Improvements in GPPGA score in patients experiencing a generalized pustular psoriasis flare: Effisayil 1 study results

Milan J. Anadkat[1], Mark G. Lebwohl[2], Boni Elewski[3], Ulrich Mrowietz[4], Shinichi Imafuku[5], Jinhua Xu[6], Ling Li[7], Manuel Quaresma[8], Christian Thoma[9], Hervé Bachelez[10,11]

[1]Washington University School of Medicine, Division of Dermatology, St. Louis, MO, USA; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]University of Alabama School of Medicine, Birmingham, AL, USA; [4]Psoriasis-Center, Department of Dermatology, University Medical Center Schleswig-Holstein, Campus Kiel, Kiel, Germany; [5]Department of Dermatology, Faculty of Medicine, Fukuoka University, Fukuoka, Japan; [6]Department of Dermatology, Huashan Hospital, Fudan University, Shanghai, China; [7]Boehringer Ingelheim Investment Co. Ltd, Shanghai, China; [8]Boehringer Ingelheim International GmbH, Ingelheim, Germany; [9]Boehringer Ingelheim International GmbH, Biberach, Germany; [10]Service de Dermatologie, Assistance Publique–Hôpitaux de Paris Hôpital Saint-Louis, Paris, France; [11]INSERM Unité 1163, Imagine Institute of Genetic Diseases, Université Paris Cité, Paris, France

Spesolimab treatment resulted in sustained clinical improvements for up to 12 weeks in patients with a GPP flare

PURPOSE

To determine the proportion of patients with a GPP flare who achieved clinically significant improvements in GPPGA pustulation subscore and total scores after treatment with spesolimab.

INTRODUCTION

- GPP is a rare, autoinflammatory skin disease characterized by episodes of widespread eruption of sterile, macroscopic pustules that can occur with or without systemic inflammation and symptoms[1,2]
- Effisayil 1 (NCT03782792) was a global, multicenter, randomized, double-blind, placebo-controlled study of spesolimab, an anti-interleukin-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 (one 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 (one sided p=0.02)
- MCIDs in GPPGA pustulation subscore and GPPGA total score in patients with a GPP flare have previously been assessed as a ≥2-point change and a ≥1-point change, respectively[4]
- Here we report the proportion of patients who achieved clinically significant improvements in GPPGA scores throughout the 12-week Effisayil 1 study, regardless of whether they achieved the defined primary or key secondary endpoints

METHODS

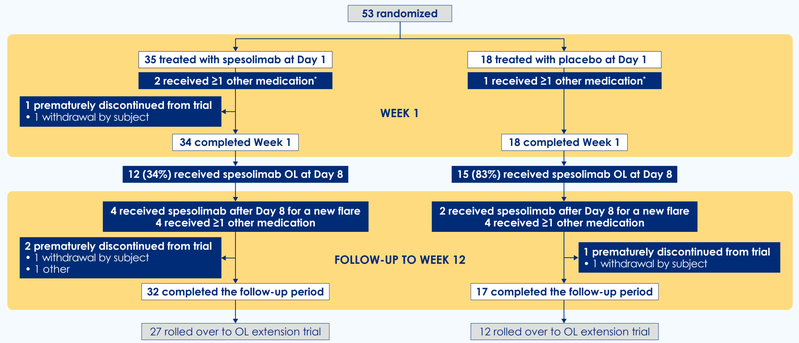
- GPPGA total score and pustulation subscore were assessed by the investigator and recorded at Days 1–7, and Weeks 1–4, 8, and 12, with improvements in GPPGA pustulation subscore by ≥2 points, and in GPPGA total score by ≥1 point calculated for each time point
- Patients who achieved a ≥2 point improvement in GPPGA pustulation subscore and a ≥1-point improvement in GPPGA total score were further assessed by achievement of the primary and key secondary endpoints at Day 8
- ITT analysis included observed values for all patients over time according to the randomized treatment received at Day 1, regardless of the use of any other medication for GPP or any additional dose of spesolimab

CONCLUSIONS

- Patients with a GPP flare treated with spesolimab achieved rapid, clinically significant improvements in pustular and skin clearance, which were sustained through Week 12
- Patients initially randomized to receive placebo who were given OL spesolimab at Day 8 also achieved clinically significant improvements in pustular and skin clearance, which were sustained through to Week 12
- These data indicate that spesolimab rapidly targets the underlying causes of GPP flares and maintains this effect over time, further supporting its use as a potential therapeutic option for patients with a GPP flare

RESULTS

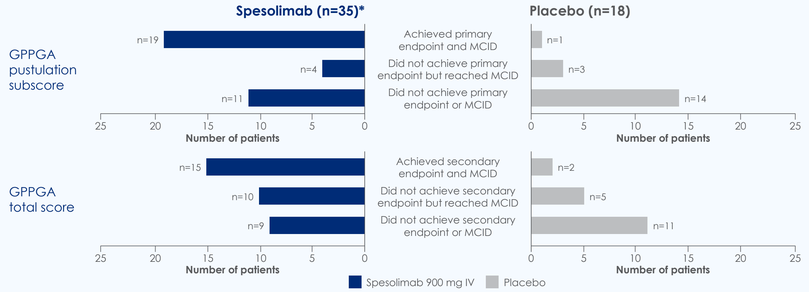
Patient disposition in the Effisayil 1 study[3]



*1 patient continued other medication beyond Week 1.

Optional OL spesolimab for persistent flare symptoms at Day 8 was received by 12 patients in the spesolimab arm and 15 patients in the placebo arm; spesolimab for a new flare was received by 4 patients in the spesolimab arm, two of whom had received OL spesolimab at Day 8; 2 patients in the placebo arm received spesolimab for a new flare, one of whom had received OL spesolimab at Day 8

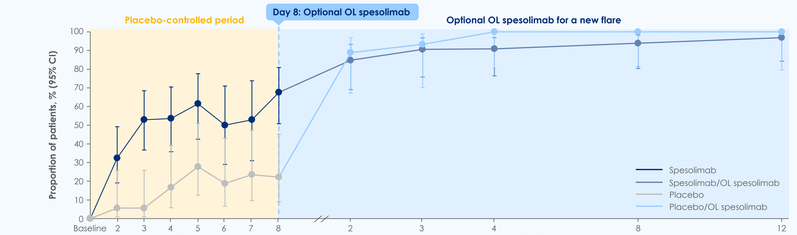
Number of patients initially randomized to spesolimab or placebo who achieved MCIDs in GPPGA pustulation subscore and GPPGA total score at Day 8



*One patient in the spesolimab arm prematurely discontinued the trial and was not assessed at Week 1. The primary endpoint was a GPPGA pustulation subscore of 0 (no visible pustules) at Day 8, and the key secondary endpoint was a GPPGA total score of 0 or 1 (clear / almost clear skin), at Day 8. MCIDs in GPPGA pustulation subscore and total score in patients with a GPP flare were assessed as a ≥2 point change and a ≥1 point change, respectively. Two patients in the spesolimab arm, and one patient in the placebo arm received other medication for GPP during Week 1 of the study. Use of any other medication for GPP was regarded as non-response for primary and key secondary endpoint analysis.

Most patients who received spesolimab achieved the primary endpoint and MCID (n=19) or MCID alone in GPPGA pustulation subscore (n=4) at Day 8. Most patients who received placebo did not achieve the primary endpoint or MCID in GPPGA pustulation subscore (n=14) at Day 8. Similar results were observed for the GPPGA total score

Proportion of patients who achieved an improvement in GPPGA pustulation subscore by ≥2 points from baseline – ITT analysis

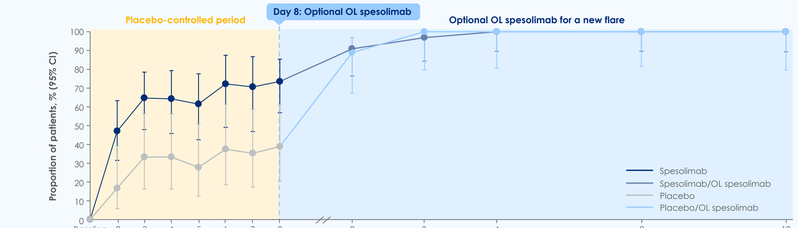


	Baseline	2	3	4	5	6	7	8	2	3	4	8	12
Spesolimab (n)	35	34	34	34	34	34	34	34	33	32	33	33	32
Placebo (n)	18	18	18	18	18	18	18	18	18	15	16	17	15

ITT: observed cases regardless of the use of any other medication for GPP or any additional dose of spesolimab. Among 35 patients randomized to receive spesolimab, OL spesolimab was received by 12 patients at Day 8 due to persistent flare symptoms. OL spesolimab was received by 4 of these patients after Day 8 due to a new flare, 2 of whom had received OL spesolimab at Day 8. Among 18 patients randomized to receive placebo, OL spesolimab was received by 15 patients at Day 8 due to persistent flare symptoms. OL spesolimab was received by 2 of these patients after Day 8 due to a new flare, one of whom had received OL spesolimab at Day 8.

MCIDs in GPPGA pustulation subscore were observed in 68% of patients initially randomized to receive spesolimab at Week 1 and sustained in 97% of these individuals at Week 12. In patients initially randomized to placebo who received OL spesolimab at Day 8, rapid, clinically significant improvements in GPPGA pustulation subscore were seen in 89% of patients by Week 2 (one week after spesolimab). This improvement in GPPGA pustulation score reached 100% in these patients by Week 12

Proportion of patients who achieved an improvement in GPPGA total score by ≥1 point from baseline – ITT analysis



	Baseline	2	3	4	5	6	7	8	2	3	4	8	12
Spesolimab (n)	35	34	34	34	34	34	34	34	33	32	33	33	32
Placebo (n)	18	18	18	18	18	18	18	18	18	15	16	17	15

ITT: observed cases regardless of the use of any other medication for GPP or any additional dose of spesolimab. Among 35 patients randomized to receive spesolimab, OL spesolimab was received by 12 patients at Day 8 due to persistent flare symptoms. OL spesolimab was received by 4 of these patients after Day 8 due to a new flare, 2 of whom had received OL spesolimab at Day 8. Among 18 patients randomized to receive placebo, OL spesolimab was received by 15 patients at Day 8 due to persistent flare symptoms. OL spesolimab was received by 2 of these patients after Day 8 due to a new flare, one of whom had received OL spesolimab at Day 8.

MCIDs in GPPGA total score were observed in 74% of patients initially randomized to receive spesolimab at Week 1. In patients initially randomized to receive placebo who were given OL spesolimab at Day 8, rapid, clinically significant improvements in GPPGA total score were seen in 89% of individuals by Week 2 (1 week after spesolimab administration). These improvements were sustained in 100% of all patients by Week 12

Abbreviations

CI, confidence interval; GPP, generalized pustular psoriasis, GPPGA, Generalized Pustular Psoriasis Physician Global Assessment; ITT, intention to treat; IV, intravenous; MCID, minimal clinically important difference; OL, open-label

References

1. Navarini AA, et al. *J Eur Acad Dermatol Venereol* 2017;31:1792–1799; 2. Fujita H, et al. *J Dermatol* 2018;45(1):35–1270; 3. Bachelez H, et al. *New Engl J Med* 2021;385:2431–2440; 4. Gradi B, et al. Presentation at SPIN 2022; Abstract #P121.

Disclosures & Acknowledgements

The study was supported and funded by Boehringer Ingelheim. **MJA** declares paid activities as a current advisor or consultant for BioLinq, Boehringer Ingelheim, Eli Lilly, Novocure, Protagonist, and Springworks; has served as prior consultant or advisor for Abbvie, Adgero, Amgen, Aspire Bariatrics, AstraZeneca, Biogen, Bristol Myers Squibb, ImClone, Innovaderm, OnQuality, Therakos, Veloce, and UCB; has served as an investigator for Abbvie, AnaptysBio, Biogen, Boehringer-Ingelheim, ChemoCentryx, Eli Lilly, InCyte, Inflamrx, Horus Biosciences, Lutris, Moonlake, Novartis, OnQuality, UCB, Veloce, XBiotech, and Xoma. **MGL** declares paid consulting activities for Ashfirm Bio, Almirall, AnaptysBio, Arcutis, Aristea, Arrive Technology, Avotres Therapeutics, Biamx, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, CorEvitas, Dermavant Sciences, Dr. Reddy's, Evelo, Evommune, Facilitate International Dermatologic Education, Forte, Foundation for Research and Education in Dermatology, Helsinn, LEO Pharma, Meiji, Mindera, Pfizer, and Verrica; and receiving research grants from AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Dermavant Sciences, Eli Lilly, Incyte, Janssen, Ortho Dermatologics, Regeneron, and UCB. **BE** declares being an investigator for AbbVie, Amgen (previously Celgene), AnaptysBio, Bausch Health (formerly Valeant Pharmaceuticals), Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Incyte, LEO Pharma, Menlo, Merck, Novartis, Pfizer, Regeneron, Sun Pharmaceutical Industries, UCB, and Vanda; and a consultant for Amgen (previously Celgene), Arcutis, Bausch Health (formerly Valeant Pharmaceuticals), Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, LEO Pharma, Novartis, and UCB. **UM** declares being an advisor and/or receiving speaker's honoraria and/or grants and/or participating in clinical trials for AbbVie, Aditxt, Almirall, Amgen (previously Celgene), Aristea, Boehringer Ingelheim, Bristol Myers Squibb, Dr. Reddy's, Eli Lilly, Foamix, Formycon, Immunic, Janssen, LEO Pharma, Medac, MethoPharm, Novartis, Phi-Stone, Pierre Fabre, Sanofi Aventis, and UCB. **SI** declares receiving grants, consulting fees, and/or speaker's fees from Abbvie, Amgen, Eisai, Eli Lilly, Janssen, Kyowa Kirin, LEO Pharma, Maruho Pharmaceutical, Mitsubishi Tanabe, Novartis, Sun Pharmaceutical Industries, Taiho Yakuhin Koryo, Torii Yakuhin, and UCB. **JX** declares receiving grants, consulting fees, and/or speaker's fees from AbbVie, Bayer, Boehringer Ingelheim, Kyowa Kirin, La Roche-Posay China, Novartis, Pfizer, and Sanofi. **LL**, **MQ**, and **CT** are employees of Boehringer Ingelheim. **HB** declares paid consulting activities for AbbVie, Almirall, BIOCAD, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermavant Sciences, Eli Lilly, Janssen, Kyowa Kirin, LEO Pharma, Mylan, Novartis, UCB, and Xion Pharmaceuticals; receiving grant support from Boehringer Ingelheim, Janssen, LEO Pharma, Novartis, and Pfizer; and participating on a data safety monitoring board/advisory board for Avillion. 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.

Scan QR code for an interactive, electronic, device-friendly copy of this poster https://bit.ly/3JFqGzU

Click the icon to access an interactive microsite for this Smart poster