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Imsidolimab, an IL-36 Receptor Antagonist, Was Effective and Well-Tolerated for Treatment, Maintenance of Response, and Prevention of Flares in Patients With Generalized Pustular Psoriasis Results From the Phase 3 Trials, GEMINI-1 and GEMINI-2

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BACKGROUND & INTRODUCTION

- Generalized pustular psoriasis (GPP) is a chronic, systemic, inflammatory skin disease that can be severe, debilitating, and life threatening
- GPP is characterized by intermittent flares with eruptions of sterile pustules on erythematous skin. Systemic features such as high fever, general malaise, leukocytosis, and elevated C-reactive protein also occur; extracutaneous organ involvement can lead to substantial morbidity and mortality[1]
- Loss of function mutations in the gene encoding IL-36 receptor antagonist were identified in a subset of patients with GPP, suggesting that IL-36 is a key cytokine in the pathogenesis of GPP[2]
- Imsidolimab is an investigational IgG4 antibody that specifically binds to the IL-36 receptor and antagonizes IL-36 signaling, reducing the functional activity of IL-36 cytokines
- In the Phase 2 GALLOP trial (NCT03619902), imsidolimab was well tolerated and demonstrated rapid and sustained improvements in symptoms and pustular eruptions in patients with GPP flare,[3] providing supporting evidence to advance to Phase 3 studies
- The results of 2 completed Phase 3 trials, GEMINI-1 (NCT05352893) and GEMINI-2 (NCT05366855), of imsidolimab in patients with GPP are reported here

METHODS

GEMINI-1

- Randomized, double-blind, placebo (PBO)-controlled, global study evaluated the safety and efficacy of an induction dose of imsidolimab 750mg or 300mg IV versus PBO for treatment of GPP flare
- Adults, 18 to 80 years of age, with clinically confirmed diagnosis of GPP flare of moderate to severe intensity defined as:
  - Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) score ≥3
  - Pustulation Rating Scale (PRS) score ≥3
  - Active flare and pustules ≥5% of body surface area (BSA)
- Patients were randomized (1:1:1) to a single dose of imsidolimab 750mg IV, imsidolimab 300mg IV, or PBO IV and followed until they rolled over to GEMINI-2 (**Figure 1**)
- Primary endpoint: GPPPGA score of clear (0) or almost clear (1) collectively across all GPP disease attributes (pustulation, erythema, scaling) at Week 4
- Key secondary endpoint: PRS of 0 or 1 at Week 1

GEMINI-2

- Long-term extension of GEMINI-1: randomized, double-blind, PBO-controlled study of imsidolimab 200mg SC every 4 weeks vs PBO for maintenance and prevention or delaying recurrence of a re-flare (GPPPGA ≥3) relative to a single IV induction dose (**Figure 1**)

GEMINI-1 and GEMINI-2 Study Designs

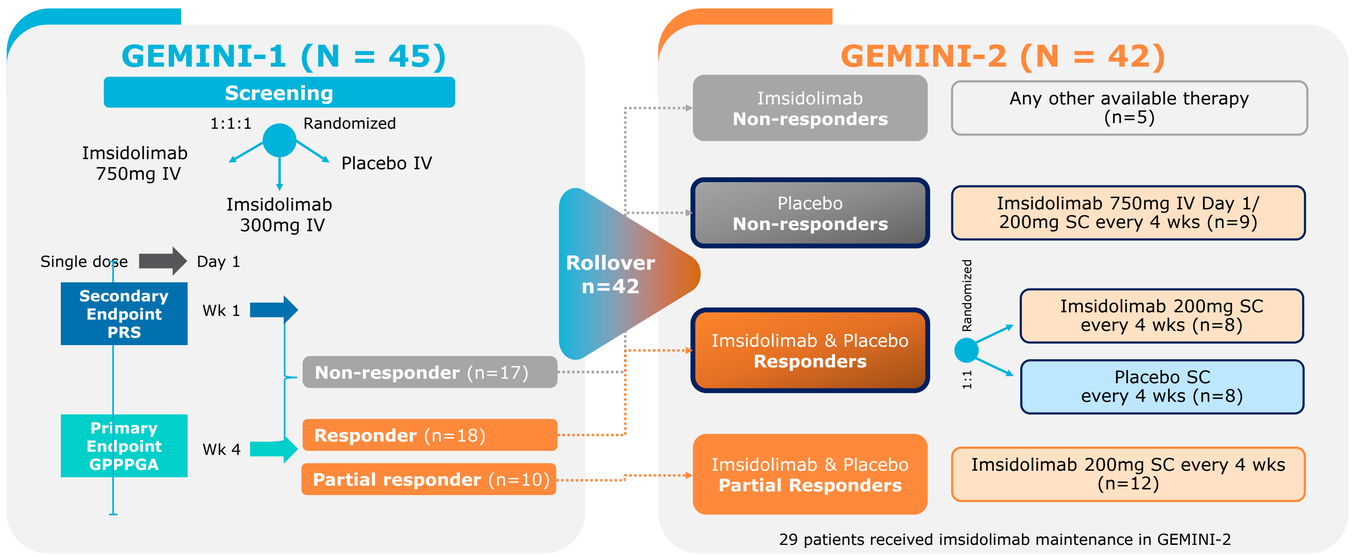


Figure 1. Study design and patient numbers per groups in GEMINI-1 and GEMINI-2

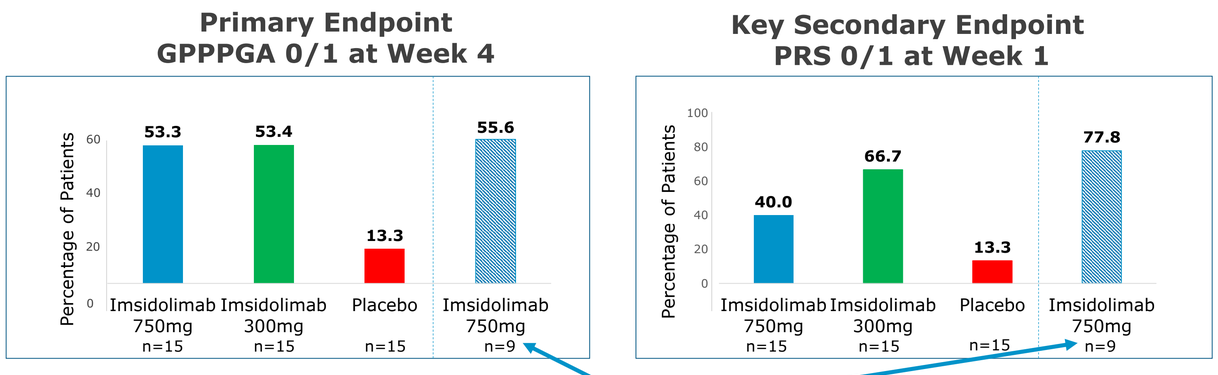
- Patients in GEMINI-1 could rollover into GEMINI-2 if they were a responder or partial responder at Week 4. Patients who had no improvement or worsened (non-responder) between Week 1 and Week 4 could rollover into GEMINI-2 to receive rescue therapy
- Treatment in GEMINI-2 was based on their responder status in GEMINI-1 (**Figure 1**)
- Patients were followed for at least 24 weeks and up to maximum of 92 weeks
- Topline PBO-controlled data from the responders re-randomized in GEMINI-2 and observational data from the PBO non-responders who received imsidolimab 750mg IV as rescue therapy and 200mg SC for maintenance in GEMINI-2 are presented

Responder Definitions

- Responder: Completed Week 4 of GEMINI-1 with GPPPGA score of 0 or 1 collectively across all GPP disease attributes (pustulation, erythema, scaling)
- Partial responder: Completed Week 4 of GEMINI-1 but did not have GPPPGA score of 0 or 1
- Non-responder: No improvement or worsened

RESULTS

GEMINI-1: Imsidolimab 750mg and 300mg IV were Effective in the Treatment of GPP Flare in GEMINI-1 & in Crossover PBO Patients in GEMINI-2 (750mg IV)



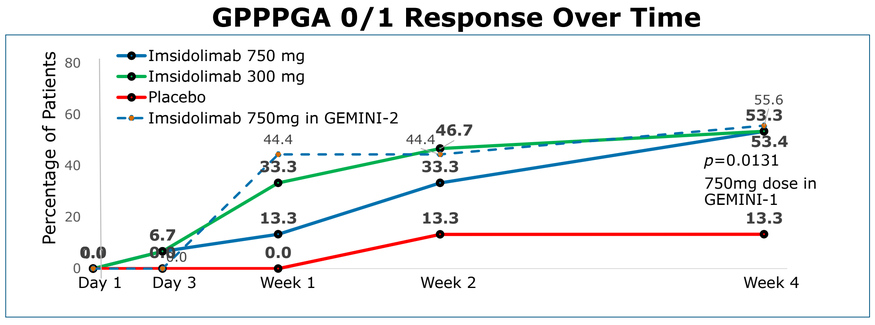
Single doses of imsidolimab were highly effective at inducing GPPPGA response vs. PBO

Observational data from PBO non-responders in GEMINI-1 who crossed over to GEMINI-2 rescued with imsidolimab 750mg IV showed similar results to GEMINI-1

Single doses of imsidolimab had a rapid onset of effect within days to 1 week vs. PBO

Figure 2. Percentage of patients achieving GPPPGA 0/1 at Week 4 and PRS 0/1 at Week 1 in GEMINI-1 after a single IV dose of imsidolimab 750mg, 300mg, or PBO

GEMINI-1: Rapid and Clinically Meaningful Improvement of GPP was Obtained With Single Dose Imsidolimab 750mg IV and 300mg IV



- Significantly more patients who received imsidolimab 750mg IV in GEMINI-1 achieved the primary endpoint of GPPPGA 0/1 at Week 4 vs. PBO (**Figure 3**)

Figure 3. Percentage of patients who received a single dose of imsidolimab 750mg IV, imsidolimab 300mg IV, or PBO in GEMINI-1 and achieved GPPPGA score of 0/1. The dashed line is the percentage of PBO non-responders who crossed over to GEMINI-2 rescued with imsidolimab 750mg IV (observational data)

Safety and Tolerability

GEMINI-1

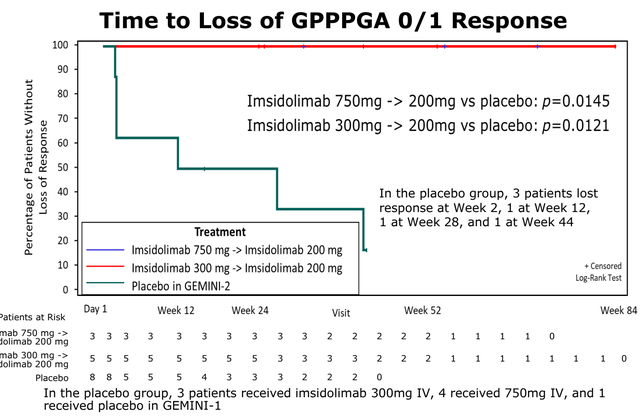
- Treatment-emergent adverse events (TEAE) were similar across treatment groups
- No SAEs or severe AEs in imsidolimab-treated patients
- No cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) or Guillain-Barre Syndrome (GBS)
- Low incidence and no elevation of infections vs. placebo
- No infusion reactions reported
- Of the 30 patients treated with imsidolimab, 1 treated with 750 mg (3%) had detectable non-neutralizing anti-drug antibodies (ADA)

GEMINI-2

- TEAEs were similar in imsidolimab and PBO groups
- No SAEs led to study treatment discontinuation/withdrawal
- Similar to GEMINI-1: No DRESS or GBS, low incidence and no elevation of infections vs placebo, no infusion reaction, and uncommon ADA

GEMINI-2: Imsidolimab 200mg SC Every 4 Weeks Maintained Response & Prevented GPP Re-flaring Regardless of GEMINI-1 Imsidolimab Dose

- Imsidolimab (n=8): 100% maintained a GPPPGA score of 0/1 and 0 flared
- PBO (n=8): 25% maintained a GPPPGA score of 0/1 and 62.5% flared (GPPPGA ≥3)
- Imsidolimab significantly maintained GPPPGA response regardless of GEMINI-1 dose (**Figure 4**)
- PBO crossover patients who received imsidolimab 750mg IV/200mg SC in GEMINI-2 (n=9): 77.8% maintained remission for at least 24 weeks (observational data)



In the placebo group, 3 patients received imsidolimab 300mg IV, 4 received 750mg IV, and 1 received placebo in GEMINI-1

Figure 4. Kaplan-Meier curve of time to loss of response with imsidolimab 200mg SC (shown by dose of imsidolimab received in GEMINI-1) and PBO every 4 weeks

CONCLUSIONS

- Rapid and clinically meaningful improvement of GPP was obtained with single IV doses of imsidolimab 300mg and 750mg
- Regardless of the single IV dose received in GEMINI-1 (300 mg or 750 mg), maintenance dosing with every 4-week 200mg SC imsidolimab maintained clearance of GPP and prevented flares during at least 24 weeks of follow-up
- These findings from a randomized, double-blind, placebo-controlled trial were further supported with observational data from patients receiving open-label imsidolimab
- Across the trials, imsidolimab administered IV or SC was well tolerated
  - Low incidence and no elevation of infections vs placebo
  - No infusion reactions were reported
- Overall, ADAs were non-neutralizing and detection was uncommon
- Imsidolimab represents a promising therapeutic option for patients with GPP

ACKNOWLEDGEMENTS

1. GEMINI-1 and GEMINI-2 trials were supported by Anaptys
2. Disclosures: AR, HB, EWYY, MB, PC, JCS, MD, JEG were investigators for GEMINI-1 and GEMINI-2. AR, HB, & JEG are advisors for Anaptys. AS, BR, PR, KS, MD, and PL are employees and stockholders of Anaptys. Other disclosures available upon request
3. Medical writing support was provided by Susan Sutch, PharmD and funded by Anaptys
4. Anaptys is grateful to all investigators and to the patients and their caregivers for participation in these studies

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Presented at European Academy of Dermatology & Venereology, Amsterdam, The Netherlands, 25-28 September 2024