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Real-World Experience with Spesolimab for Generalized Pustular Psoriasis: A Four-Case Series

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Introduction & Objectives:

Generalized pustular psoriasis (GPP) is a rare and potentially life-threatening autoinflammatory skin disease, characterized by sudden flares of sterile pustules and systemic symptoms. Recent advances have identified the IL-36 pathway as a key player in its pathogenesis, leading to the development of spesolimab, a humanized anti-IL-36R monoclonal antibody. In the Effisayil-1 trial, spesolimab showed rapid and sustained efficacy. While clinical trial data support its use, our contribution lies in presenting real-world clinical experience with spesolimab in four patients with severe GPP flares, reinforcing its effectiveness and utility in routine practice beyond controlled trial settings.

Materials & Methods:

This is a retrospective study in. We collected clinical data from the medical records of four patients diagnosed with severe GPP flares who were treated with spesolimab.

Results:

		PATIENT 1	PATIENT 2	PATIENT 3	PATIENT 4
SOCIO-DEMOGRAPHIC DATA	AGE AT DIAGNOSIS	63	51	72	80
	GENDER	♀	♀	♀	♂
	HISTORY OF PSORIASIS/ PSORIATIC ARTHROPATHY	Yes / Yes	Yes / Yes	Yes / No	No/ No (debut)
	PREVIOUS TREATMENTS RECEIVED	Topical corticosteroids, phototherapy, methotrexate, cyclosporine, acitretin, adalimumab, etanercept, apremilast	Topical corticosteroids, acitretin, cyclosporine, methotrexate, adalimumab, infliximab, salazopyrin	Topical corticosteroids and antifungals, acitretin	No
SPESOLIMAB-TREATED OUTBREAK	TRIGGER	Abrupt withdrawal of systemic corticosteroids	Acitretin dose reduction and gastroenteritis	Unidentified	Unidentified
	CLINICAL SUBTYPE	Von Zumbusch	Annular	Von Zumbusch	Annular
	BIOPSY	Gpp-compatible	Gpp-compatible	Gpp-compatible	Gpp-compatible
	SCORES (BSA/ GPPGA – pustules subscale)	50% / 4 – 4	40% / 3- 2	80% with 15% epidermal **detachment**/ 4 – 4	40% / 3 – 3
	ANALYTICAL FINDINGS AND SYSTEMIC COMPLICATIONS	Leukocytosis, elevated acute phase reactants. Psoriatic arthritis and **urinary tract infection.**	Leukocytosis, elevated acute phase reactants and creatinine. **Urinary tract infection**, anxiety	Severe leukocytosis, very elevated acute phase reactants and creatinine. Cutaneous bacterial overinfection	Leukocytosis, elevated acute phase reactants, creatinine, bilirubin and transaminases
	TIME TO RESPONSE (DAYS) (from 1st spesolimab dose to no new pustules)	5	2	1	1
	SECOND SPESOLIMAB DOSE	Yes	No	Yes	No
	HOSPITAL STAY (DAYS)	13	5	7	2
	REMISSION DURATION	42	22	Not applicable; due to severity, maintenance treatment was initiated without awaiting	In referral since hospital discharge (33 days)
	MAINTENANCE TREATMENT	Ixekizumab 80mg/4weeks	Acitretin 20mg/day and topical corticosteroids	Bimekizumab 320mg/ 8 weeks. Given poor response switched to Ustekinumab 90mg/12 weeks	No

Table 1

GPP is a rare and clinically heterogeneous disease, with four subtypes. In our cohort, two patients had the acute Von Zumbusch variant and two the annular subtype, illustrating the diversity of clinical patterns. Three patients had long-standing, treatment-refractory disease, while one was experiencing a first flare. Consistent with published data, 75% of our cases were women, supporting the reported female predominance.

Treatment with spesolimab led to rapid and significant improvement in all cases, with pustule clearance occurring within five days—often within the first 24 hours—objectively measured by the Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) scale. Two patients achieved complete pustular clearance with a single dose, without needing re-treatment. Systemic symptoms such as fever, pain, and psoriatic arthritis resolved alongside skin improvement.

Patient 4, who was treatment-naïve, showed the fastest and most sustained response. He achieved complete remission after just one dose, including normalization of transaminases, and has remained flare-free without maintenance therapy. This case suggests that early intervention with spesolimab may offer a window of opportunity for long-term disease control with minimal therapeutic exposure.

Patient 3 presented with a particularly severe flare, requiring admission to a burn unit due to >15% skin detachment. The response to spesolimab was striking, with dramatic improvement within 24 hours, further underscoring its utility in life-threatening cases.

The treatment was well tolerated. Two patients developed uncomplicated urinary tract infections, which resolved promptly with oral antibiotics and had no impact on treatment efficacy.

Three patients are currently receiving maintenance therapy, while one remains in sustained remission off-treatment. These real-world findings support spesolimab not only as an effective rescue therapy, but also as a potential disease-modifying option in selected patients.

Conclusion:

Our real-world data confirm the rapid and sustained efficacy of spesolimab in GPP flares, with responses seen within hours—even in refractory cases. A single dose was sufficient in half of the patients, including one treatment-naïve case now in remission without maintenance. These results support spesolimab as a powerful first-line option and highlight the need for further studies on early intervention and long-term disease control.