Spesolimab efficacy in patients with a generalized pustular psoriasis (GPP) flare according to the presence of systemic inflammation at baseline

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Treatment with spesolimab led to rapid pustular and skin clearance compared with placebo, irrespective of baseline systemic inflammation in patients with GPP presenting with a flare

PURPOSE

To determine the efficacy and safety of spesolimab according to the extent of baseline systemic inflammation in patients with GPP presenting with a flare.

INTRODUCTION

- GPP is a rare, potentially life-threatening neutrophilic skin disease characterised by episodes of widespread eruption of sterile pustules that can occur with or without systemic inflammation and symptoms[1,2]
- Effisayil™ 1 (NCT03782792) was a global, multicentre, randomised, double-blind, placebo-controlled study of spesolimab, an anti-IL-36 receptor antibody, in patients with GPP presenting with a flare. At Week 1:[3]
  - The primary endpoint (GPPGA pustulation subscore of 0: no visible pustules) was achieved by 54% of patients receiving spesolimab vs 6% receiving placebo (two-sided p<0.001)
  - The key secondary endpoint (GPPGA total score of 0 or 1: clear or almost clear skin) was achieved by 43% of patients receiving spesolimab vs 11% receiving placebo (two-sided p=0.02)
- Here we report a subgroup analysis of the Effisayil™ 1 study, comparing patient characteristics and assessing the effects of spesolimab in patients with a GPP flare with or without systemic inflammation at baseline

CONCLUSIONS

- Baseline characteristics and demographics were consistent between patients with and without systemic inflammation; however, patients with systemic inflammation at baseline had more extensive and severe skin lesions than those without, and patients with elevated CRP were more likely to be hospitalised than those without elevated CRP
- Spesolimab achieved rapid pustular and skin clearance compared with placebo, irrespective of baseline systemic inflammation, and these effects were sustained until the end of the 12-week study
- SAEs were more common in patients with systemic inflammation at baseline than those without. SAEs and AEs were comparable between spesolimab and placebo arms
- These data support the use of spesolimab to treat GPP flares in patients with or without systemic inflammation

METHODS

- In Effisayil™ 1, 53 patients with a GPP flare were randomised 2:1 to receive a single dose of IV spesolimab 900 mg or placebo and followed for 12 weeks
- Patients could receive optional OL spesolimab on Day 8 for persistent flare symptoms; any use of other medication to treat GPP or use of spesolimab to treat a new GPP flare was considered non-response
- Patients were assigned to subgroups based on systemic inflammation at baseline, defined as an elevated CRP (>ULN [10 mg/L]) or elevated neutrophil count (>ULN [7.23x10^9/L])
- Scan the QR code at the bottom of the poster for full study design details

RESULTS

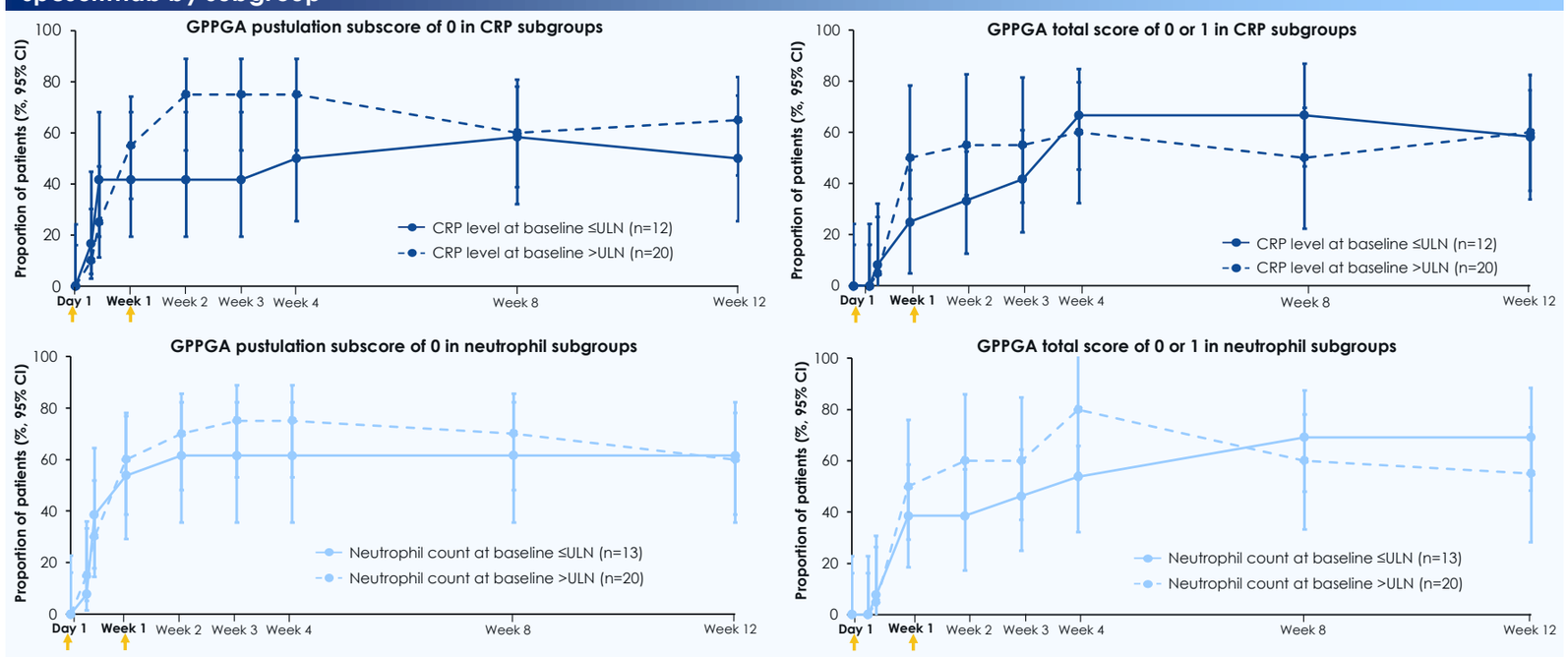
Baseline demographics and characteristics by subgroup

Characteristic	Baseline CRP ≤ULN (n=15)	Baseline CRP >ULN (n=33)	Baseline neutrophils ≤ULN (n=19)	Baseline neutrophils >ULN (n=30)
Mean age, years (SD)	45.8 (11.2)	42.0 (11.3)	46.1 (8.8)	39.9 (11.7)
Mean weight, kg (SD)	81.3 (36.5)	67.8 (16.9)	69.0 (17.6)	71.2 (24.6)
BMI, kg/m^2 (SD)	29.4 (11.5)	25.7 (6.0)	25.3 (6.5)	27.4 (8.2)
Sex, n (%)				
Female	9 (60.0)	22 (66.7)	12 (63.2)	22 (73.3)
Male	6 (40.0)	11 (33.3)	7 (36.8)	8 (26.7)
Race, n (%)				
Asian	9 (60.0)	18 (54.5)	14 (73.7)	15 (50.0)
White	6 (40.0)	15 (45.5)	5 (26.3)	15 (50.0)
Pooled study site, n (%)				
US	3 (20.0)	0	0	2 (6.7)
Japan	2 (13.3)	0	2 (10.5)	0
Asia (excluding Japan)	5 (33.3)	18 (54.5)	11 (57.9)	14 (46.7)
Europe	5 (33.3)	10 (30.3)	4 (21.1)	10 (33.3)
Africa	0	5 (15.2)	2 (10.5)	4 (13.3)
Present/past occurrence of psoriasis, n (%)				
Yes	9 (60.0)	26 (78.8)	13 (68.4)	23 (76.7)
No	4 (26.7)	6 (18.2)	6 (31.6)	5 (16.7)
Missing	2 (13.3)	1 (3.0)	0	2 (6.7)
Ongoing plaque psoriasis, n (%)				
Yes	3 (20.0)	6 (18.2)	4 (21.1)	5 (16.7)
No	12 (80.0)	27 (81.8)	15 (78.9)	25 (83.3)
IL36RN* mutation, n (%)	3 (20.0)	8 (24.2)	5 (26.3)	8 (26.7)
Baseline CRP (mg/L), n (%)				
<3	5 (33.3)	0	2 (10.5)	2 (6.7)
≥3 to <70	10 (66.7)	18 (54.5)	9 (47.4)	17 (56.7)
≥70	0	15 (45.5)	6 (31.6)	9 (30.0)
Missing	0	0	2 (10.5)	2 (6.7)
Baseline WBC count (10^9/L), n (%)				
<10.0	9 (60.0)	9 (27.3)	19 (100.0)	1 (3.3)
≥10 to <15.0	4 (26.7)	16 (48.5)	0	22 (73.3)
≥15.0	1 (6.7)	6 (18.2)	0	7 (23.3)
Missing	1 (6.7)	2 (6.1)	0	0
GPPGA total score, n (%)				
3	12 (80.0)	27 (81.8)	14 (73.7)	26 (86.7)
4	3 (20.0)	6 (18.2)	5 (26.3)	4 (13.3)
GPPGA pustulation subscore, n (%)				
2	4 (26.7)	7 (21.2)	6 (31.6)	5 (16.7)
3	7 (46.7)	13 (39.4)	8 (42.1)	12 (40.0)
4	4 (26.7)	13 (39.4)	5 (26.3)	13 (43.3)
Mean GPPASI total score (SD)	15.1 (6.0)	30.8 (12.6)	23.5 (13.7)	27.6 (12.6)
Median DLQI total score (IQR)†	16.0 (12.0)	20.5 (10.0)	22.0 (16.0)	19.0 (8.0)
Median PSS score (IQR)‡	9.0 (7.0)	11.0 (3.0)	10.0 (5.0)	11.0 (2.0)
Median pain VAS score (IQR)§	75.5 (26.0)	80.6 (28.4)	75.5 (27.1)	79.4 (23.8)
Median FACIT-Fatigue scale total score (IQR)¶	23.0 (26.0)	10.0 (15.0)	16.0 (16.0)	10.5 (25.0)
Hospitalised for current GPP flare, n (%)				
Yes	3 (20.0)	20 (60.6)	9 (47.4)	14 (46.7)
No	10 (66.7)	13 (39.4)	10 (52.6)	15 (50.0)
Missing	2 (13.3)	0	0	1 (3.3)
Median number of days in hospital for current GPP flare (IQR)	9.0 (9.0)	8 (5.5)	8.0 (3.0)	8.5 (7.0)

Patients receiving placebo or spesolimab were pooled for each subgroup. *For CRP, seven patients in the >ULN subgroup were missing data, for neutrophils, two patients in the ≤ULN subgroup and five patients in the >ULN subgroup were missing data. †DLQI scores range from 0 (no effect) to 30 (extremely large effect). ‡PSS score ranges from 0 to 16, with higher scores indicating more severe symptoms. §Pain VAS score ranges from 0 (no pain) to 100 (severe pain). ¶FACIT-Fatigue score ranges from 0 to 52, with lower scores indicating greater impact of fatigue on daily activities.

Baseline and clinical characteristics were generally consistent between patients with and without systemic inflammation at baseline. Patient-reported fatigue was more impaired in patients with baseline systemic inflammation than those without, and patients with elevated baseline CRP were more likely to be hospitalised compared with baseline CRP ≤ULN

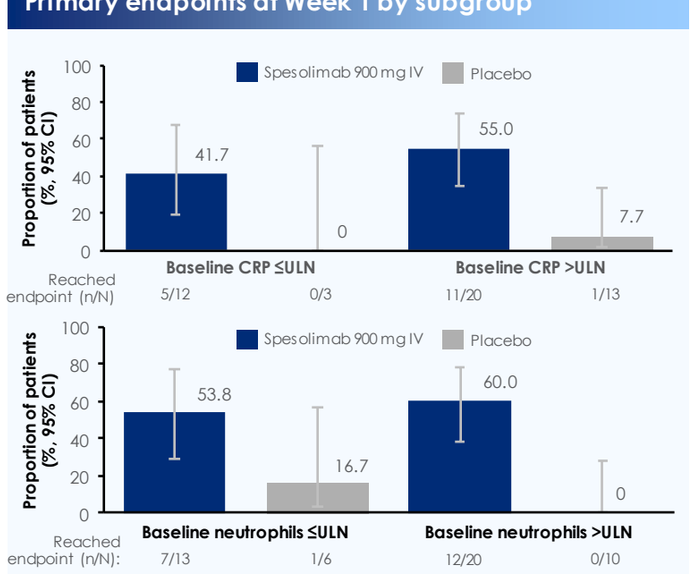
Achievement of GPPGA pustulation subscore of 0 and GPPGA total score of 0 or 1 over time in patients who received spesolimab by subgroup



Treatment effect in patients who received up to two doses of spesolimab: Day 1 (n=35) and optional dose at Day 8 (n=12). Missing values, any use of other medications for GPP, or use of spesolimab for the treatment of a new GPP flare were regarded as non-response for this analysis. Arrowheads indicate the days of IV spesolimab administration.

Patients achieved rapid pustular and skin clearance, sustained over 12 weeks irrespective of baseline systemic inflammation

Primary endpoints at Week 1 by subgroup



Two patients in the spesolimab arm and one patient in the placebo arm received another medication for GPP within the first week; one patient in the spesolimab arm discontinued before completing Week 1. Missing values, any use of other medications for GPP, or use of spesolimab for the treatment of a new GPP flare were regarded as non-response for this analysis.

Patients who received spesolimab achieved the primary endpoint regardless of systemic inflammation at baseline

Safety profile up to Week 1 by CRP subgroup

	Baseline CRP ≤ULN (10 mg/L)			Baseline CRP >ULN (10 mg/L)		
	Spesolimab (n=12)	Placebo (n=3)	Total (n=15)	Spesolimab (n=20)	Placebo (n=13)	Total (n=33)
Patients with any AE	8 (66.7)	1 (33.3)	9 (60.0)	13 (65.0)	8 (61.5)	21 (63.6)
Patients with severe AEs (RCTC grade 3 or 4)	0	0	0	2 (10.0)	1 (7.7)	3 (9.1)
Patients with Investigator-defined drug related AEs	2 (16.7)	0	2 (13.3)	8 (40.0)	5 (38.5)	13 (39.4)
Patients with AEs leading to drug discontinuation	0	0	0	0	0	0
Patients with SAEs	0	0	0	2 (10.0)	0	2 (6.1)
Requires or prolongs hospitalisation	0	0	0	2 (10.0)	0	2 (6.1)
Is life-threatening	0	0	0	0	0	0
Persistent or significant disability/incapacity	0	0	0	0	0	0
Other medically important serious event	0	0	0	0	0	0
Resulted in death	0	0	0	0	0	0

SAEs were more common in patients with higher CRP at baseline compared with lower CRP. Similar safety results were observed in neutrophil subgroups

Abbreviations

AE, adverse event; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; DLQI, Dermatology Life Quality Index; FACIT, Functional Assessment of Chronic Illness Therapy; GPP, generalized pustular psoriasis; GPPASI, Generalized Pustular Psoriasis Area and Severity Index; GPPGA, Generalized Pustular Psoriasis Physician Global Assessment; IL, interleukin; IQR, interquartile range; IV, intravenous; OL, open-label; PSS, Psoriasis Symptom Scale; RCTC, Rheumatology Common Toxicity Criteria; SAE, serious adverse event; SD, standard deviation; ULN, upper limit of normal; VAS, visual analogue scale; WBC, white blood cell.

References

1. Navarini A, et al. *J Eur Acad Dermatol Venereol* 2017;31:1792–1799; 2. Fujita H, et al. *J Dermatol* 2018;45:1235–1270; 3. Bachelez H, et al. *New Engl J Med* 2021;385:2431–2440.

Disclosures & Acknowledgements

The study was supported and funded by Boehringer Ingelheim. **TFT** declares conducting clinical trials or paid consulting activities for AbbVie, Boehringer Ingelheim, Celgene, Eli Lilly, GlaxoSmithKline, Janssen-Cilag, MSD, Novartis International, Pfizer and UCB. **SI** has served as a consultant and/or paid speaker for and/or accepted a research grant from and/or participated in clinical trials sponsored by companies including AbbVie, Amgen, Boehringer Ingelheim, Eisai, Eli Lilly, Janssen, Kyowa Kirin, LEO Pharma, Maruho Pharmaceutical, Mitsubishi Tanabe, Novartis, Sun Pharmaceutical Industries, Taiho Yakuhin Kogyo, Torii Yakuhin and UCB. **WS** is an investigator for and/or has served as a consultant and/or paid speaker for and/or accepted a research grant from AbbVie, Almirall, Amgen (previously Celgene), Bristol Myers Squibb, Boehringer Ingelheim, GSK, Janssen, Lilly, LEO Pharma, medi GmbH Bayreuth, MSD, Novartis, Pfizer, Roche, Sanofi Genzyme and UCB. **MAV** declares paid activities as an advisor, speaker or consultant for AbbVie, Almirall, Boehringer Ingelheim, Eli Lilly, Janssen-Cilag, Medac, Biogen, Bristol Myers Squibb and Novartis. **BE** is an investigator for AbbVie, Amgen (previously Celgene), AnaptysBio, Bausch Health (formerly Valeant Pharmaceuticals), Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Incyte, LEO Pharma, Menlo, MSD, Novartis, Pfizer, Regeneron, Sun Pharmaceutical Industries, UCB, and Vanda; and is a consultant for Amgen (previously Celgene), Arcutis, Bausch Health (formerly Valeant Pharmaceuticals), Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, LEO Pharma, Novartis, and UCB. **LL**, **MQ** and **CT** are employees of Boehringer Ingelheim. **SEC** declares paid activities as an advisor, speaker, or consultant for AbbVie, Boehringer Ingelheim, Eli Lilly, Janssen, LEO Pharma, MSD, Novartis, Pfizer, Sanofi and UCB. The authors met the 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 the poster. Boehringer Ingelheim was given the opportunity to review the poster for medical and scientific accuracy, as well as intellectual property considerations. James Parkinson, PhD, of OPEN Health Communications (London, UK) provided writing, editorial, and formatting support, which was contracted and funded by Boehringer Ingelheim.

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