Real-world efficacy of spesolimab: Reports from four patients with generalized pustular psoriasis

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These 4 cases provide real-world evidence of the efficacy and safety of spesolimab in treating GPP

AIM

- To describe 4 cases in which patients with GPP were treated successfully with spesolimab in both inpatient and outpatient settings

INTRODUCTION

- GPP is a chronic, inflammatory skin disease characterized by sudden and widespread pustular eruptions, often accompanied by systemic symptoms[1]
- GPP can be life-threatening if left untreated, due to complications such as sepsis and multi-organ failure[1–3]
- Dysregulation of the IL-36 pathway appears to play a key role in the pathophysiology of GPP[4,5]
- Spesolimab is a first-in-class humanized monoclonal antibody that binds specifically to the IL-36 receptor, and antagonizes IL-36 signaling
- Spesolimab is currently the only US FDA-approved treatment for GPP flares in adults, and is approved for GPP flare treatment in many other countries
- Per the label, spesolimab should be administered as a single 900 mg dose by IV infusion over 90 minutes. If flare symptoms persist, an additional 900 mg IV dose may be administered 1 week after the initial dose[6]

KEY THEMES

Key Themes

	Spesolimab treatment offers rapid improvement in symptoms and QoL for patients with GPP
	Burden of disease is associated with GPP (e.g. need for hospitalization; impact on daily activities; decreased psychosocial well-being)
	Triggers for GPP flare include corticosteroids and HCQ
	There may be difficulties in diagnosing GPP (e.g. exclude AGEP)
	Diagnosis of GPP is based on clinical features (skin biopsy not required)

CONCLUSIONS

- These cases provide real-world evidence that spesolimab is an effective and safe treatment for GPP flares. Spesolimab treatment results in rapid improvement in symptoms and patient QoL
- When used in an inpatient setting for severe GPP, spesolimab treatment allowed for rapid patient improvement and discharge the next day
- Triggers for GPP flares may include corticosteroids (use and dose tapering) and HCQ
- The early symptoms of GPP can be difficult to distinguish from AGEP
- Per recent guidelines from the National Psoriasis Foundation, diagnosis of GPP should be based on clinical features, and treatment of this life-threatening disease should not be delayed while waiting for skin biopsy results[7]

CASE PRESENTATIONS

Patient case summaries

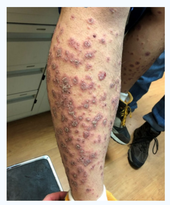
Case report	Case 1	Case 2	Case 3	Case 4
Patient demographics	18-year-old Asian male	58-year-old White female	36-year-old American Indian male	40-year-old White female
GPP presentation	Plaques studded with pustules mainly affecting trunk and legs	Pustules affecting axilla and neck 2 weeks after initiating HCQ and intra-articular corticosteroids for undiagnosed joint pain Pustules spread to whole body despite oral corticosteroid treatment for suspected AGEP	Pustules affecting whole body following high-dose IV corticosteroid treatment for unrelated reasons Systemic symptoms including dyspnea, generalized weakness requiring use of a wheelchair, swelling of face, extremities, and genitals	Annular pustular plaques on extremities and trunk 3 weeks after initiating HCQ treatment Rapid worsening and generalization of pustules with tapering of corticosteroids Systemic symptoms including fever, chills, rigors, joint aches, malaise, fatigue
Required hospitalization	No	No	Yes	Yes
Initial diagnosis	GPP	AGEP; biopsy showed subcorneal pustular dermatosis	GPP	AGEP; biopsy showed subcorneal neutrophilic pustules
Comorbidities	Plaque psoriasis; autism; obesity; autoimmune hepatitis	Non-specific arthritis (later diagnosed as PsA); Raynaud's disease; diverticulitis	Plaque psoriasis; hypertension; obesity; T2D; obstructive sleep apnea	Granuloma annulare
Spesolimab treatment*	Two spesolimab (900 mg IV) infusions, given 7 days apart; outpatient infusion center	Two spesolimab (900 mg IV) infusions, given 7 days apart; home infusion service	Two spesolimab (900 mg IV) infusions, given 20 days apart; outpatient infusion center	Two spesolimab (900 mg IV) infusions, given 8 days apart; inpatient (#1); outpatient infusion center (#2)
Concomitant treatment	Topical triamcinolone	Corticosteroid (dose taper completed day before infusion #2)	Guselkumab; topical triamcinolone	Cyclosporine; corticosteroid (dose taper); topical triamcinolone
Previous treatment	Topicals (triamcinolone, calcipotriene, and salicylic acid); acitretin	Corticosteroid; cyclosporine	Topical triamcinolone; antibiotics	Corticosteroid; cyclosporine; topical triamcinolone; cyproheptadine
Other information	-	*Pseudomonas* infection on lower leg	Patient received high-dose IV corticosteroids on the same day of spesolimab infusion #1	-

*Per the label, spesolimab should be administered as a single 900 mg dose by IV infusion over 90 minutes. If flare symptoms persist, an additional 900 mg IV dose may be administered 1 week after the initial dose[6]

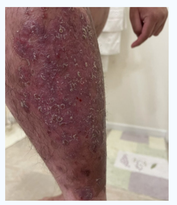
Case 1: 18-year-old Asian male

- Initially diagnosed with guttate psoriasis; topical therapy failed; acitretin was stopped due to intolerance
- Spesolimab was given ~4 weeks after rash onset
- Following the first spesolimab infusion, there was slight improvement in pustules; however, new pustules continued to develop. Following the second infusion, pustules cleared within 2 weeks (**Figure 1**)
- Before spesolimab treatment, the patient was bullied at school because his skin lesions were thought to be contagious. The patient's confidence improved following clearance of the pustules

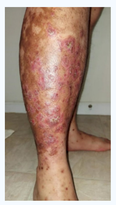
Figure 1. Skin on lower leg before and after spesolimab treatment



Right lower leg: pre-spesolimab



Right lower leg: 5 days post-spesolimab infusion #1



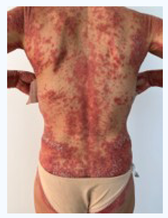
Right lower leg: 5 days post-spesolimab infusion #2

This case highlights the severe impact GPP can have on QoL. The patient was embarrassed to wear shorts and was also bullied. Skin lesions improved following treatment with spesolimab

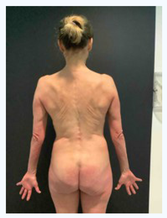
Case 2: 58-year-old White female

- Received HCQ for joint pain (later diagnosed as psoriatic arthritis); developed a pustular rash
- Rash was initially diagnosed as AGEP and was treated with corticosteroids; this was followed by worsening of the pustular rash
- Spesolimab was given ~3 weeks after rash onset
- Following the first spesolimab infusion there were no new pustules within 24 hours. The patient continued to have erythematous patches with desquamation
- The patient's skin was fully clear 3 weeks following the second spesolimab infusion, though many areas resolved much earlier (**Figure 2**)

Figure 2. Skin on back before and after spesolimab treatment



Back: pre-spesolimab



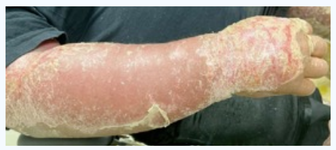
Back: 10 days post-spesolimab infusion #2

This case highlights the difficulty in distinguishing between GPP and AGEP. This case also highlights the rapid response seen with spesolimab treatment

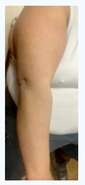
Case 3: 36-year-old American Indian male

- The patient presented to the ED (reason unknown; not GPP) and received corticosteroids. He re-presented within days with a pustular rash, received further corticosteroids, and was referred to the Dermatology service. He was examined by a dermatologist 2 days later. He had a rapidly worsening pustular rash and systemic symptoms; his ADLs were severely affected. Hospitalization was required
- The patient experienced a significant delay in receiving spesolimab, due to reimbursement issues between the hospital and patient's insurance provider (Indian Health Services); hospitalization was therefore prolonged
- Spesolimab was given ~4 weeks after rash onset
- The patient showed ~50% improvement at 1 week following the first spesolimab infusion; some residual erythema and pustules
- He was completely clear of pustules 24 hours after receiving the second spesolimab infusion (**Figure 3**)
- Spesolimab rapidly improved the patient's QoL; pain and generalized weakness resolved completely, and he could resume normal ADLs within 1 week of spesolimab treatment

Figure 3. Skin on arm before and after spesolimab treatment



Right arm: pre-spesolimab



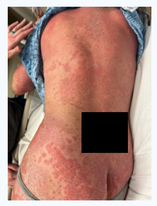
Right arm: 3 weeks post-spesolimab infusion #2

This case highlights corticosteroid use as a trigger for GPP flares. This case also illustrates logistical barriers to receiving spesolimab treatment (e.g. with insurance provider)

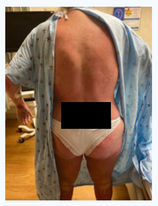
Case 4: 40-year-old White female

- Presented with granuloma annulare, was treated with HCQ, and subsequently developed a pustular rash
- Rash was initially diagnosed as AGEP and was treated with corticosteroids. This was followed by rapid worsening of the rash, and systemic symptoms; hospitalization was required
- Spesolimab was given ~12 days after rash onset
- The patient experienced a 75% improvement in itching, pain, and pustules within 24 hours of the first spesolimab infusion (**Figure 4**) and was discharged from hospital the next day
- Further symptoms on her face and acral regions cleared within 24 hours of the second infusion of spesolimab

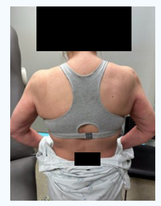
Figure 4. Skin on back before and after spesolimab treatment



Back: pre-spesolimab



Back: 14 hours post-spesolimab infusion #1



Back: 48 hours post-spesolimab infusion #2

This case highlights the importance of the availability of spesolimab in an inpatient setting to decrease hospitalization times for individuals with severe disease

Abbreviations

ADL, activity of daily living; AGEP, acute generalized exanthematous pustulosis; ED, emergency department; FDA, Food and Drug Administration; GPP, generalized pustular psoriasis; HCQ, hydroxychloroquine; IL-36, interleukin-36; IV, intravenous; PsA, psoriatic arthritis; QoL, quality of life; T2D, type 2 diabetes

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