

Characterization of flares in patients with generalized pustular psoriasis – a population-based study from the French National Health Data System database (SNDS)

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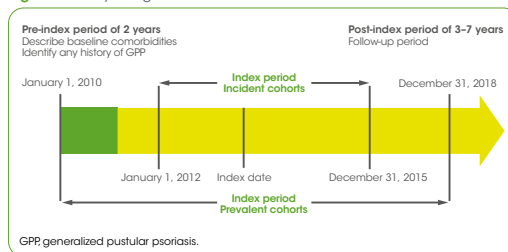
Background

- Generalized pustular psoriasis (GPP) is a rare, autoinflammatory skin disease characterized by erythema, edema, and the sudden widespread eruptions of visible pustules, which may or may not be preceded by a history of plaque psoriasis^{1,2}
- The clinical course of GPP is highly variable as it can be relapsing with recurrent flares or persistent with intermittent flares³
- Known triggers of GPP flares are infections, stress, and the administration or discontinuation of certain medications⁴
- GPP flares can lead to life-threatening complications such as septic shock, renal failure, cholangitis and respiratory abnormalities, such as neutrophilic pneumonitis and acute respiratory distress syndrome, and death⁴
- There are no approved GPP-specific therapies in the United States and Europe, and the evidence that supports currently recommended treatments, such as acitretin, methotrexate and cyclosporine, is insufficient^{5,6}
- There are limited real-world data characterizing patients with GPP flares, and the impact of flares on disease progression, morbidity, and mortality due to the difficulty identifying GPP flares in administrative claims databases
- Here, the results of an observational retrospective study based on the French National Health Data System (SNDS), aimed at characterizing GPP flares frequency and severity by analyzing hospital admissions, intensive care unit admissions, and length of stay, are reported

Methods

- This study was conducted in France using secondary administrative claims data obtained from the SNDS database, which covers almost the entire French population (~66 million inhabitants) and contains data from the national health insurance database (SNIIRAM), the national hospital discharge database (PMSI) and death statistics (CépiDC)
- Patients with GPP were identified and organized into two cohorts:
 - Prevalent cohort, which included all patients diagnosed with GPP if they had ≥ 1 hospital admission with primary, related or associated diagnosis of GPP (ICD-10 code L40.1) between January 1, 2010 and December 31, 2018 (Figure 1)
 - Incident cohort, which included patients newly diagnosed with GPP (ICD-10 code L40.1) with no history of GPP before the date of the first hospitalization at (the index date) (Figure 1)
- Patients with GPP flares were derived from the GPP incident cohort and were identified between 2012 and 2015 if they had a primary diagnosis of GPP (ICD-10 code L40.1) in a medical, surgical, or obstetric inpatient setting during the study period and ≥ 3 days of hospitalization
- The following outcomes among patients with GPP flares were described:
 - Characteristics of patients with GPP flares
 - Number of flares per patient during the follow-up
 - Mortality in patients with GPP flares
 - Hospitalization of patients with GPP flares
- Descriptive statistical analyses were conducted for baseline and outcomes measures

Figure 1. Study design

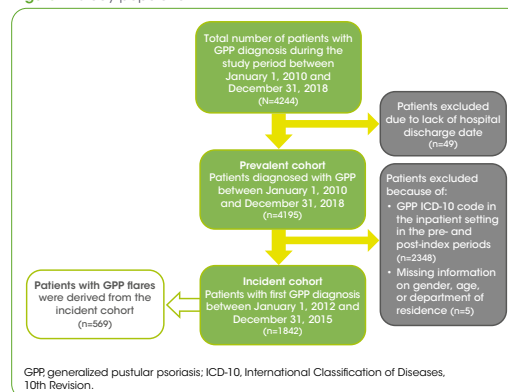


Results

Patient population

- In total, 4195 patients with GPP were identified based on the SNDS database with at least one hospitalization for GPP (ICD-10 code L40.1) or with a GPP in the chronic disease list. These patients constituted the prevalent cohort for the study (Figure 2)
- The incident cohort included 1842 incident cases of GPP that were identified between January 1, 2012 and December 31, 2015, after excluding patients with any history of GPP (ICD-10 code in the pre-index period 2 years before the index date) and patients with missing demographic data (Figure 2)
- Most patients with GPP (47%) were aged between 26 and 60 years at index date with a mean age of 58 years
 - Approximately 53% of the identified patients were males

Figure 2. Study population



Characterization of patients with GPP flares

- A total of 569 patients with GPP flares were identified within the incident cohort, with a median of 1 flare and a mean of 1.4 flares per patient (Table 1)
- The total number of flares was 811, corresponding to 0.4 flares/person/year
- The mean time to first flare was approximately 36 days
- Most GPP flares occurred within the first year of follow-up, and the recurrence decreased over the years (Table 1)

Mortality in patients with GPP flares

- The median time from the first flare to all-cause death was 546 days, and from the last flare to all-cause death was 386 days (Table 2)
- The most frequent primary causes of death among patients with GPP were heart disease, sepsis, and liver diseases
- The proportion of GPP patients who died within 4 weeks after their last flare was 2.6%, with a median time to death of 14 days
- Among patients with GPP flares, rate of all-cause death throughout the observation period was 24.4%

Hospitalization in patients with GPP flares

- The mean length of hospital stay due to a flare was approximately 12 days (Table 3)
- Of the patients with GPP flares, 25.0% were admitted to an intensive care unit (ICU). Most ICU admissions were reported in the non-neurovascular ICU and resuscitation in a non-pediatric unit
 - The mean length of stay in the ICU was approximately 18 days
- Of the patients with flares, 34.3% were graded with ≥ 3 severity (severe/most severe)
- Approximately 49% of the patients with GPP flares had at least 1 visit to a dermatologist after their first flare (Table 3)

Table 1. Characteristics of patients with GPP flares

	Patients with GPP flares (n=569)
Gender, n (%)	
Female	301 (52.9)
Age groups, years, n (%)	
0-12 years	13 (2.3)
13-25 years	22 (3.8)
26-60 years	271 (47.6)
>60 years	263 (46.2)
Number of flares per patient during the follow-up period	
Mean \pm SD	1.4 \pm 1.2
Median (min, max)	1 (1, 12)
Number of flares during the follow-up period, n (%)	
1	452 (79.4)
2	70 (12.3)
3	22 (3.9)
4	8 (1.4)
≥ 5	17 (3.0)
Number of flares per person-year	
Number of flares	811
Total person-years	1927
Number of flares per person-year	0.4
Time to first flare, days	
Mean \pm SD	35.7 \pm 185.2
Median (min, max)	0 (0, 1928)

GPP, generalized pustular psoriasis; SD, standard deviation.

Table 2. Mortality in patients with GPP flares

	Patients with GPP flares (n=569)
All-cause death, n (%)	139 (24.4)
Time to death after the first flare, days	
Mean \pm SD	703.8 (636.5)
Median	546
Time to death after the last flare, days	
Mean \pm SD	580.9 \pm 588.7
Median	386
Death within 4 weeks after the last flare, n (%)	15 (2.6)
Time to death after the last flare, days	
Mean \pm SD	15.5 \pm 7.7
Median	14

GPP, generalized pustular psoriasis; SD, standard deviation.

Discussion

- This is the first study to develop an algorithm to specifically identify patients with GPP flares in an administrative/claims database
 - The algorithm used, while not validated, should be considered conservative. It may underestimate the actual number of flares because hospitals may use other diagnosis codes. Furthermore, the algorithm would not identify patients with GPP flares treated in outpatient settings
- The study has several strengths, including large sample size, a longitudinal study design with an extended follow-up, the availability of death dates and causes of deaths
- Admissions to the ICU were relatively common during flares, and in general there was a relatively high median length of stay in the hospital; this is consistent with previously published data in which the duration of hospitalization was reported to be between 10 and 14 days⁷
- Although the recurrence of flares tended to decrease over time, the incidence of GPP flares persists for a long time
- GPP flares were associated with high mortality rates, which is consistent with previously reported data in which mortality rate among GPP patients was reported to be up to 32%, and flare-related deaths ranged between 5 and 10%⁷
- In conclusion, this is the first study to use a nationwide administrative/claims data base to characterize the epidemiology and burden of GPP, characterize the recurrency of GPP flares, and evaluate impact of GPP flares on disease on mortality, morbidity, hospitalization, and ICU admissions

Table 3. Hospitalizations in patients with GPP flares

	Patients with GPP flares (n=569)
Length of stay, days	
Mean \pm SD	11.5 \pm 10.5
Median (min, max)	8 (0, 99)
Length of stay – first flare, days	
Mean \pm SD	11.0 \pm 10.2
Median (min, max)	8 (0, 99)
Length of stay – second flare, days	
Mean \pm SD	13.4 \pm 12.9
Median (min, max)	8 (0, 57)
Admission in ICU, n (%)	142 (25.0)
Number of visits to ICU	
Intensive care in a neurovascular unit	16 (6.6)
Intensive care in a non-neurovascular unit	117 (48.0)
Resuscitation in a non-pediatric unit	110 (45.1)
Resuscitation in a pediatric unit	1 (0.4)
Length of stay in ICU, days	
Mean \pm SD	17.7 \pm 24.1
Median (min, max)	12 (0, 176)
Number of flares in patients with available GHM codes, n (%)	783 (96.6)
Severity level of hospitalization*, n (%)	
1	223 (27.5)
2	240 (29.6)
3	256 (31.6)
4	64 (7.9)
Missing	28 (3.5)
≥ 1 GP visit after the first flare, n (%)	556 (97.7)
≥ 1 dermatologist visit after the first flare, n (%)	276 (48.5)

*Severity level calculated according to GHM codes, from the least severe (level 1) to the most severe (level 4).

GHM [Les groupes homogènes de malades]; Diagnosis-Related Groups (DRG); GP, general practitioner; GPP, generalized pustular psoriasis; ICU, intensive care unit; SD, standard deviation.

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Disclosures

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