Global consensus on the clinical course, treatment and management of generalized pustular psoriasis (GPP)

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Using a Delphi panel approach, we have established global consensus on the clinical course, diagnosis, treatment goals and management of GPP; the evidence-based algorithm we have subsequently developed will provide much needed guidance for physicians to implement in clinical practice

PURPOSE

To conduct a Delphi panel study to gain advanced insights into the clinical course, diagnosis, treatment goals and management of GPP

INTRODUCTION

- GPP is a rare, neutrophilic skin disease, with a prevalence ranging from 0.02–1.4 per 10,000 people worldwide[1–5]
- ERASPEN and JDA have published guidelines for the classification and diagnosis of GPP, respectively;[1,2] however, the evidence base for these guidelines is limited
- Few clinical trials have been conducted in GPP due to the rarity of the disease and lack of international consensus on criteria for diagnosis and treatment goals
- As a result, there is a general paucity of information to inform optimal management of patients with GPP

CONCLUSIONS

- Global consensus among expert dermatologists was reached on:
  - Key clinical and histological features supporting GPP diagnosis and flare definition
  - GPP being distinct from plaque psoriasis, although both conditions may occur in the same patient
  - Treatment goals of rapid, sustained control of cutaneous and systemic symptoms, and long-term prevention of new flares
  - Multidisciplinary disease management and assessment tools for monitoring disease severity in clinical practice

METHODS

- An SLR was conducted to identify published literature and develop statements for four key domains of GPP:
  - Clinical course and flare definition
  - Diagnosis
  - Treatment goals
  - Holistic management of GPP
- The Delphi panel comprised 21 expert dermatologists
- Statements were rated on a Likert scale (1 [strong disagreement] to 7 [strong agreement]); consensus was reached when statements were agreed on by ≥80% of panelists

SLR and statement development → Global experts rated statements in 2 Delphi panel rounds → Clinical management algorithm developed

RESULTS

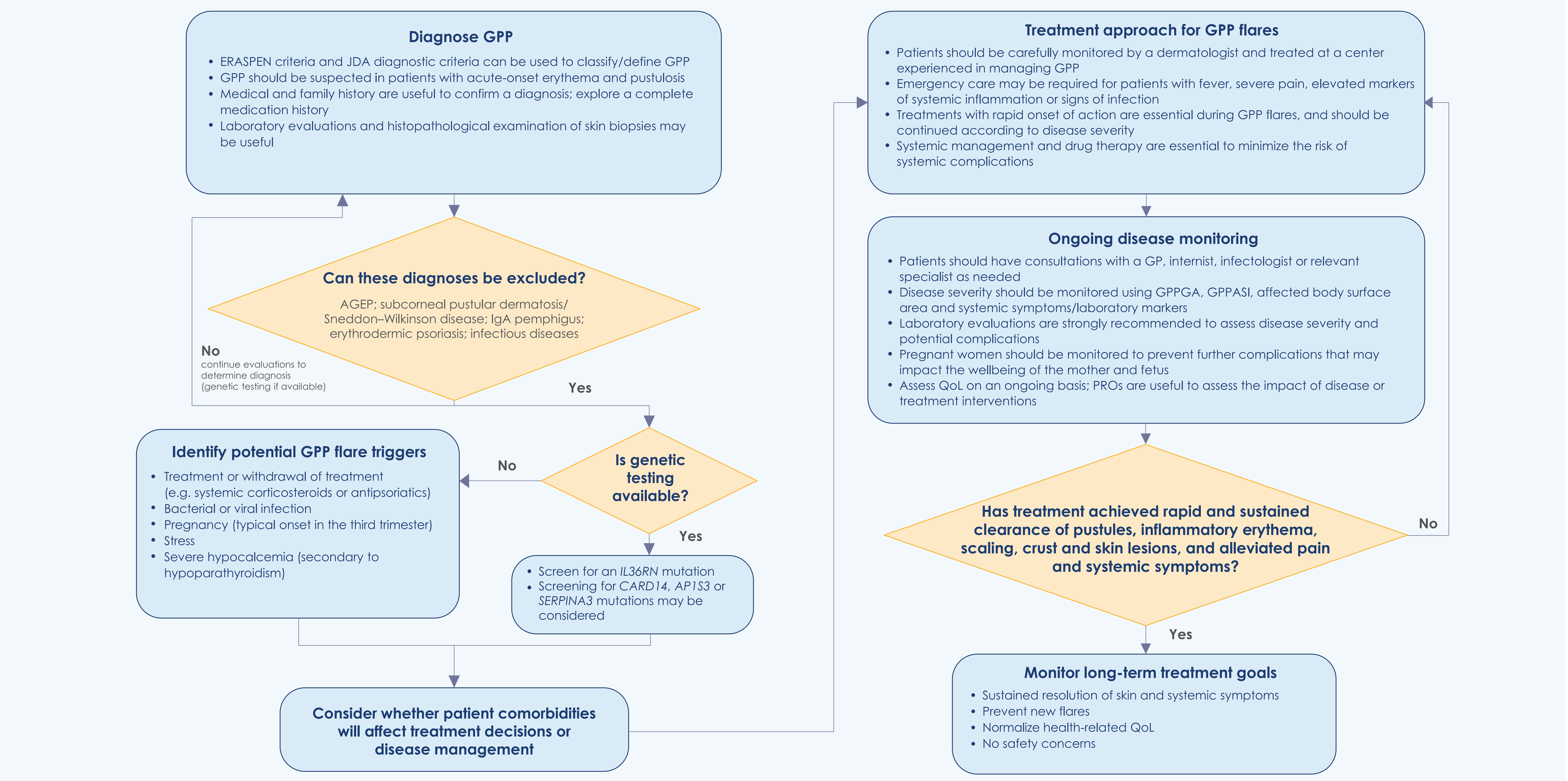
Consensus after 2 Delphi panel rounds

Domain/subdomain	Statements, n	Agreement, n (%)
Round 1		
Round 1 total	**185**	**141 (76.2)**
Domain 1: Clinical course and flare definition		
GPP definition/classification	21	16 (76.2)
Flare definition and GPP clinical course	9	9 (100.0)
Potential triggers and disposing factors	27	13 (48.1)
Prognosis	24	23 (95.8)
Domain 1 total	81	61 (75.3)
Domain 2: Diagnosis		
Criteria	2	2 (100.0)
Clinical diagnosis of GPP	3	3 (100.0)
Laboratory tests relevant for the diagnosis of GPP	15	9 (60.0)
Genetic screening in GPP diagnosis	2	1 (50.0)
Histopathologic features of GPP	5	4 (80.0)
Differential diagnosis	14	5 (35.7)
Domain 2 total	41	24 (58.5)
Domain 3: Treatment goals		
Flare/acute-phase treatment goals	9	9 (100.0)
Long-term goals	8	8 (100.0)
Domain 3 total	17	17 (100.0)
Domain 4: Holistic management of GPP		
Domain 4 total	46	39 (84.8)
Round 2		
Round 2 total	**28**	**16 (57.1)**
Domain 1: Clinical course and flare definition		
GPP definition/classification	3	0
Potential triggers and disposing factors	2	0
Domain 1 total	5	0
Domain 2: Diagnosis		
Laboratory tests relevant for the diagnosis of GPP	3	1 (33.3)
Genetic screening in GPP diagnosis	2	2 (100.0)
Histopathologic features of GPP	7	7 (100.0)
Differential diagnosis	2	0
Domain 2 total	14	10 (71.4)
Domain 4: Holistic management of GPP		
Domain 4 total	9	6 (66.7)
Rounds 1 and 2		
Total	**213**	**157 (73.7)**

- **Overall, dermatologists reached consensus on 73.7% of statements, and these formed the basis of the clinical management algorithm**
- **All dermatologists reached consensus on statements on treatment goals, and high levels of agreement were reported for statements on holistic management**
- **More evidence is needed in areas with low consensus, such as potential triggers and disposing factors, laboratory tests relevant for the diagnosis of GPP and differential diagnoses**

Clinical management flow diagram for GPP based on consensus statements

For a detailed clinical management algorithm that summarizes all consensus statements, please scan the QR code at the bottom of the poster


Diagnose GPP
• ERASPEN criteria and JDA diagnostic criteria can be used to classify/define GPP
• GPP should be suspected in patients with acute-onset erythema and pustulosis
• Medical and family history are useful to confirm a diagnosis; explore a complete medication history
• Laboratory evaluations and histopathological examination of skin biopsies may be useful
Can these diagnoses be excluded?
AGEP; subcorneal pustular dermatosis/ Sneddon–Wilkinson disease; IgA pemphigus; erythrodermic psoriasis; infectious diseases
No
continue evaluations to determine diagnosis (genetic testing if available)
Yes
Is genetic testing available?
No
Yes
Identify potential GPP flare triggers
• Treatment or withdrawal of treatment (e.g. systemic corticosteroids or antipsoriatics)
• Bacterial or viral infection
• Pregnancy (typical onset in the third trimester)
• Stress
• Severe hypocalcemia (secondary to hypoparathyroidism)
• Screen for an IL36RN mutation
• Screening for CARD14, AP1S3 or SERPINA3 mutations may be considered
Consider whether patient comorbidities will affect treatment decisions or disease management
Treatment approach for GPP flares
• Patients should be carefully monitored by a dermatologist and treated at a center experienced in managing GPP
• Emergency care may be required for patients with fever, severe pain, elevated markers of systemic inflammation or signs of infection
• Treatments with rapid onset of action are essential during GPP flares, and should be continued according to disease severity
• Systemic management and drug therapy are essential to minimize the risk of systemic complications
Ongoing disease monitoring
• Patients should have consultations with a GP, internist, infectologist or relevant specialist as needed
• Disease severity should be monitored using GPPGA, GPPASI, affected body surface area and systemic symptoms/laboratory markers
• Laboratory evaluations are strongly recommended to assess disease severity and potential complications
• Pregnant women should be monitored to prevent further complications that may impact the wellbeing of the mother and fetus
• Assess QoL on an ongoing basis; PROs are useful to assess the impact of disease or treatment interventions
Has treatment achieved rapid and sustained clearance of pustules, inflammatory erythema, scaling, crust and skin lesions, and alleviated pain and systemic symptoms?
No
Yes
Monitor long-term treatment goals
• Sustained resolution of skin and systemic symptoms
• Prevent new flares
• Normalize health-related QoL
• No safety concerns

Clinical course and flare definition
- GPP presents as primary, macroscopically visible pustules of variable size on inflamed skin, classically affecting non-acral areas, and is associated with systemic symptoms
- The clinical course of GPP is highly variable; it can be relapsing or persistent and is generally unstable and prolonged without treatment

Diagnosis
- GPP should be suspected in patients with acute-onset erythema and pustulosis, and a complete medical history should be explored
- Genetic testing is helpful for the diagnosis of GPP, not just as a research tool

Treatment goals
- In the acute phase, the aim of treatment should be to achieve rapid and sustained clearance of pustules, inflammatory erythema, scaling, crust and skin lesions
- In the long-term, treatment should prevent the occurrence of new flares, achieve sustained resolution of skin and systemic symptoms, and improve health-related QoL, without any safety concerns

Holistic management of GPP
- Disease severity should be monitored using GPPGA, GPPASI, affected body surface area and systemic symptom and laboratory marker assessments; the impact of treatment on patient QoL can be monitored using PROs
- Due to the range of complications and comorbidities associated with GPP, a multidisciplinary approach is required; consultations with a GP, internist, infectologist or other specialist should be carried out as needed

Abbreviations

AGEP, acute generalized exanthematous pustulosis; ERASPEN, European Rare and Severe Psoriasis Expert Network; GP, general practitioner; GPP, generalized pustular psoriasis; GPPASI, Generalized Pustular Psoriasis Area and Severity Index; GPPGA, Generalized Pustular Psoriasis Physician Global Assessment; Ig, immunoglobulin; JDA, Japanese Dermatological Association; PRO, patient-reported outcome; QoL, quality of life; SLR, systematic literature review.

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Data sharing statement

To ensure independent interpretation of clinical study results and enable authors to fulfill their role and obligations under the ICMJE criteria, Boehringer Ingelheim grants all external authors access to relevant clinical study data. In adherence with the Boehringer Ingelheim Policy on Transparency and Publication of Clinical Study Data, scientific and medical researchers can request access to clinical study data after publication of the primary manuscript in a peer-reviewed journal, regulatory activities are complete, and other criteria are met. Researchers should use the https://vivli.org/ link to request access to study data and visit https://www.mystudywindow.com/msw/datasharing for further information.

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