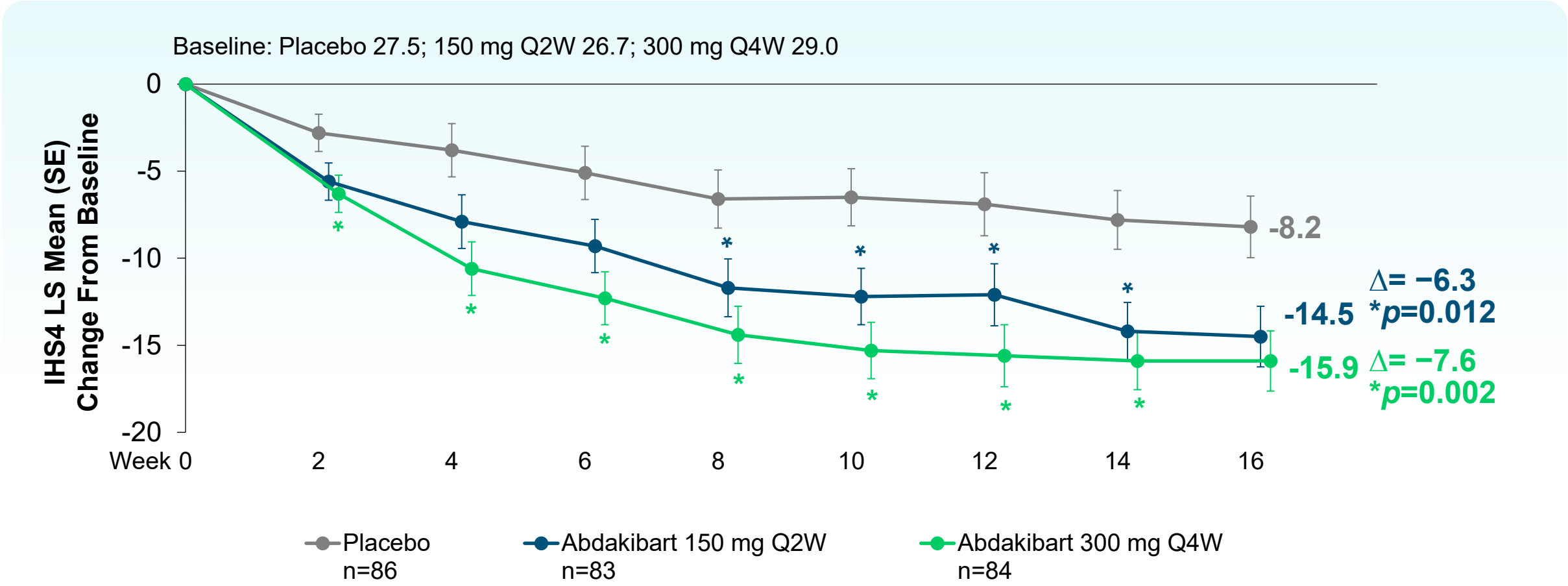
AN, abscess and inflammatory nodule; ANdT, abscesses, inflammatory nodules, and draining tunnels; BMI, body mass index; dT, draining tunnel; HS, hidradenitis suppurativa; IHS4, International Hidradenitis Suppurativa Severity Score System; Q2W, every 2 weeks; Q4W, every 4 weeks; SD, standard deviation.

The primary endpoint of HiSCR75 was met for both dose groups at week 16



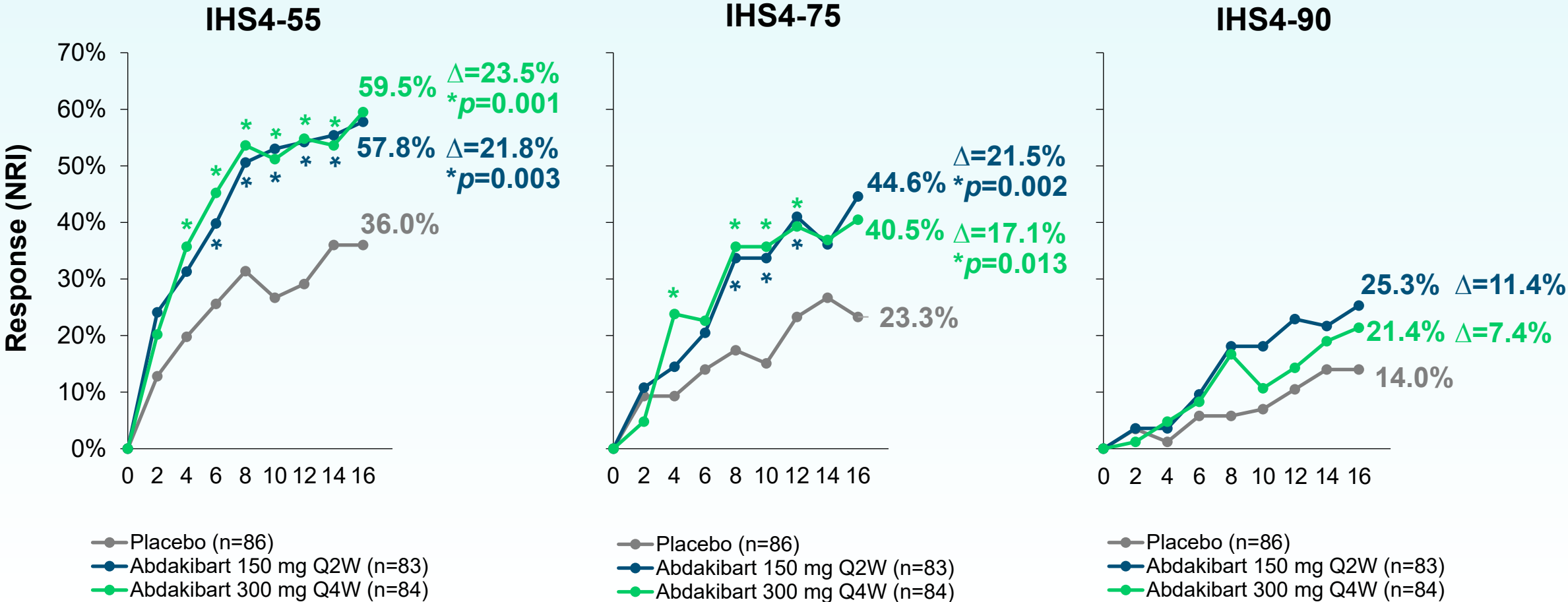
*Nominal $p < 0.05$ vs placebo.
CI, confidence interval; Δ , difference between treatment arm and placebo; HiSCR, Hidradenitis Suppurativa Clinical Response; NRI, non-response imputation; Q2W, every 2 weeks; Q4W, every 4 weeks.
Participants who experience an intercurrent event using the composite strategy (i.e., use of rescue antibiotics before week 16, discontinuation of study treatment due to an adverse event or lack of efficacy) are treated as non-responders following the intercurrent event. Participants with missing data are imputed as non-responders.
Difference in responder rate, corresponding CIs and p-value are obtained using a Mantel-Haenszel (MH) test stratified by the randomization stratification factors. The estimated MH risk difference is summarized along with the two-sided 95% CI using MH stratum weights and the Sato variance estimator.

Statistically significant decreases in IHS4 scores were observed for abdakibart vs placebo



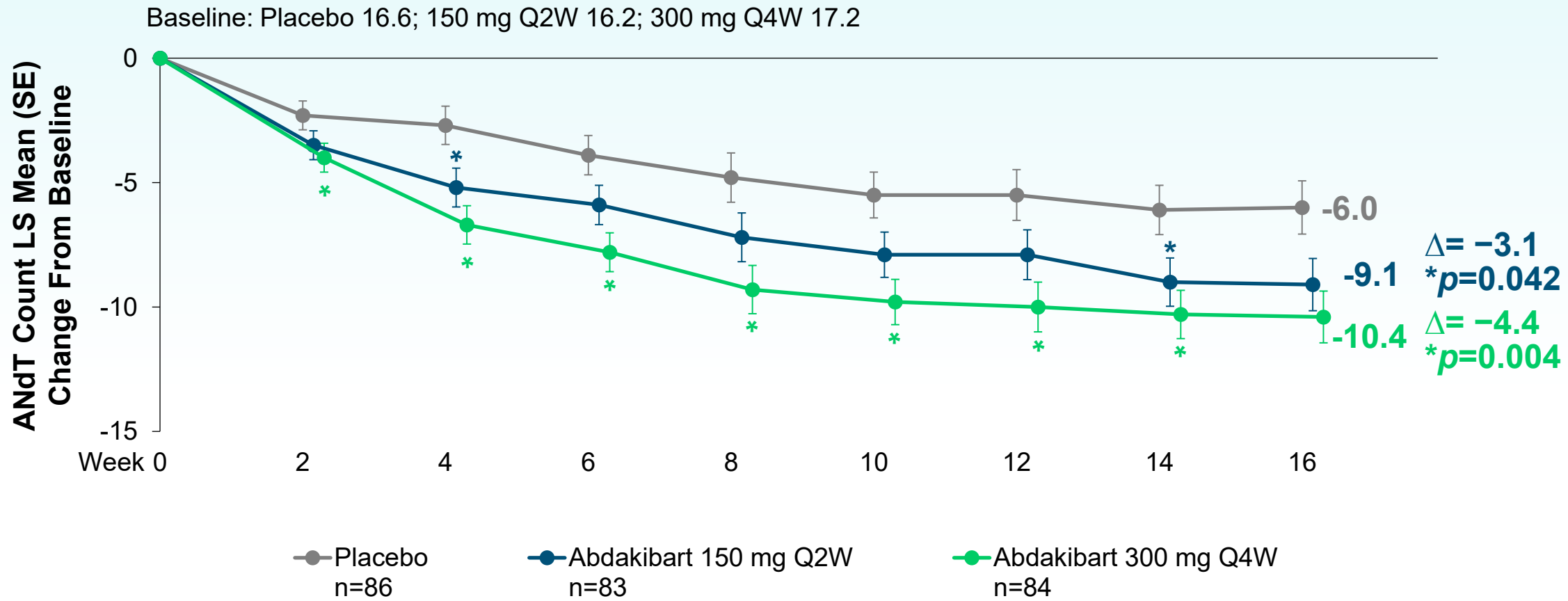
*Nominal $p < 0.05$ vs placebo.
 Δ , difference between treatment arm and placebo; IHS4 International Hidradenitis Suppurativa Severity Score System; LS, least squares; Q2W, every 2 weeks; Q4W, every 4 weeks; SE, standard error.
Data after an intercurrent event using the composite strategy (both missing and observed) are not used in the analysis. All other missing data are left as missing.
LS means are based on a mixed effects model for repeated measures (MMRM) where the change from baseline is the dependent variable, treatment group, visit, treatment-by-visit interaction and the randomization stratification factors (baseline weight [≤ 90 kg, > 90 kg], baseline Hurley Stage [II, III]) are the fixed effects, and baseline score is included as a covariate.

Rates of IHS4-55/75/90 response were greater with abdakibart vs placebo



*Nominal $p < 0.05$ vs placebo.
 CI, confidence interval; Δ, difference between treatment arm and placebo; IHS4 International Hidradenitis Suppurativa Severity Score System; NRI, non-response imputation; Q2W, every 2 weeks; Q4W, every 4 weeks.
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Greater decreases in ANdT count were observed for abdakibart vs placebo



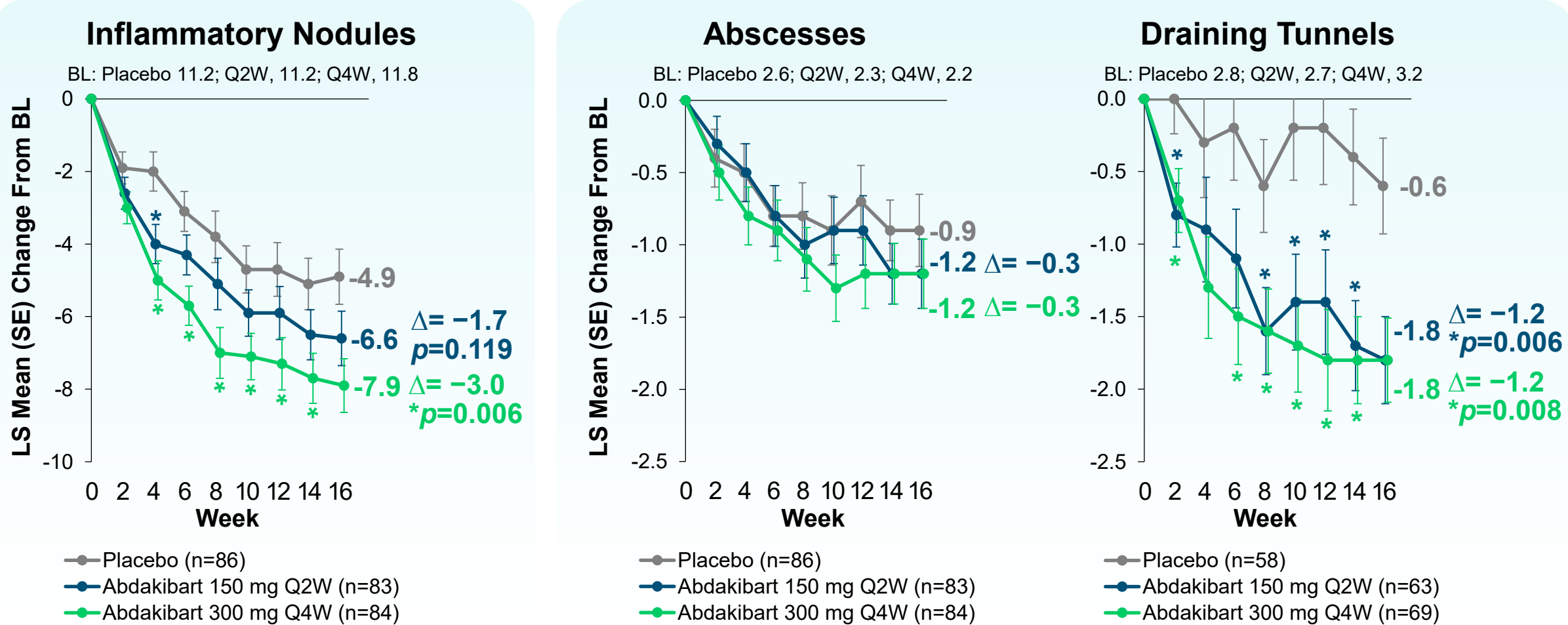
*Nominal $p < 0.05$ vs placebo.

Δ, difference between treatment arm and placebo; ANdT, abscesses, inflammatory nodules, and draining tunnels; ISH4 International Hidradenitis Suppurativa Severity Score System 4; LS, least squares; Q2W, every 2 weeks; Q4W, every 4 weeks; SE, standard error.

Data after an intercurrent event using the composite strategy (both missing and observed) are not used in the analysis. All other missing data are left as missing.

LS means are based on a mixed effects model for repeated measures (MMRM) where the change from baseline is the dependent variable, treatment group, visit, treatment-by-visit interaction and the randomization stratification factors (baseline weight [≤ 90 kg, > 90 kg], baseline Hurley Stage [II, III]) are the fixed effects, and baseline score is included as a covariate.

Greater decreases from baseline in inflammatory nodules, abscesses, and dT were observed for abdakibart vs placebo



*Nominal $p < 0.05$ vs placebo. Nominal p -values for changes from baseline in abscess count with abdakibart vs placebo were > 0.05 at all visits.

Δ , difference between treatment arm and placebo; BL, baseline; LS, least squares; Q2W, every 2 weeks; Q4W, every 4 weeks; SE, standard error.

Data after an intercurrent event using the composite strategy (both missing and observed) are not used in the analysis. All other missing data are left as missing.

LS means are based on a mixed effects model for repeated measures (MMRM) where the change from baseline is the dependent variable, treatment group, visit, treatment-by-visit interaction and the randomization stratification factors (baseline weight [≤ 90 kg, > 90 kg], baseline Hurley Stage [II, III]) are the fixed effects, and baseline score is included as a covariate.

Rates of TEAEs, including SAEs were similar to placebo; few adverse events of special interest were reported

	Placebo	Abdakibart	
		150 mg Q2W	300 mg Q4W
Participants, n (%)	n=86	n=83	n=83
Any TEAE*	46 (53.5)	43 (51.8)	46 (55.4)
Any TESAE	2 (2.3)	2 (2.4)	1 (1.2)
Non-cardiac chest pain	0	0	1 (1.2)
Major depressive disorder	0	1 (1.2)	0
Hidradenitis	2 (2.3)	1 (1.2)	0
Any TEAE leading to study drug discontinuation	2 (2.3)	2 (2.4)	1 (1.2)
Deaths	0	0	0

	Placebo	Abdakibart	
		150 mg Q2W	300 mg Q4W
Participants, n (%)	n=86	n=83	n=83
Hypersensitivity reaction	0	0	0
Injection site reaction	4 (4.7)	3 (3.6)	5 (6.0)
Leukopenia	0	0	0
Neutropenia	0	0	0
Serious infections	0	0	0
MACE	0	0	0
Malignancy	0	0	0
Opportunistic infections	0	0	0
Tuberculosis	0	0	0

MACE, major adverse cardiovascular event; Q2W, every 2 weeks; Q4W, every 4 weeks; SAE, serious adverse event; TEAE, treatment emergent adverse event; TESAE, treatment emergent serious adverse event.

One participant randomized to abdakibart 300 mg Q4W did not receive study drug and therefore is not included in safety population.

*The most common TEAE reported in all 3 treatment groups was headache.

Conclusions

LOTUS enrolled patients with moderate to severe HS, including both biologic naïve as well as patients with prior exposure ($\approx 40\%$ in the abdakibart arms) to anti-TNF and/or anti-IL17 agents

Using a rigorous testing procedure, the primary endpoint of HiSCR75 response was met for both abdakibart dose groups in the phase 2 LOTUS trial in participants with moderate to severe HS

Efficacy of abdakibart was demonstrated with rapid ($< 2\text{-}4$ weeks) improvements in clinically meaningful outcomes, including HiSCR, IHS4 scores, IHS4-55/75, inflammatory nodule count, dT count, and ANdT count

Abdakibart was well-tolerated with a favorable safety profile through week 20

These findings validate IL-1 β as a promising new mechanism and support further investigation of abdakibart for the treatment of moderate to severe HS



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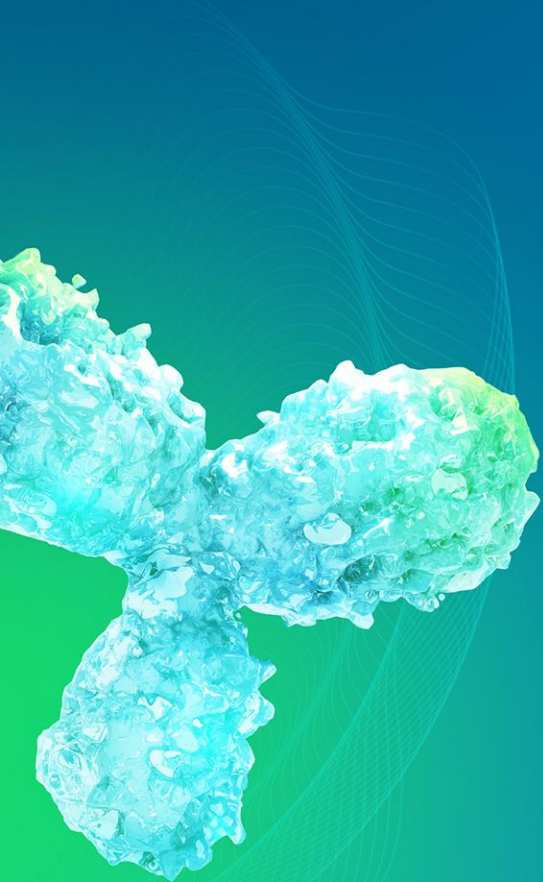
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