Efficacy of spesolimab for the treatment of GPP flares across prespecified patient subgroups in the Effisayil 1 study

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Subgroup analyses from the Effisayil 1 study showed that the efficacy of spesolimab (pustular and skin lesion clearance) was consistent across all prespecified patient populations, including those with or without *IL36RN* mutations

PURPOSE

To investigate the consistency of the spesolimab treatment effect by conducting a subgroup analysis of the primary and key secondary endpoints from the Effisayil 1 study, according to patient demographics and clinical characteristics at baseline.

INTRODUCTION

- GPP is a rare and potentially life-threatening autoinflammatory disease characterized by recurrent flares of widespread sterile pustules, with or without systemic inflammation[1,2]
- Effisayil 1 (NCT03782792) was a multicenter, randomized, double-blind, placebo-controlled study of spesolimab, an anti-IL-36 receptor antibody, in patients presenting with a GPP flare. Within 1 week of a single dose of spesolimab, rapid pustular and skin clearance was observed compared with placebo[3]
  - Primary endpoint (GPPGA pustulation subscore of 0; no visible pustules): 54% vs 6% (one-sided p<0.001)
  - Key secondary endpoint (GPPGA total score of 0 or 1; clear or almost clear skin): 43% vs 11% (one-sided p=0.0118)

CONCLUSIONS

- Estimates of spesolimab treatment effect in each patient subgroup were generally similar to those of the overall population for both the primary and key secondary endpoints
- The efficacy of spesolimab (pustular and skin clearance) compared with placebo was consistent across all prespecified subgroups
- However, it should be noted that several subgroups had very few patients
- These data provide further evidence supporting the use of spesolimab to treat all patients presenting with a GPP flare

METHODS

- The efficacy of spesolimab was evaluated in prespecified patient subgroups from Effisayil 1, if at least 2 categories of the subgroup included ≥5 patients: sex, age, race, BMI, GPPGA pustulation subscore at baseline, GPPGA total score at baseline, JDA GPP severity score at baseline, presence of plaque psoriasis at baseline, and *IL36RN* mutation status
- Scan the QR code at the bottom of this poster to see full details of the Effisayil 1 study design[3,4]

RESULTS

Baseline demographics and clinical characteristics

Characteristic	Spesolimab (n=35)	Placebo (n=18)
Age, years, mean (SD)	43.2 (12.1)	42.6 (8.4)
Female, n (%)	21 (60.0)	15 (83.3)
Race, n (%)		
Asian	16 (45.7)	13 (72.2)
White	19 (54.3)	5 (27.8)
BMI, kg/m², mean (SD)	27 (8)	26 (10)
IL36RN mutation positive*, n (%)	8 (22.9)	6 (33.3)
GPPGA total score, n (%)		
3 (moderate)	28 (80.0)	15 (83.3)
4 (severe)	7 (20.0)	3 (16.7)
GPPGA pustulation subscore, n (%)		
2 (mild)	6 (17.1)	5 (27.8)
3 (moderate)	16 (45.7)	7 (38.9)
4 (severe)	13 (37.1)	6 (33.3)
Pain VAS, median (IQR)	79.8 (70.5–87.8)	70.0 (50.0–89.4)
JDA GPP severity index, n (%)		
Mild	9 (25.7)	5 (27.8)
Moderate	19 (54.3)	8 (44.4)
Severe	4 (11.4)	4 (22.2)
Missing	3 (8.6)	1 (5.6)
Mean (SD)	7.9 (3.0)	8.4 (2.8)
Median (min, max)	8.0 (2, 14)	8.0 (4, 14)
Medication for GPP prior to randomization, n (%)†	**18 (51.4)**	**9 (50.0)**
Clobetasol propionate	5 (14.3)	1 (5.6)
Acitretin	4 (11.4)	1 (5.6)
Cyclosporin	2 (5.7)	3 (16.7)
Betamethasone valerate	2 (5.7)	2 (11.1)
Methotrexate	1 (2.9)	3 (16.7)
Betamethasone dipropionate	1 (2.9)	2 (11.1)
Betamethasone; calcipotriol	2 (5.7)	1 (5.6)
Emulsifying wax; paraffin, liquid, white soft paraffin	1 (2.9)	2 (11.1)

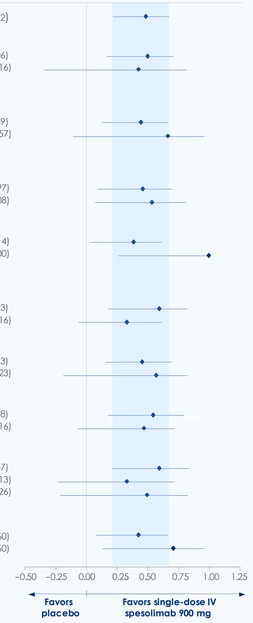
Genotyping data were available for 46 patients. DNA sequencing was not performed in 7 patients.
*Patients who were homozygous or heterozygous for an IL36RN mutation were considered positive;
†Background medication for GPP in at least 3 patients of the overall population.

The placebo arm included a higher proportion of female and Asian patients than the spesolimab arm; clinical characteristics were generally balanced between study arms

Subgroup analysis of GPPGA pustulation subscore of 0 at Week 1

Forest plot of risk difference for GPPGA pustulation score of 0 at Week 1

Subgroup (n/N)*	Response rate, % of patients	Risk difference (95% CI)
Overall (19/35 vs 1/18)	54.3 vs 5.6	0.487 (0.215–0.672)
Baseline GPPGA total score		
3 (16/28 vs 1/15)	57.1 vs 6.7	0.505 (0.163–0.706)
4 (3/7 vs 0/3)	42.9 vs 0.0	0.429 (−0.343–0.816)
Presence of plaque psoriasis at baseline		
No (15/29 vs 1/15)	51.7 vs 6.7	0.451 (0.117–0.659)
Yes (4/6 vs 0/3)	66.7 vs 0.0	0.667 (−0.109–0.957)
Baseline GPPGA pustulation subscore		
<4 (12/22 vs 1/12)	54.5 vs 8.3	0.462 (0.089–0.697)
=4 (7/13 vs 0/6)	53.8 vs 0.0	0.538 (0.070–0.808)
Baseline JDA GPP severity index		
Mild or moderate (13/28 vs 1/13)	46.4 vs 7.7	0.387 (0.038–0.614)
Severe (4/4 vs 0/4)	100.0 vs 0.0	1.000 (0.261–1.000)
Background medication before randomization		
No (14/20 vs 1/10)	70.0 vs 10.0	0.600 (0.177–0.823)
Yes (5/15 vs 0/8)	33.3 vs 0.0	0.333 (−0.069–0.616)
Sex		
Female (11/21 vs 1/15)	52.4 vs 6.7	0.457 (0.151–0.693)
Male (8/14 vs 0/3)	57.1 vs 0.0	0.571 (−0.191–0.823)
Race		
Asian (10/16 vs 1/13)	62.5 vs 7.7	0.548 (0.173–0.798)
White (9/19 vs 0/5)	47.4 vs 0.0	0.474 (−0.073–0.716)
BMI		
<25 kg/m² (9/15 vs 0/9)	60.0 vs 0.0	0.600 (0.204–0.837)
25 to <30 kg/m² (5/10 vs 1/6)	50.0 vs 16.7	0.333 (−0.231–0.713)
≥30 kg/m² (5/10 vs 0/3)	50.0 vs 0.0	0.500 (−0.215–0.826)
IL36RN mutation positive†		
No (9/21 vs 0/11)	42.9 vs 0.0	0.429 (0.081–0.660)
Yes (7/8 vs 1/6)	87.5 vs 16.7	0.708 (0.126–0.960)



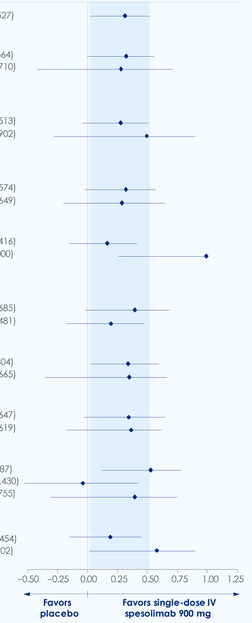
Missing values or any use of other medication for GPP within the first week of the trial were regarded as non-response for the analysis of these endpoints.
*Single-dose IV spesolimab 900 mg vs placebo; subgroup analysis by age was not performed, as only 2 patients were aged ≥65 years; †Patients who were homozygous or heterozygous for an *IL36RN* mutation were considered positive.

The efficacy of spesolimab (GPPGA pustulation subscore of 0) was consistent across patient subgroups

Subgroup analysis of GPPGA total score of 0 or 1 at Week 1

Forest plot of risk difference for GPPGA total score of 0 or 1 at Week 1

Subgroup (n/N)*	Response rate, % of patients	Risk difference (95% CI)
Overall (15/35 vs 2/18)	42.9 vs 11.1	0.317 (0.022–0.527)
Baseline GPPGA total score		
3 (13/28 vs 2/15)	46.4 vs 13.3	0.331 (0.000–0.564)
4 (2/7 vs 0/3)	28.6 vs 0.0	0.286 (−0.418–0.710)
Presence of plaque psoriasis at baseline		
No (12/29 vs 2/15)	41.4 vs 13.3	0.280 (−0.044–0.513)
Yes (3/6 vs 0/3)	50.0 vs 0.0	0.500 (−0.283–0.902)
Baseline GPPGA pustulation subscore		
<4 (9/22 vs 1/12)	40.9 vs 8.3	0.326 (−0.025–0.574)
=4 (6/13 vs 1/6)	46.2 vs 16.7	0.295 (−0.206–0.649)
Baseline JDA GPP severity index		
Mild or moderate (9/28 vs 2/13)	32.1 vs 15.4	0.168 (−0.160–0.416)
Severe (4/4 vs 0/4)	100.0 vs 0.0	1.000 (0.261–1.000)
Background medication before randomization		
No (12/20 vs 2/10)	60.0 vs 20.0	0.400 (−0.019–0.685)
Yes (3/15 vs 0/8)	20.0 vs 0.0	0.200 (−0.176–0.481)
Sex		
Female (10/21 vs 2/15)	47.6 vs 13.3	0.343 (0.026–0.604)
Male (5/14 vs 0/3)	35.7 vs 0.0	0.357 (−0.352–0.665)
Race		
Asian (8/16 vs 2/13)	50.0 vs 15.4	0.346 (−0.031–0.647)
White (7/19 vs 0/5)	36.8 vs 0.0	0.368 (−0.178–0.619)
BMI		
<25 kg/m² (8/15 vs 0/9)	53.3 vs 0.0	0.533 (0.118–0.787)
25 to <30 kg/m² (3/10 vs 2/6)	30.0 vs 33.3	−0.033 (−0.532–0.430)
≥30 kg/m² (4/10 vs 0/3)	40.0 vs 0.0	0.400 (−0.313–0.755)
IL36RN mutation positive†		
No (6/21 vs 1/11)	28.6 vs 9.1	0.195 (−0.151–0.454)
Yes (6/8 vs 1/6)	75.0 vs 16.7	0.583 (0.018–0.902)



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The efficacy of spesolimab (GPPGA total score of 0 or 1) was consistent across patient subgroups

Abbreviations

BMI, body mass index; CI, confidence interval; FDA, US Food and Drug Administration; GPP, generalized pustular psoriasis; GPPGA, Generalized Pustular Psoriasis Physician Global Assessment; IL-36, interleukin-36; IQR, interquartile range; IV, intravenous; JDA, Japanese Dermatological Association; SD, standard deviation; VAS, visual analog scale.

References

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