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

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Overall, data from this phase IIa PoCC study, and interim analyses from the ongoing OLE study, support the development of spesolimab in HS

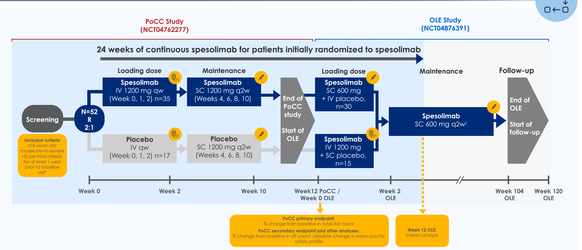
AIM

Here, for the first time, we present results from patients with HS who were treated continuously with spesolimab over a 24-week period; including data from Week 12 of a phase IIa PoCC study, and further interim analyses from Week 12 of an ongoing OLE study

INTRODUCTION

- HS is a chronic, debilitating, recurrent inflammatory disorder characterized by painful abscesses, inflammatory nodules, and draining tunnels[1,2]
  - These lesions typically affect inverse body regions with skin folds, such as the axillary, groin, gluteal, and perianal regions
  - There is a high unmet need for effective targeted therapies
- The pro-inflammatory IL-36 signaling pathway has been implicated in the HS inflammatory network[3]
  - Spesolimab, an anti–IL-36R monoclonal antibody, selectively inhibits IL-36R signaling and downstream inflammatory pathways

METHODS



*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.
[1]At Week 12, patients could have their dose of spesolimab increased to SC 1200 mg q2w if required (based on change in HS-PGA score from baseline).
No formal statistical testing was performed. Last dose was given at Week 104.
In the PoCC study, patients with disease worsening were eligible to receive systemic antibiotics; HS disease worsening was defined as ≥ 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

- In the PoCC study, total counts for all HS lesions decreased over 12 weeks of treatment with spesolimab
  - Moreover, a greater proportion of patients in the spesolimab arm experienced a decrease in dT count at Week 12 than in the placebo arm
- The observed decreases in lesion counts and the percentage change in dTs were sustained over 24 weeks of continuous spesolimab treatment
- Similarly, patients treated with spesolimab had a decrease in IHS4 score that was sustained up to Week 24 of continuous spesolimab treatment
- Patients previously randomized to placebo also had a decrease in HS lesion count and IHS4 score at Week 12 of the OLE
- Spesolimab was generally well-tolerated, in line with previous trials in other indications

RESULTS

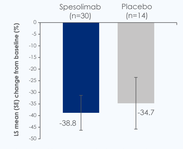
Baseline demographics and clinical characteristics

Characteristic	Baseline PoCC study N=52		Baseline OLE study N=45	
	Spesolimab (n=35)	Placebo (n=17)	Spesolimab-to-spesolimab (n=30)	Placebo-to-spesolimab (n=15)
Sex, n (%)				
Female	21 (60.0)	10 (58.8)	19 (63.3)	8 (53.3)
Male	14 (40.0)	7 (41.2)	11 (36.7)	7 (46.7)
Age, years, mean (SD)	35.7 (11.3)	34.1 (11.0)	35.5 (10.8)[1]	35.7 (10.7)[1]
BMI, kg/m², mean (SD)	33.2 (8.2)	30.4 (5.6)	33.4 (8.4)	30.6 (5.7)
Prior TNFi treatment, n (%)				
TNFi-failure	10 (28.6)	4 (23.5)	9 (30.0)	3 (20.0)
TNFi-naïve	25 (71.4)	13 (76.5)	21 (70.0)	12 (80.0)
HS severity*, n (%)				
Mild	0	0	3 (10.0)	2 (13.3)
Moderate	8 (22.9)	2 (11.8)	14 (46.7)	2 (13.3)
Severe	27 (77.1)	15 (88.2)	13 (43.3)	11 (73.3)
AN count, mean (SD)	11.6 (9.3)	18.9 (15.7)	7.5 (15.5)	17.7 (23.4)
Inflammatory nodule count, mean (SD)	9.5 (9.3)	15.6 (12.2)	6.8 (15.4)	11.9 (15.8)
dT count, mean (SD)	3.6 (4.0)	4.5 (4.6)	2.1 (3.1)	5.9 (6.0)

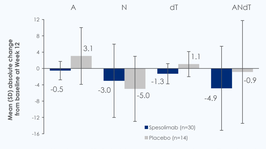
*HS severity was based on IHS4 criteria.
[1]For the OLE study, baseline age refers to the mean age at the beginning of the PoCC study.

Efficacy: Week 12 data from PoCC study

Percentage change from baseline in total AN count



Absolute change from baseline in lesion counts at Week 12

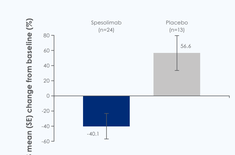


LS means were estimated by REML-based MMRM including the fixed, categorical effects of treatment at each visit, prior use of TNF-α inhibitor strata, and the continuous effect of baseline at each visit as well as random effects of subject. Analyses use data up to the use of rescue therapy; data after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

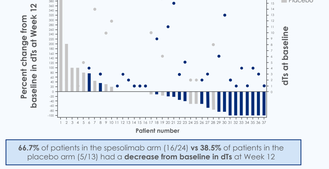
A decrease in all lesion types was observed in the spesolimab arm by Week 12

Efficacy: Week 12 data from PoCC study

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 dTs** at Week 12

LS means, differences, and CIs 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 use data up to the use of rescue therapy; data after the use of rescue therapy are censored.

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

Efficacy: Interim analysis OLE at Week 12

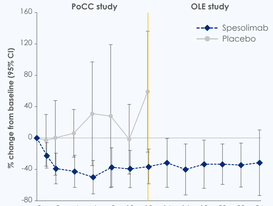
Measure	Baseline* (defined as the last observation before the first dose of spesolimab)		Week 12 of OLE		Absolute change from baseline to Week 12 of OLE	
	Spesolimab-to-spesolimab n=26 (Week 0 of PoCC)	Placebo-to-spesolimab n=13 (Week 0 of OLE)	Spesolimab-to-spesolimab (24 weeks of treatment) n=26	Placebo-to-spesolimab (12 weeks of treatment) n=13	Spesolimab-to-spesolimab (24 weeks of treatment) n=26	Placebo-to-spesolimab (12 weeks of treatment) n=13
Abscess count Mean	1.5	5.4	1.2	3.5	**-0.2**	**-1.9**
Inflammatory nodule count Mean	10.3	10.3	6.3	8.6	**-4.1**	**-1.7**
dT count Mean	3.6	5.4	2.3	4.5	**-1.3**	**-0.9**
IHS4 score Mean	27.7	42.6	18.0	33.7	**-9.8**	**-8.9**
DLQI score Mean	15.1	9.9	11.9[1]	12.5	**-3.2**[1]	**2.5**

*Baseline data are given for the subset of patients with data available at Week 12 (n=26 for prior spesolimab, n=13 for prior placebo). [1]n=27. Patients in the spesolimab-to-spesolimab arm received spesolimab for 12 weeks in the PoCC study, and a further 12 weeks in the OLE study; patients in the placebo-to-spesolimab arm received spesolimab for 12 weeks in the OLE study only.

After 24 weeks of continuous spesolimab treatment, sustained decreases from baseline were observed in AN, dT, and IHS4 score

Efficacy: Over 24 weeks of spesolimab treatment

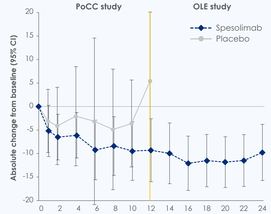
Percentage change from baseline in dT count



Number of patients:

Placebo	13	13	13	13	13	13	13	13	13															
Spesolimab	24	22	24	23	22	22	24	22	23	23	24	22	20	21										

Absolute change from baseline in IHS4



Number of patients:

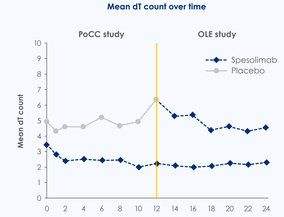
Placebo	15	15	15	15	14	15	15	14																
Spesolimab	30	27	30	29	27	28	30	27	29	29	30	28	25	26										

Patients in the spesolimab-to-spesolimab arm received spesolimab for 12 weeks in the PoCC study, and a further 12 weeks in the OLE study; patients in the placebo-to-spesolimab arm received spesolimab for 12 weeks in the OLE study only.

Decreases from baseline in dT count and IHS4 score observed in the 12-week PoCC study were sustained over the first 12 weeks of the OLE study

Efficacy at Week 24 across treatment arms

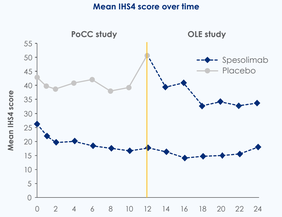
Mean dT count over time



Number of patients:

Placebo	15	15	15	15	14	15	15	14	14	14	13	13	13	13										
Spesolimab	30	27	30	29	27	28	30	27	29	29	30	28	25	26										

Mean IHS4 score over time



Number of patients:

Placebo	15	15	15	15	14	15	15	14	14	14	13	13	13	13										
Spesolimab	30	27	30	29	27	28	30	27	29	29	30	28	25	26										

Patients in the spesolimab-to-spesolimab arm received spesolimab for 12 weeks in the PoCC study, and a further 12 weeks in the OLE study; patients in the placebo-to-spesolimab arm received spesolimab for 12 weeks in the OLE study only.

Decreases in dT count and IHS4 score were observed in patients after switching from placebo to spesolimab

Safety profile

AEs up to Week 12, n (%)	PoCC study (Week 1–12)		OLE study (Week 12–24)	
	Spesolimab (n=36)*	Placebo (n=16)	Spesolimab-to-spesolimab (n=30)	Placebo-to-spesolimab (n=15)
Any AE	28 (77.8)	14 (87.5)	21 (70.0)	9 (60.0)
Severe AEs[‡]	0	0	1 (3.3)	0
Serious AEs[‡]	0	1 (6.3)	1 (3.3)	1 (6.7)
Investigator-defined drug-related AEs[§]	15 (41.7)	3 (18.8)	9 (30.0)	3 (20.0)
AEs leading to treatment discontinuation	0	1 (6.3)	1 (3.3)	2 (13.3)
Investigator-defined AESIs	0	0	0	0
Most common AEs[¶]				
Headache	4 (11.1)	3 (18.8)	3 (10.0)	0
Nasopharyngitis	3 (8.3)	3 (18.8)	1 (3.3)	0
Nausea	4 (11.1)	0	0	0
Fatigue	4 (11.1)	0	0	0
Injection site erythema	4 (11.1)	0	2 (6.7)	0
Injection site pain	3 (8.3)	1 (6.3)	2 (6.7)	0

Data cut-off at Week 12 of the OLE trial: Last Patient Completed April 21, 2022
*2 patients received inverted treatment at Week 2; therefore, 36 patients were exposed to spesolimab. ‡Severe AEs were those with an RCTC Grade of 3 or 4. [†]1 patient in the OLE study treated with prior placebo was reported to have an unrelated event of acute hepatitis C; 1 patient in the OLE study was reported to have Guillain-Barré syndrome by the investigator and was assessed as causally related by the investigator. A panel of independent neurologists deemed this as a case of peripheral neuropathy. A causal association with spesolimab was assessed to be unlikely by the panel.
§The higher percentage of drug-related AEs in the spesolimab arm is mostly due to injection site reactions. ¶At the preferred term level.

Spesolimab had a favorable safety profile, and was in line with previous trials

Abbreviations

A, abscess; AE, adverse event; AESI, adverse event of special interest; AN, abscess and inflammatory nodule; ANdT, abscess, inflammatory nodule and draining tunnel; BMI, body mass index; CI, confidence intervals; DLQI, Dermatology Life Quality Index; dT, draining tunnel; HS, hidradenitis suppurativa; HS-PGA, hidradenitis suppurativa Physician Global Assessment; IHS4, International Hidradenitis Suppurativa Severity Score System; IL-36, interleukin-36; IL-36R, interleukin-36 receptor; IV, intravenous; LS, least squares; MMRM, mixed model repeated measures; OLE, open-label extension; PoCC, proof-of-clinical-concept; REML, restricted maximum likelihood; qw, every week; q2w, every 2 weeks; RCTC, Rheumatology Common Toxicity Criteria; SC, subcutaneous; SD, standard deviation; SE, standard error; TNF-α, tumor necrosis factor alpha; TNFi, tumor necrosis factor inhibitor.

References

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2. Zouboulis CC, et al. *Dermatology* 2015;231:184–190.
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Disclosures & Acknowledgments

This study was supported and funded by Boehringer Ingelheim.

AA is a consultant for AbbVie, Boehringer Ingelheim, Infiaflx, Kymera, Novartis, and UCB, and investigator for Boehringer Ingelheim and Processa Pharmaceuticals. **EP** is a consultant and advisory board member for, and has received speaker fees from AbbVie, Amgen, AstraZeneca, Baxter, Celgene, ChemoCentryx, Eli Lilly, Galderma, Infiaflx, Janssen, LEO Pharma, Novartis, Pfizer, Sandoz, and UCB, and grant support (to Erasmus Medical Center) from AbbVie, Celgene, Center for Human Drug Research, Novartis, Pfizer, Janssen, and UCB. **ABK** is a consultant and investigator for AbbVie, Bristol Myers Squibb, Janssen, Eli Lilly, Novartis, Pfizer, and UCB; an investigator for Incyte and AnaptysBio; a consultant for Bayer, Boehringer Ingelheim, Ventyx Biosciences, MoonLake, Eli Lilly, Concert Pharma, Evommune, Sonoma Bio, and Sanofi; receives fellowship funding from Janssen and AbbVie; and serves on the Board of Directors for Almirall. **JGK** declares receiving consultant fees/honoraria from AbbVie, Aclaris Therapeutics, Allergan, Almirall, Amgen, Arena, Aristea, Asana Biosciences, Aurigene, Bausch Health, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Escalier Biosciences, Galapagos, Janssen, Eli Lilly, MoonLake, Nimbus, Novartis, Pfizer, Sanofi, Sienna Biopharmaceuticals, Sun Pharmaceutical Industries, Target PharmaSolutions, UCB, and Ventyx Biosciences, and grant support (to The Rockefeller University) from AbbVie, Airos, Allergan, Amgen, Avillion, Biogen, Botanix, Boehringer Ingelheim, Bristol Myers Squibb, Escure, Innovaderm Research, Incyte, Janssen, Kyowa Kirin, Eli Lilly, Nimbus Lakshmi, Novan, Novartis, Pfizer, Regeneron, UCB, and Vitae Pharmaceuticals. **SM, HW, NBI,** and **ACHD** are employees of Boehringer Ingelheim International GmbH. **CCZ** declares receiving disease-relevant consultancy fees/honoraria from AbbVie, Bayer, Boehringer Ingelheim, Incyte, Infiaflx, Janssen, Novartis, Regeneron, and UCB; has received speaker fees from AbbVie, Almirall, and UCB; is President of the European Hidradenitis Suppurativa Foundation e.V., Coordinator of the ALLOCATE skin group of EBN Skin, and Chair of the Acne, Rosacea and Hidradenitis Suppurativa Task Force group of the European Academy of Dermatology and Venereology; is Editor of the *European Academy of Dermatology and Venereology* News, and co-copyright holder of IHS4 on behalf of the EHSF e.V.; and his employer has received disease-relevant grants from AbbVie, Boehringer Ingelheim, Infiaflx, Novartis, and UCB for his participation as a clinical investigator.
The authors met criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors did not receive payment related to the development of this poster. Boehringer Ingelheim was given the opportunity to review the poster for medical and scientific accuracy, as well as intellectual property considerations. Isabella Goldsbrough, PhD, of Hyperion, OPEN Health Communications, provided writing, editorial, and formatting support, which was contracted and funded by Boehringer Ingelheim.

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Presented at: Fall Clinical Dermatology Conference® 23, Las Vegas, NV, USA; October 19–22, 2023.
Originally presented at: 25th World Congress of Dermatology (WCD), Singapore; July 3–8, 2023.