Spesolimab for hidradenitis suppurativa: A proof-of-concept study

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A Phase IIa proof-of-clinical-concept study in patients with moderate-to-severe hidradenitis suppurativa (HS)

AIM

This Phase IIa proof-of-clinical-concept study aimed to explore the effect of spesolimab, an anti-IL-36R monoclonal antibody,[1] in patients with moderate-to-severe HS

INTRODUCTION

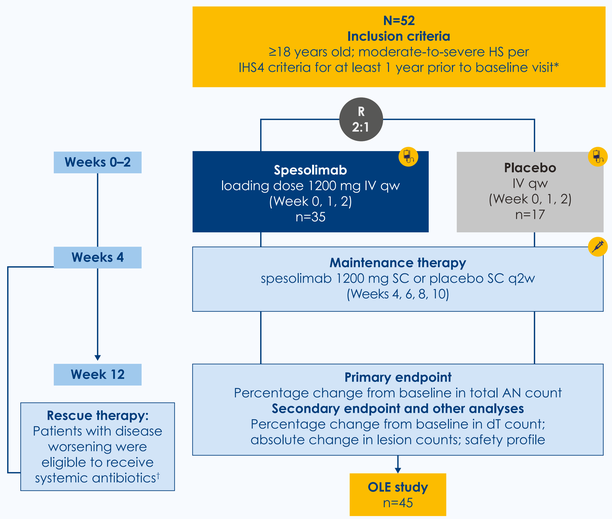
- HS is a chronic, recurrent inflammatory disorder characterized by painful abscesses (A), inflammatory nodules (N), and draining tunnels (dT) primarily affecting inverse body regions with skin folds, and it has a high unmet need for effective targeted therapies.[2] IL-36 signaling has been implicated in the HS inflammatory network

METHODS

- This was an exploratory study. No formal statistical testing was performed; results are descriptive

Study design (NCT04762277)

EudraCT protocol 2020-003672-40



*Patients eligible for inclusion also had HS lesions in ≥2 distinct body areas; total AN count ≥5; total dT count ≤20; were biologic-naïve or had failed on previous TNF-α inhibitor treatment for HS and had an inadequate response to oral antibiotics for HS in the past year.
†HS disease worsening was defined as a 150% increase in AN count from baseline; rescue monotherapy with either doxycycline 100 mg orally twice daily, or an alternative per investigator discretion could be given for a maximum of 2 weeks, and for not more than a total of 4 weeks over the course of the study.

CONCLUSIONS

- Overall, these results support the development of spesolimab in HS
- Changes in total AN count were similar between treatment groups at Week 12. However, all lesion types decreased with spesolimab treatment
- A greater proportion of patients in the spesolimab arm experienced a decrease in dT count at Week 12 than in the placebo arm
- Spesolimab was generally well tolerated, in line with previous trials in other indications

RESULTS

Baseline patient demographics

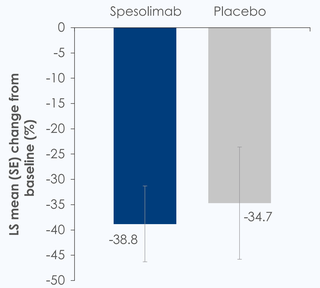
Characteristic	Spesolimab (n=35)	Placebo (n=17)
Sex, n (%)		
Female	21 (60.0)	10 (58.8)
Male	14 (40.0)	7 (41.2)
Age, years, mean (SD)	35.7 (11.3)	34.1 (11.0)
HS severity*, n (%)		
Moderate	8 (22.9)	2 (11.8)
Severe	27 (77.1)	15 (88.2)
AN count, mean (SD)	11.6 (9.3)	18.9 (15.7)
Inflammatory nodule count, mean (SD)	9.5 (9.3)	15.6 (12.2)
Draining tunnel count, mean (SD)	3.6 (4.0)	4.5 (4.6)

*HS severity was based on IHS4 criteria.

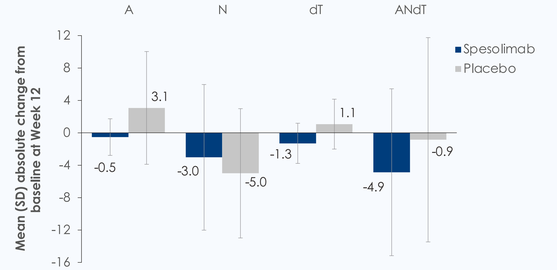
Baseline characteristics were similar between spesolimab and placebo groups

Change from baseline in the primary endpoint and all lesion types

Percentage change from baseline in total AN count



Absolute change from baseline in lesion counts at Week 12

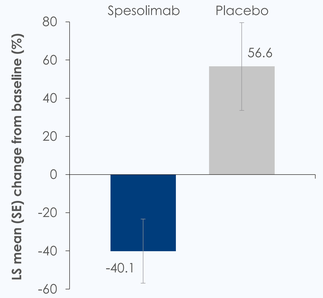


LS means were estimated by REML-based MMRM including the fixed, categorical effects of treatment at each visit, prior use of TNF-α inhibitor strata and the continuous effect of baseline at each visit as well as random effects of subject. Analyses used data up to the use of rescue therapy; data after the use of rescue therapy were censored. Results are presented descriptively; patients with non-missing values are included in the summary.

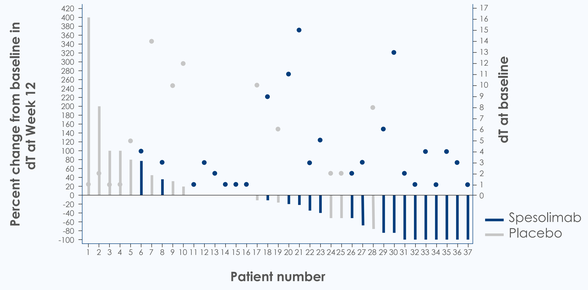
A decrease in all lesion types was observed in the spesolimab arm by Week 12

Change from baseline in dT count

Percentage change from baseline in dT count



Percentage change from baseline in dT count: individual patient data



66.7% of patients in the spesolimab arm (16/24) **vs 38.5% of patients** in the placebo arm (5/13) had a **decrease from baseline in dT** at Week 12.

LS means, differences and confidence intervals were estimated by REML-based MMRM including the fixed, categorical effects of treatment at each visit, prior use of TNF-α inhibitor strata and the continuous effect of baseline at each visit as well as random effects of subject. Analyses used data up to the use of rescue therapy; data after the use of rescue therapy were censored.

A greater proportion of patients in the spesolimab vs the placebo arm had a decrease from baseline in dT at Week 12

Adverse Events

AEs up to Week 12, n (%)	Spesolimab (n=36)*	Placebo (n=16)
Any AE	28 (77.8)	14 (87.5)
Severe AEs‡	0	0
Investigator-defined drug-related AEs‡	15 (41.7)	3 (18.8)
AEs leading to treatment discontinuation	0	1 (6.3)
Investigator defined AESIs	0	0
Most common AEs§		
Headache	4 (11.1)	3 (18.8)
Nasopharyngitis	3 (8.3)	3 (18.8)
Nausea	4 (11.1)	0
Fatigue	4 (11.1)	0
Injection site erythema	4 (11.1)	0
Injection site pain	3 (8.3)	1 (6.3)

*At Week 2, two patients received inverted treatment; therefore, 36 patients were exposed to spesolimab.
‡Severe AEs were those with an RCTC Grade of 3 or 4.
†The higher percentage of drug-related AEs in the spesolimab arm was mostly due to injection site reactions.
§At the preferred term level.

The safety profile of spesolimab was in line with previous trials; no patient receiving spesolimab had a serious AE

Abbreviations
AN, abscess and inflammatory nodule; ANdT, abscess, inflammatory nodule and draining tunnel; AE, adverse event; AESI, adverse event of special interest; dT, draining tunnel; HS, hidradenitis suppurativa; IHS4, International Hidradenitis Suppurativa Severity Score System; IV, intravenous; LS, least squares; MMRM, mixed model repeated measures; OLE, open-label extension; qw, once weekly; q2w, once every 2 weeks; R, randomized; RCTC, Rheumatology Common Toxicity Criteria; REML, restricted maximum likelihood; SC, subcutaneous; SD, standard deviation; SE, standard error; TNF, tumor necrosis factor.

References
1. Bachelez H, et al. *N Engl J Med* 2021;385:2431–2440. 2. Zouboulis CC, et al. *Dermatology* 2015;231:184–190.

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