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Flare frequency and patient characteristics in generalized pustular psoriasis (GPP) – A multicentre observational study

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Despite current treatments, patients with GPP still experience frequent moderate and severe flares, highlighting the unmet clinical need in this patient population

PURPOSE

To investigate the frequency of GPP flares, clinical characteristics and treatment history of patients diagnosed with GPP in the past 10 years at 29 medical facilities in Japan.

INTRODUCTION

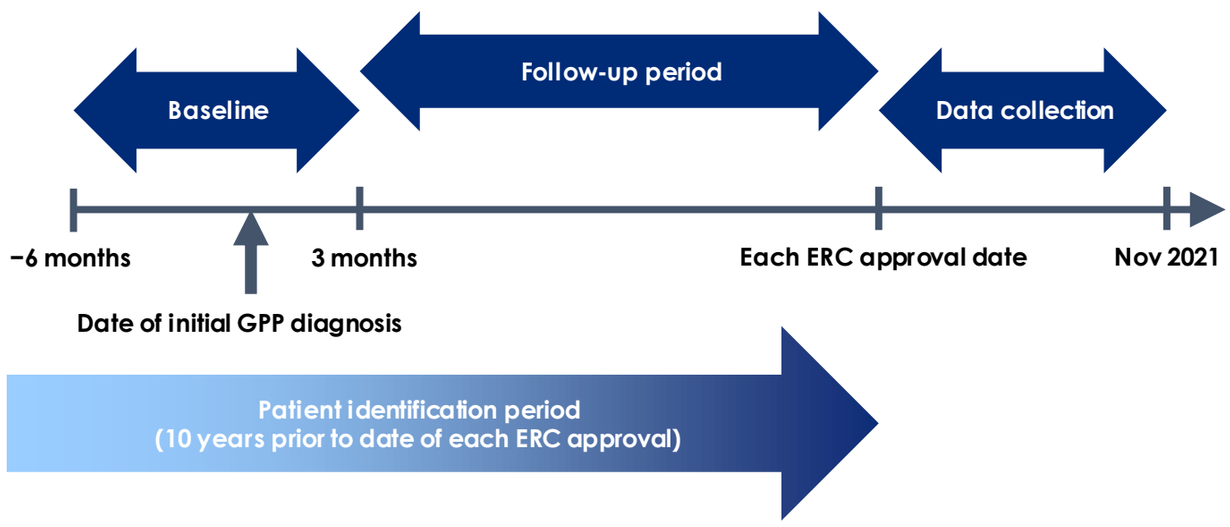
- GPP is a severe and rare relapsing–remitting disease characterised by recurrent pustules and erythematous eruptions, with complications such as respiratory and circulatory failure, and even death[1,2]
- Multiple treatment modalities for GPP, including corticosteroids and TNF-α inhibitors, have been approved in Japan[2,3]
- While epidemiological studies of GPP have been performed in Japan,[2] data relating to the frequency and severity of GPP flares have not been reported, and data regarding the current treatment landscape and genetic mutations associated with GPP are limited

CONCLUSIONS

- The study population of 205 patients with GPP represents a large sample for a chart review
- At baseline, 177 patients had a GPP flare (severe, 99; moderate, 52; mild, 26)
- During follow-up, 70 patients reported 106 flares (severe, 50; moderate, 55; mild, 1) and the overall incidence of acute GPP flares was 11.5 per 100 person-years
- These data highlight that even under current treatment conditions in Japan, patients with GPP still experience moderate and severe flares and an unmet medical need exists

METHODS

- **Design:** A retrospective chart review study
- **Inclusion criteria:** Patients diagnosed with GPP (2006 JDA criteria), with ≥6 months' continuous observation within 10 years of protocol approval by the ERC of each institution
- **Data:** Patient demographics, medical history, treatment dose and frequency, laboratory tests, and flare history
- **Primary endpoint:** Flare frequency and severity (adjudicated by an expert committee)
- **Secondary endpoints:** Patient demographics at initial diagnosis and GPP treatment during follow-up



RESULTS

Baseline demographics and medical history

Parameter	N=205
Age	n=205
Median (Q1–Q3), years	53.0 (42.0–66.0)
Mean (SD), years	52.0 (19.3)
Sex	n=205
Female, n (%)	99 (48.3)
Height	n=149
Median (Q1–Q3), cm	162.0 (153.0–167.0)
Mean (SD), cm	158.0 (17.9)
Body weight	n=156
Median (Q1–Q3), kg	61.5 (51.7–72.0)
Mean (SD), kg	61.6 (17.9)
BMI	n=146
Median (Q1–Q3), kg/m^2	23.8 (21.0–26.9)
Mean (SD), kg/m^2	24.2 (5.1)
Family history of GPP, n/N (%)	7/155 (4.5)
Family history of psoriasis-related diseases, n/N (%)*	6/120 (5.0)
Presence of GPP-associated mutations in patients with retrospective testing available, n/N (%)*	
IL36RN	12/39 (30.8)
CARD14	2/16 (12.5)
AP1S3	0/2 (0.0)

*Number of patients tested (N) vs the number of patients positive (n)

The patient population included a similar proportion of males and females and the mean age was 52 years; *IL36RN* mutations were the most frequently observed GPP-associated mutations (30.8%)

Baseline JDA severity determination*

A. Assessment of skin symptoms		
Overall score, mean (SD)		**4.8 (2.5)**
Erythema area (total)	≥75: Severe (3 points)	88 (42.9)
	25 to <75: Moderate (2 points)	72 (35.1)
	<25: Mild (1 point)	30 (14.6)
Erythema area with pustules	≥50: Severe (3 points)	33 (16.1)
	10 to <50: Moderate (2 points)	81 (39.5)
	<10: Mild (1 point)	50 (24.4)
Oedema area	≥50: Severe (3 points)	23 (11.2)
	10 to <50: Moderate (2 points)	64 (31.2)
	<10: Mild (1 point)	30 (14.6)
B. Evaluation of systemic symptoms and laboratory findings		
Overall score, mean (SD)		**3.3 (2.4)**
Fever (°C)	≥38.5: 2 points	35 (17.1)
	37 to <38.5: 1 point	79 (38.5)
	<37: 0 points	77 (37.6)
WBC (/μL)	≥15,000: 2 points	51 (24.6)
	10,000 to <15,000: 1 point	63 (30.7)
	<10,000: 0 points	85 (41.5)
CRP (mg/dL)	≥7.0: 2 points	61 (29.8)
	0.3 to <7.0: 1 point	94 (45.9)
	<0.3: 0 points	41 (20.0)
Serum albumin (g/dL)	<3.0: 2 points	45 (22.0)
	3.0 to <3.8: 1 point	58 (28.3)
	≥3.8: 0 points	87 (42.4)
Total score: A + B, mean (SD)		**8.1 (4.1)**

Data are presented as n (%), unless otherwise specified. Assessment of skin symptoms included: erythema, pustules and oedema (0–9 points). Evaluation of systemic symptoms and laboratory findings included: fever, WBC count, serum CRP and serum albumin (0–8 points).
*JDA severity classification: mild, 0–6 points; moderate, 7–10 points; severe, 11–17 points.

Based on JDA severity determinations, 74 patients (36.1%) had mild GPP, 63 (30.7%) had moderate GPP, and 68 (33.2%) had severe GPP

Flare frequency

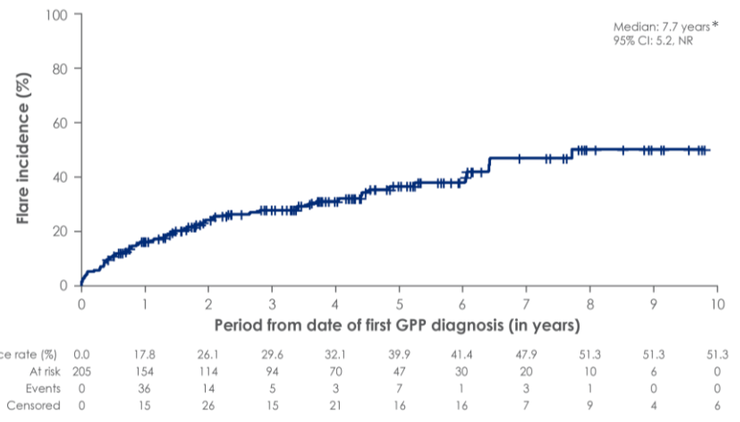
Baseline	Patients (N=205)
All flares, n (%)	**177 (86.3)**
Mild	26 (12.7)
Moderate	52 (25.4)
Severe	99 (48.3)

Follow-up	Patients, n (%)	Number of occurrences	Frequency (of occurrence), per 100 person-years
All flares	**70* (34.1)**	**106**	**11.5**
Mild	1 (0.5)	1	0.1
Moderate	40 (19.5)	55	6.0
Severe	36 (17.6)	50	5.4

Flares and severity were reviewed by the Data Review Committee. Flares for which the time of onset was unclear or the severity was difficult to evaluate were assessed based on the flare definition, which was defined by the Data Review Committee.
*When only the most severe flare for each patient was counted, 34 patients (15.0%) had a moderate flare and 36 (17.6%) had a severe flare.

During follow-up, 106 flares were observed in 70 patients (34.1%): 47 (22.9%) had 1 flare, 14 (6.8%) had 2 flares, and nine (4.4%) had ≥3 flares

Flare occurrence during follow-up: Time to onset of the first GPP flare



*Refers to median time to onset of the first GPP flare.

The cumulative incidence of flares from the date of diagnosis was 17.8% at 1 year, 29.6% at 3 years, and 39.9% at 5 years

Abbreviations
BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; ERC, Ethics Review Committee; GPP, generalized pustular psoriasis; JDA, Japanese Dermatological Association; NR, not reached; Q, quartile; SD, standard deviation; TNF, tumour necrosis factor; WBC, white blood cell.

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