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Efficacy of spesolimab for generalized pustular psoriasis (GPP) flare treatment according to GPP Area and Severity Index (GPPASI) score at baseline

Melinda Gooderham[1], Shinichi Imafuku[2], Ricardo Romiti[3], Dagmar Wilsmann-Theis[4], Min Zheng[5], Ling Li[6], Manuel Quaresma[7], Christian Thoma[8], Mark G. Lebwohl[9]

[1]School of Medicine, Queen's University and Centre for Dermatology and Probity Medical Research, Peterborough, ON, Canada; [2]Department of Dermatology, Faculty of Medicine, Fukuoka University, Fukuoka, Japan; [3]Psoriasis, Trichology and Collagen Diseases Department, University of São Paulo, State of São Paulo, Brazil; [4]Department of Dermatology and Allergy, University of Bonn, Bonn, Germany; [5]Department of Dermatology, Second Affiliated Hospital, Zhejiang University, School of Medicine, Hangzhou, Zhejiang, China; [6]Boehringer Ingelheim Investment Co., Ltd, Shanghai, China; [7]Boehringer Ingelheim International GmbH, Ingelheim, Germany; [8]Boehringer Ingelheim International GmbH, Biberach, Germany; [9]Icahn School of Medicine at Mount Sinai, New York, NY, USA

The treatment effect achieved with spesolimab in patients presenting with a GPP flare is consistently superior to placebo, independent of the extent and severity of disease at baseline

PURPOSE

To evaluate the efficacy of spesolimab treatment in patients with a GPP flare according to the extent and severity of GPP at baseline, assessed by GPPASI score.

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[1–3]
- Effisayil 1 was a global, multicentre, randomised, double-blind, placebo-controlled study of spesolimab, an anti-interleukin-36 receptor antibody, in 53 patients with a GPP flare (NCT03782792). Spesolimab treatment led to rapid pustular and skin clearance at 1 week:[4,5]
  - Primary endpoint (GPPGA pustulation subscore of 0; no visible pustules): 54% vs 6% (two-sided p<0.001)
  - Key secondary endpoint (GPPGA total score of 0 or 1; clear or almost clear skin): 43% vs 11% (two-sided p=0.02)

CONCLUSIONS

- Patients with a GPP flare and higher GPPASI at baseline experienced a greater symptom burden and impact on QoL and were more likely to be hospitalised than patients with a lower GPPASI at baseline
- Pustular and skin clearance following spesolimab treatment were consistently superior to placebo, and independent of the extent and severity of GPP at baseline

METHODS

- Patients with a GPP flare (N=53) were randomised (2:1) to receive IV spesolimab 900 mg or placebo at baseline and were followed for 12 weeks. Patients were eligible to receive OL spesolimab for persistent flare symptoms on Day 8[4,5]
- For this analysis, patients were assigned to two subgroups based on GPPASI scores below (lower GPPASI) or above (higher GPPASI) the median (27.2) for the population at baseline
- Analyses included the proportion of patients achieving a GPPGA pustulation subscore of 0 or a GPPGA total score of 0 or 1 at Week 1 and over the 12-week study
- The proportion of patients treated with spesolimab who achieved a 50% (GPPASI 50) reduction in GPPASI score from baseline over the 12-week study was also assessed
- Results are for patients who received up to two doses of spesolimab; missing GPPGA values, any use of other medication to treat GPP or use of spesolimab to treat a new GPP flare were considered non-response

RESULTS

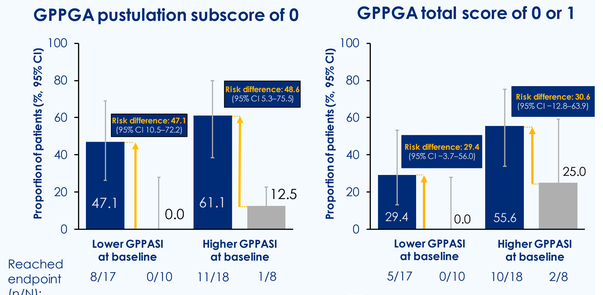
Baseline demographics and clinical characteristics

Characteristic	Lower GPPASI at baseline (≤ median 27.2) (n=27)	Higher GPPASI at baseline (> median 27.2) (n=26)
Mean age, years (SD)	43.9 (10.8)	42.1 (11.2)
Female, n (%)	19 (70.4)	17 (65.4)
Race, n (%)*		
Asian	19 (70.4)	10 (38.5)
White	8 (29.6)	16 (61.5)
Pooled study site, n (%)		
US	3 (11.1)	0
Japan	2 (7.4)	0
Asia (excluding Japan)	15 (55.6)	10 (38.5)
Europe	7 (25.9)	9 (34.6)
Africa	0	7 (26.9)
Mean BMI, kg/m² (SD)	28.1 (10.0)	25.9 (6.1)
Mean weight, kg (SD)	75.1 (30.3)	68.9 (17.3)
***IL36RN* mutation, n (%)†**	7 (25.9)	7 (26.9)
GPPGA total score, n (%)		
3	24 (88.9)	19 (73.1)
4	3 (11.1)	7 (26.9)
GPPGA pustulation subscore, n (%)		
2	6 (22.2)	5 (19.2)
3	16 (59.3)	7 (26.9)
4	5 (18.5)	14 (53.8)
GPPASI total score, n (SD)	15.1 (5.3)	38.4 (9.7)
DLQI total score, median (IQR)	16.0 (10.0)	23.0 (8.0)
PSS total score, median (IQR)	10.0 (4.0)	11.5 (4.0)
FACIT-Fatigue total score, median (IQR)	23.0 (20.0)	6.5 (10.0)
Pain VAS score, median (IQR)	71.9 (29.6)	81.8 (16.8)
Hospitalised for current GPP flare, n (%)	6 (22.2)	19 (73.1)

Data for each subgroup include both treatment arms.
*Self-reported by the patients; †Genotyping information available for 46 patients; *IL36RN* mutation status was unknown in 1 patient (3.7%) with lower GPPASI at baseline and in 6 patients (23.1%) with higher GPPASI at baseline.

Compared with patients with a lower GPPASI at baseline, patients with a higher GPPASI at baseline were more likely to present with a GPPGA total score or pustulation subscore of 4, reported a greater impact on patient-reported outcomes and QoL, and were more likely to require hospitalisation for a current flare

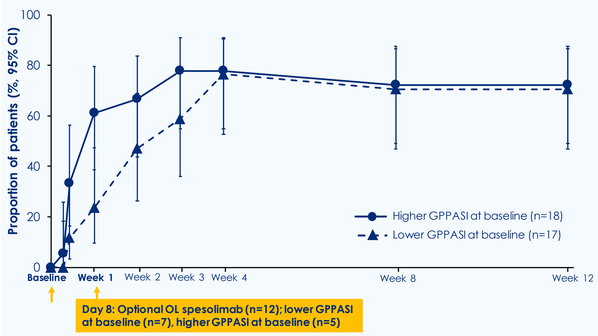
Primary and secondary endpoints in patients by GPPASI subgroup at Week 1



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 spesolimab arm discontinued before completing Week 1. Missing values or any use of other medication for GPP within the first week of the trial were regarded as non-response for the analysis of these endpoints.

Primary and key secondary endpoints were achieved by a similar proportion of patients in the spesolimab arm, regardless of GPPASI subgroup, and the treatment effect compared with placebo was consistent in each subgroup

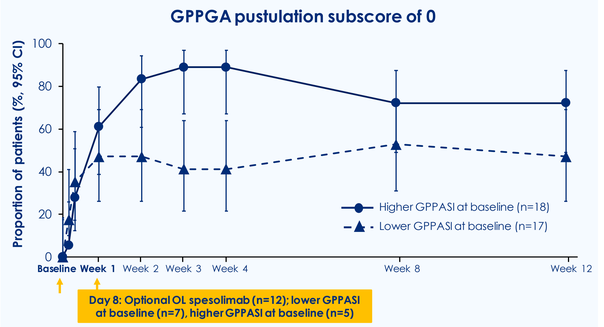
Proportion of patients treated with spesolimab* who achieved GPPASI 50 by GPPASI subgroup



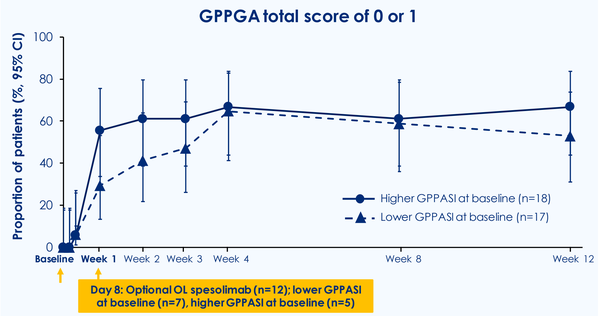
*Treatment effect in patients who received up to two doses of spesolimab: Day 1 (n=35) and optional dose at Day 8 (n=12). Missing values, any use of other medication for GPP or spesolimab for the treatment of a new GPP flare were regarded as non-response for this analysis.

GPPASI 50 was achieved by 23.5% of patients in the lower GPPASI group and 61.1% in the higher GPPASI group at Week 1, and by 70.6% and 72.2% of patients at Week 12, respectively

Proportion of patients treated with spesolimab* with a GPPGA pustulation subscore of 0 or GPPGA total score of 0 or 1 by GPPASI subgroup



Improvements observed with spesolimab treatment in both subgroups were sustained at Week 12: a GPPGA pustulation subscore of 0 was achieved by 47.1% of patients with a lower GPPASI at baseline and 72.2% of patients with a higher GPPASI at baseline



*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 medication for GPP or spesolimab for the treatment of a new GPP flare were regarded as non-response for this analysis.

At Week 12, a GPPGA total score of 0 or 1 was achieved by 52.9% of patients with a lower GPPASI at baseline and 66.7% of patients with a higher GPPASI at baseline

Abbreviations
BMI, body mass index; CI, confidence interval; DLQI, Dermatology Life Quality Index; FACIT, Functional Assessment of Chronic Illness Therapy; GPP, generalized pustular psoriasis; GPPASI, Generalised Pustular Psoriasis Area and Severity Index; GPPGA, Generalized Pustular Psoriasis Physician Global Assessment; IQR, interquartile range; IV, intravenous; OL, open-label; PSS, Psoriasis Symptom Scale; QoL, quality of life; SD, standard deviation; VAS, visual analogue scale

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