

Epidemiology, Characteristics of Disease, and Unmet Needs of Patients with Generalized Pustular Psoriasis: A Large Italian Delphi Consensus

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Keywords

Delphi consensus · Generalized pustular psoriasis · Incidence · Italian population · Prevalence · Rare diseases · Systemic inflammation

Abstract

Introduction: Generalized pustular psoriasis (GPP) is a rare and chronic, debilitating skin condition characterized, in its acute flare phase, by clinically severe and potentially life-threatening systemic manifestations. Data on GPP are still scanty, particularly in Europe and at a national level. The aim of this study was to provide expert indications on several disease-related and patient-related aspects of GPP, with

specific focus to the Italian context. **Methods:** We conducted an iterative eDelphi study following the recommended criteria for reporting methods and results. After a thorough bibliographic review aimed to identify unknown or controversial issues in GPP, the following areas were investigated through a few specific questions/statements for each area: (1) disease epidemiology; (2) disease characteristics, with specific interest toward GPP flares; (3) diagnosis and diagnostic delay; (4) GPP treatment; (5) GPP patient journey and use of healthcare resources in Italy; (6) unmet needs and quality of life. An Executive Board of 9 principal investigators

Annalisa Scopinaro and Stefano Piaserico are co-last authors. Gabriella Fabbrocini is deceased.

revised and approved the topics to be examined and overviewed the whole project. A total of 35 experts from different Italian areas, including 34 board-certified Italian dermatologists and 1 representative of patients' associations, took part in the study. **Results:** A high agreement in responses from Italian experts emerged during two eDelphi iterations on – among several other aspects – GPP prevalence and incidence in Italy, use of European Rare and Severe Psoriasis Expert Network diagnostic criteria, flare frequency and duration, best diagnostic and care pathway, and main unmet needs of Italian patients. On the other hand, a broad spectrum of treatments (of different drug classes) was reported both in the acute and chronic phases of GPP, and no consensus on the issue was thus achieved. **Conclusions:** Consensus findings from this Delphi study of GPP experts may be useful to fill gaps of knowledge and improve awareness of this rare disease, as well as to help clinical and public health management of GPP in Italy.

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Introduction

Generalized pustular psoriasis (GPP) is a rare and chronic, systemic, inflammatory, debilitating condition characterized by widespread eruption of primary, non-infectious, and macroscopically visible pustules on non-acral skin [1, 2]. GPP is a biologically complex auto-inflammatory disease that often co-occurs with plaque psoriasis; is sometimes associated with systemic inflammation; and may have acute, subacute, or – more rarely – chronic symptoms [3]. Acute flares of disease represent a dermatological emergency being characterized by clinically severe and potentially life-threatening systemic manifestations (i.e., distributing shock) and requiring access to the emergency department, hospital, or intensive care unit (ICU) [4, 5].

Information on the epidemiology of GPP is still scanty, and data are largely heterogeneous, with prevalence in Europe ranging between about 0.2 and 50 cases per 100,000 inhabitants and an incidence between 0.6 and 8 cases per million person-years in the few available European studies [6–8]. Due to the rarity of GPP, several other aspects of this disease are still poorly studied and understood, including its pathogenesis, management, treatment, as well as the key unmet needs of patients [2, 9–11]. Further, although diagnostic criteria were established in 2014 in Japan [12] and in 2017 in Europe [1] in landmark publications, both definitions are still subject to some limitations [11]. In particular, a workshop

of international experts noted that the Japanese Dermatological Association guidelines do not include the presence/absence of psoriatic plaques in the definition of GPP, whereas the European Rare and Severe Psoriasis Expert Network (ERASPEN) guidelines do not consider a few common characteristics of GPP, i.e., typical histopathological results and the clinical finding of lakes of pus [11].

Within the framework of rare diseases, such as GPP, where quantitative data are lacking, opinions of experts involved in the diagnostic and management pathways may provide, through adequate methodologies of consensus, valuable tools to the overall care of the disease [13–15]. Delphi methods are increasingly used and may help, at a national level, to define the standards and identify potential gaps in the pathway of care. Therefore, from June to November 2022, we performed an online iterative Delphi study – i.e., a robust method to investigate consensus on health topics [16] – of clinicians who are an expert in GPP in Italy, in order to give additional indications on the epidemiology, characteristics, management, and unmet needs related to the disease, with specific focus to the Italian context.

Materials and Methods

We conducted an eDelphi study on several aspects of GPP following the recommended criteria for reporting methods and results [16, 17]. The study was originally designed by academic Master Delphi experts (P.M., C.G.) [18], and since the start of the project, we considered any relevant requirements of a high-quality Delphi study, including anonymity, iteration, controlled feedback, and statistical stability of consensus [19]. We assessed consensus both through the presentation of the main findings of our survey and through the quantitative computation of the level of agreement among participants to the survey [20]. A detailed flowchart describing the course of the Delphi process is given in Figure 1. The following areas were investigated, through a few specific questions/statements for each area, in order to explore the level of agreement of Italian experts on various debated epidemiological and clinical topics of GPP: (1) disease epidemiology; (2) disease characteristics, with specific interest toward GPP flares; (3) diagnosis and diagnostic delay; (4) GPP treatment; (5) GPP patient journey and use of healthcare resources in Italy; (6) unmet needs and quality of life. The phases of the Delphi study are described extensively below.

Literature Review and Identification of the Areas of Investigation

In March 2022, we conducted a review of the scientific literature and of gray literature information to explore the available materials and identify unknown or controversial issues in GPP. PubMed/MEDLINE and EMBASE were used for the bibliographic review of scientific articles, through the broad search string “generalized pustular psoriasis OR generalized pustular psoriasis” (search date:

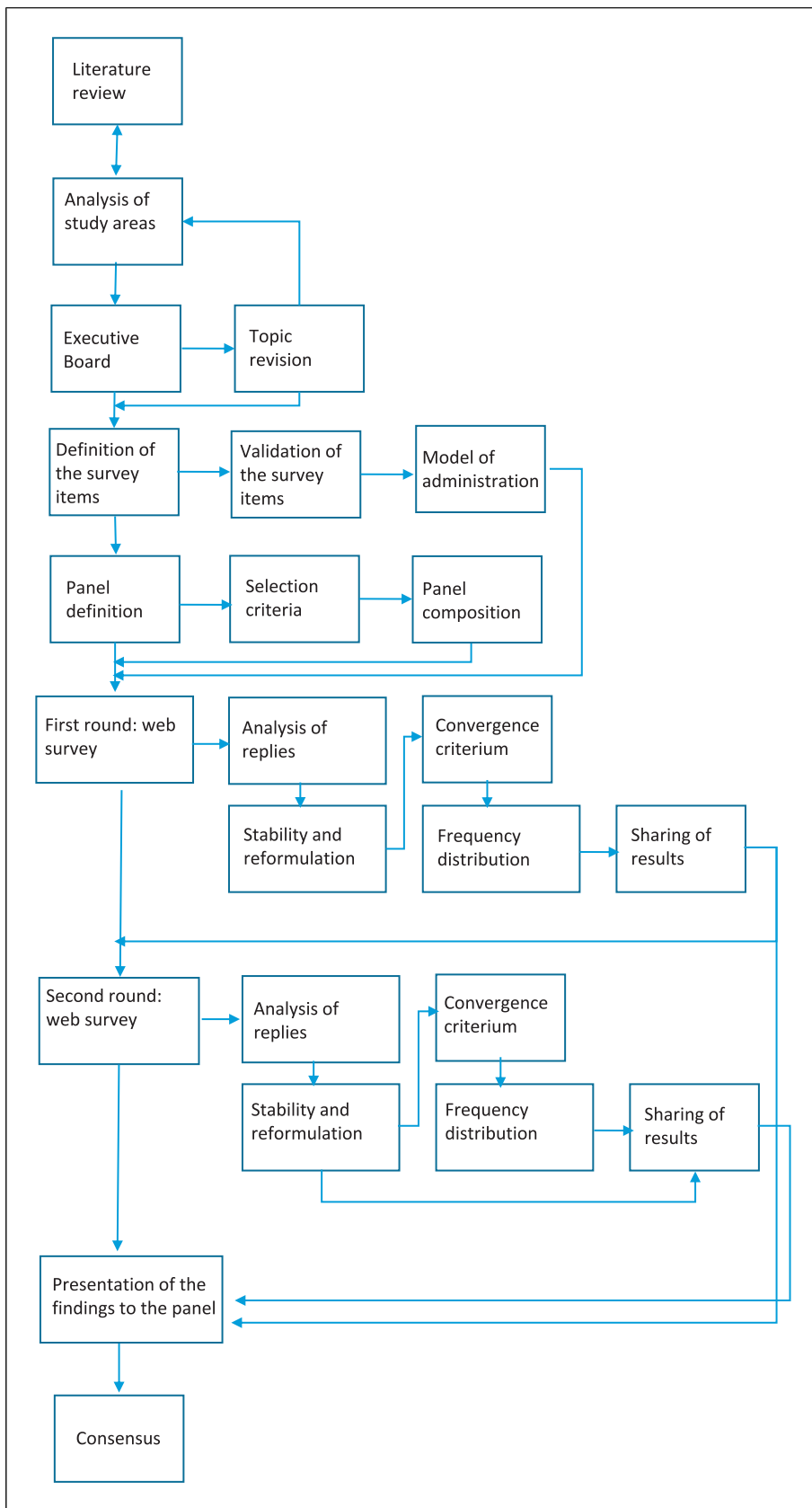


Fig. 1. Flowchart describing the Delphi study development.

March 10, 2022), whereas the gray literature search was conducted through ad hoc searches in the websites of several national and international health institutions, medical societies, patients' associations, rare diseases organizations, and other educational sources. The search and selection process of scientific articles was conducted independently by two researchers. A total of 897 papers were initially retrieved in PubMed and 1447 in EMBASE. These articles were first screened according to their title and abstract only, to exclude those clearly not relevant to the study aims (e.g., those focused on diseases other than GPP, genetic/molecular analyses, case reports, etc.), and in a second screening phase on the basis of their full-text. With reference to the screening process of quantitative epidemiological data, only original articles reporting information on the prevalence and/or incidence of GPP were selected, and a total of 7 papers were finally included. With reference to other (qualitative) topics, inclusion criteria were extended to relevant reviews and guidelines, besides papers reporting original data analyses, and a total of 21 papers were finally included. The review was focused on – but not restricted to – the Italian healthcare environment. Six areas of investigation (reported above) were defined.

An Executive Board was formed, including a total of nine investigators among GPP clinicians ($n = 7$: L.A., F.B., G.D., G.F., C.P., F.P., and S.P.) and experts in the Delphi methodological process ($n = 2$: C.G., P.M.). They revised and approved the topics to be examined and overviewed the project.

Definition and Validation of the Questionnaire for the Survey

The questionnaire was defined using both quantitative and qualitative criteria, the final objective being to reach the highest consensus level between panelists. Questions and statements were initially defined according to the findings of the bibliographic review, particularly after the analysis of earlier guidelines, reviews, and surveys. In the first round, mostly open-ended or multiple-choice questions were proposed. A few statements were also given, and answers were collected through a Likert scale based on 4 levels (i.e., “fully disagree,” “partially disagree,” “partially agree,” “fully agree”). In case of an answer expressing disagreement, an additional open-ended question was always asked in order to collect the reason(s) for dissent. Evidence was classified through the focus level [21]. A total of 25 items were included in the first round. In the second round, in reverse, mostly statements were proposed to the panelists, using the same 4-level scale. Consensus was measured using the percentage of agreement or a combination of percentage agreement within a certain range and for a certain threshold. A total of 14 items were included in the second round.

The questionnaire of the first round was checked qualitatively [22] by assessing the validity of (i) facade, through a superficial examination of the content of the questionnaire (i.e., is the tool valid to nonexperts, too?); (ii) content, through an expert analysis of the content of the questionnaire (i.e., is the questionnaire adequately comprehensive with reference to the areas of investigations?). Although the monitoring procedures are not clear-cut, in fact, it is generally required that some experts examine the survey and overview the appropriateness of the questions/statements and the completeness of the domains.

Definition of the Panel

Experts were selected and invited according to objective criteria, on the basis of the specific scientific topic to be examined, and including board-certified Italian dermatologists with expertise in

the diagnosis and/or management of GPP and a representative of patients' associations, expert in rare diseases [23]. They were first informed on June 25, 2022, of the Delphi study by e-mail and subsequently received an invitation to participate with a link to the survey (based on the Web platform SurveyMonkey®) [24]. The first question of the survey (i.e., “During the last 5 years, did you diagnose or treat at least 1 GPP patient?”) was aimed to exclude any nonexpert in the field who was eventually by mistake invited to participate. Out of a total of 58 invited experts, 34 dermatology clinicians and 1 patient advocacy group representative (60%) satisfied the inclusion criteria and completed the first round of the survey in full. Fifteen clinicians were from Northern Italy (44%), 9 from Central Italy (26%), and 10 from Southern/Insular Italy (29%). A median number of 2 GPP patients (range: 0–19 patients) were followed in the clinicians' departments/study centers at the moment of the survey. All clinicians participating in the first round were subsequently invited to join the second round, and 29 of them (85%) participated and completed the survey in full.

Delphi Iterations

The first round of the Web survey was conducted between June 29 and July 13, 2022. On the basis of experts' replies, each item of the survey was classified according to the following focus levels.

- Moderate to high variability in first round responses → Item requires reinvestigation in round 2.
- High proportion of “I don't know” answers (i.e., >33%) → Item requires reinvestigation in round 2.
- Substantial agreement among the respondents (i.e., ≥67%) → Item does not require reinvestigation in round 2.

Results of the first round were discussed within the Executive Board. Statements were examined both through the stability of findings and frequency of responses. The convergence criterion for consensus was defined in relation to the stability of results, to a threshold, equal to two-thirds of the response frequency. With reference to the statements included in the survey, “full” or “partial” agreement, as well as “full” or “partial” disagreement, was summed together. In a few cases, after careful analysis of stability and frequency, statements with focus level “C” were revised and included in the second round [25]. This was conducted between October 19 and November 3, 2022, using the same methods and agreement criteria defined for the first round. The consistency of answers between the first and second rounds supported a general accuracy in the definition of the statements. Further, this led to full consensus or majority for most statements included in the second round (with the only exception of questions on GPP treatments), and therefore, the iterations were stopped. On December 19, 2022, the results of the Delphi study were presented and discussed with the participants of the survey. Throughout the manuscript, we use the term “majority” to refer to an agreement of 67–99% of panelists and “full consensus” to an agreement of 100% of panelists.

Results

Epidemiology of GPP

Consensus on the epidemiology of GPP was achieved during the first Delphi round. In a 4-point Likert scale, the majority of panelists agreed (76%) or completely

agreed (12%) that the prevalence of GPP in Italy is in the range 1–3 cases per million inhabitants, with a total agreement percentage of 88%. Four participants (12%) disagreed, all of them indicating a higher expected prevalence. Similarly, 62% of panelists agreed and 19% completely agreed (total agreement percentage of 81%) that the incidence of GPP in Italy ranges between 0.5 and 1 new case per million person-years, with six participants (19%) reporting disagreement. They were further asked to provide their beliefs on the correct incidence estimate, and their answers ranged between 1 and 10 new cases per million person-years.

Characteristics of GPP Flares

Various questions aimed to better define the characteristics of flares in GPP patients. The majority of participants (92%) considered that an average of 0.4 flares per patient per year – as reported in a French observational study [26] – is a realistic estimate, according to their clinical experience. No consensus was, on the other hand, achieved during the first round on the mean duration of a flare, with 59% of panelists indicating a duration of 2–4 weeks and 35% indicating 1–3 months. During the second round, we thus proposed the following statement: “Considering GPP therapies available at the moment, the mean duration of a treated GPP flare is between 2 and 8 weeks.” Almost all participants (97%) agreed with such statement, and consensus on this topic was achieved.

Clinicians were asked to report which proportion of GPP patients, based on their experience, requires access to the emergency department, hospitalization, and access to the ICU during a flare (Fig. 2). While most experts reported an infrequent need of ICU access, answers were more distributed for need of emergency department access (modal categories were 40–60% and 60–80% of patients, with 21% of answers each) and for need of hospitalization (modal category was 10–40% of patients, indicated by 32% of experts). During the second round, we separated these three topics by proposing different statements. Fifty-five percent of experts agreed and 35% completely agreed (total agreement: 90%) with a statement reporting that “more than half of patients with an acute flare require access to the emergency department.” Consensus was also achieved (90%) that about half of the patients require hospitalization during a GPP flare, although the proportion of experts “in complete agreement” with the statement was lower (28%) and that “in agreement” was higher (62%). Consensus was almost full (28 out of 29 experts, 97%) that less than 10% of patients require ICU access during a flare.

An accord on the average duration of hospitalization (independently of the hospital ward, i.e., general unit or ICU) during a GPP flare was reached during the first round of the Delphi exercise, with 79% of panelists backing the proposed mean of 12 days, based on a French observational study [26]. Eleven clinicians (32%) had no adequate expertise of patients admitted to ICU during a flare and thus did not reply to the subsequent question on the average duration of ICU stay, while 20 out of 23 experts (87% of respondents) agreed with the proposed average ICU stay alone (i.e., excluding the duration of stay in other hospital wards) of 18 days [26].

The main hospital departments where GPP patients are hospitalized due to a flare are, according to the experts, those of internal medicine and dermatology. These were indicated by more than two-thirds of panelists (74% and 68%, respectively). Of notice, 5 out of 34 participants (15%) noted, in the open-ended comments, that beds in the Italian dermatology departments are scarce.

Diagnostic Issues in GPP

In the first round, an open question was proposed to collect information on the criteria used by each clinician to diagnose GPP, and 25 out of 34 of them (74%) reported to adopt the ERASPEN criteria. A prompt, correct diagnosis of GPP is an unmet need (see below) in this rare disease. Several factors involved in the misdiagnosis of GPP were cited by panelists, with 42% of them reporting an incorrect diagnostic pathway (e.g., patients examined at emergency departments, by clinicians other than dermatologists, etc.), 24% issues related to the rarity and inadequate knowledge of the disease, and 18% errors in the diagnosis due to unclear clinical presentation of GPP, among other sparse replies. During the second Delphi round, there was full consensus between experts (60% agreed and 40% completely agreed) with a statement that proposed the three factors reported above as the main explanations related to GPP misdiagnosis.

Treatment of GPP

There was consensus between clinicians on the use of treatments in the chronic phase of GPP, with 88% reporting they “always” continue to prescribe drugs during this phase. The efficacy and safety of the available drugs was acknowledged by the majority of experts. Concerned with efficacy during a GPP flare, 68% of panelists evaluated the available drugs as “quite satisfactory,” but none of them judged the efficacy as “fully satisfactory.” Similarly, most clinicians evaluated drug safety “quite satisfactory” (68%), and only a few of them, “fully satisfactory” (9%). Consensus was also reached during the first

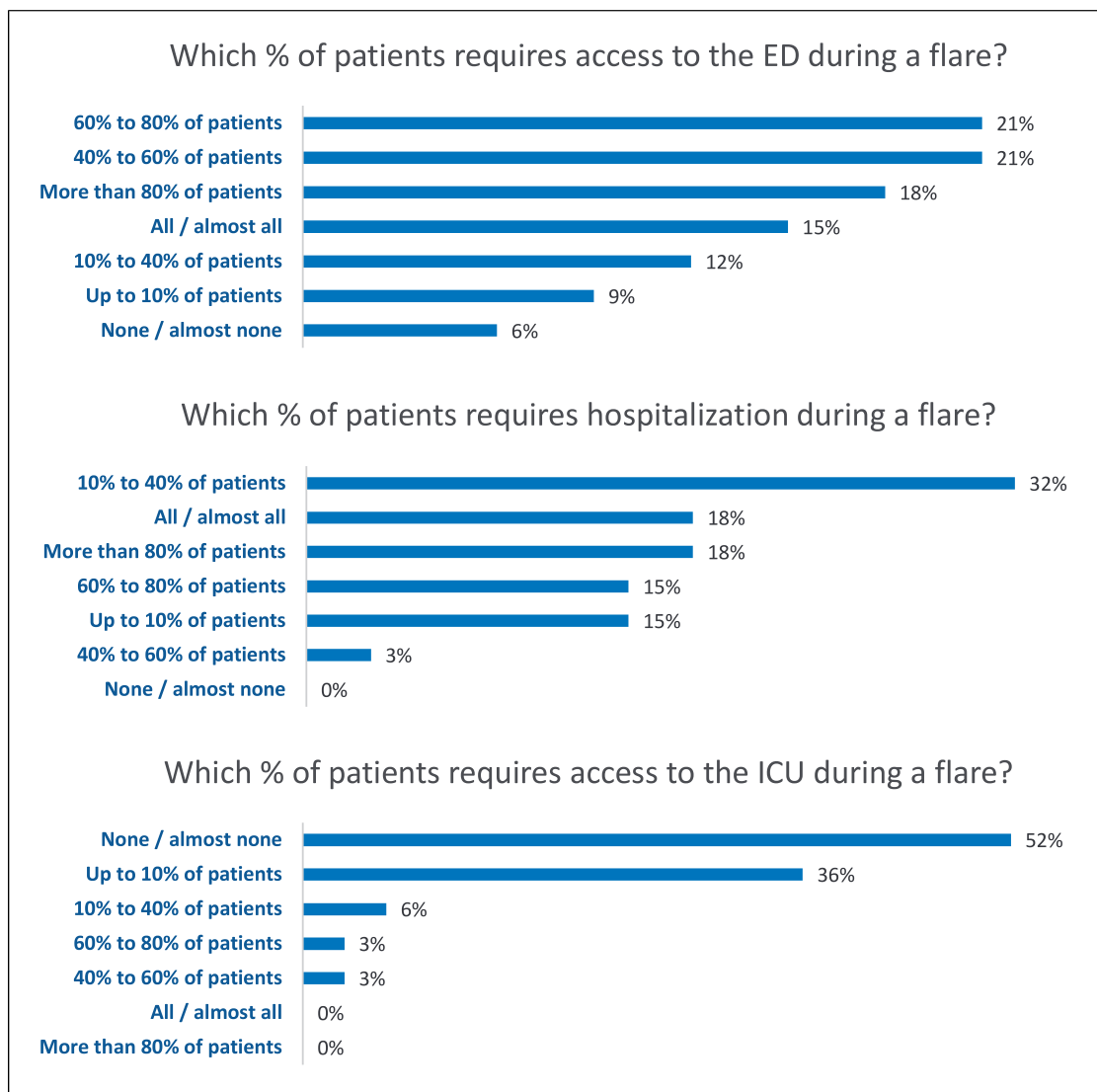


Fig. 2. Proportion of patients requiring access to the ED, hospital, or ICU during a GPP flare (first round of the survey).

round on the rapidity of action of available treatments during a flare, with a total of 82% of clinicians reporting that they act quite rapidly (i.e., in 2–4 weeks, 65% of respondents) or rapidly (i.e., about 2 weeks, 18% of respondents). Another 18% judged available treatments “slow” (i.e., 1–3 months) to resolve a flare.

Treatments used during a GPP flare (Fig. 3a) or in the chronic phase (Fig. 3b) varied widely across clinicians. In the second round, a question on which treatment(s) is used during a patient flare was proposed by grouping therapy according to the type of drug (biological, non-biological, or both), but no consensus was reached. In fact, 52% of clinicians reported to use both types, 34% non-biological drugs

and 14% biological drugs. Among clinicians reporting use of non-biological drugs, we asked whether a biological drug was subsequently prescribed in case of treatment failure after 1 week: 32% of clinicians answered “Yes, always,” 60% “Yes, sometimes,” and 8% “No, never.” Among clinicians reporting biological drugs use, 63% prescribed anti-IL-17, 47% anti-IL23, 42% anti-TNF α , and 16% anti-IL12/23 drugs.

Italian GPP Patients’ Journey and Use of Healthcare Resources

Four subsequent aspects of the clinical pathway of patients with GPP in Italy were investigated through open-ended questions. The first question was focused on

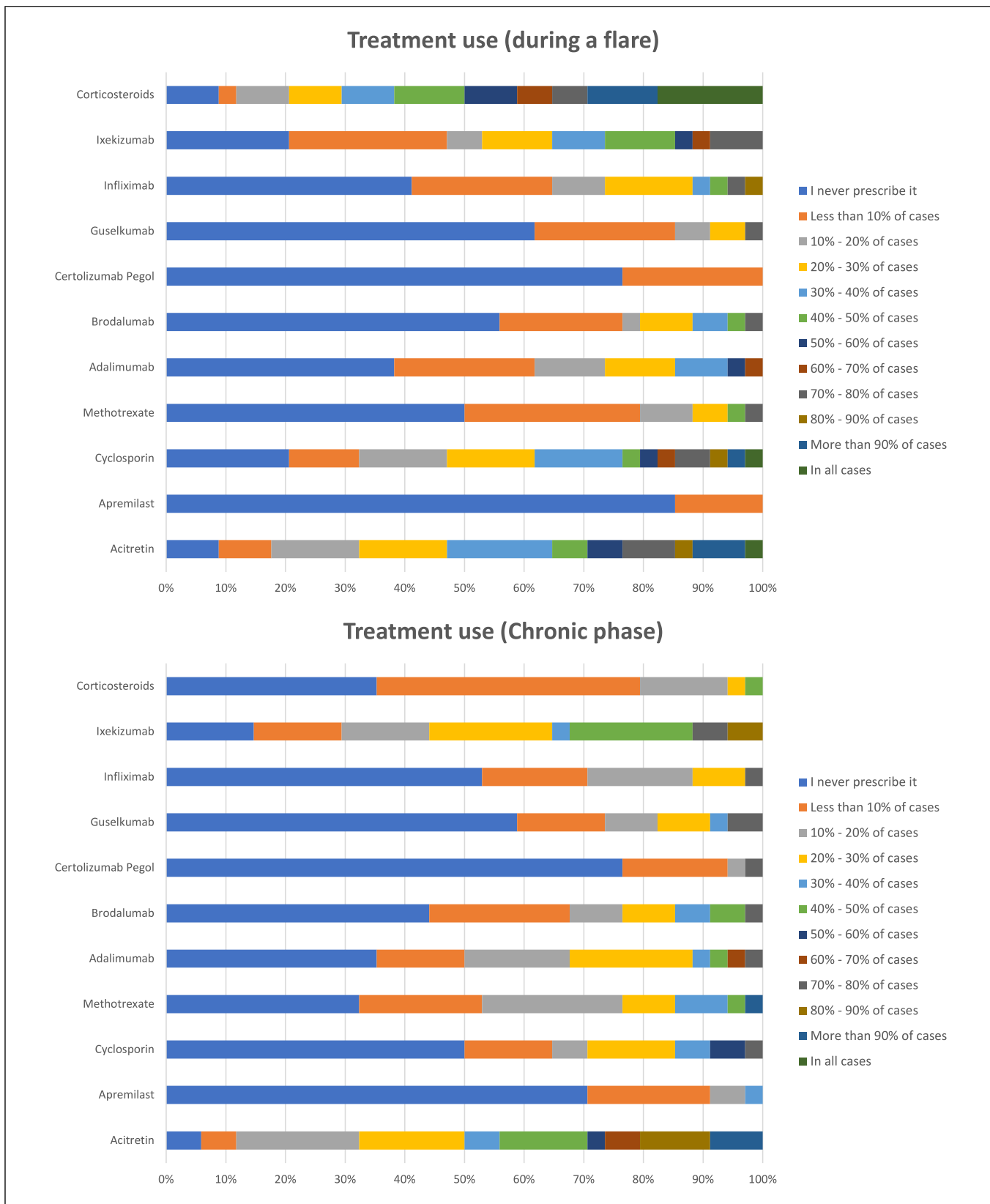


Fig. 3. Treatments used by clinicians during the acute and chronic phases of GPP (first round of the survey).

the first encounter of the GPP patient in the healthcare pathway that, according to the panelists, occurs most frequently at an emergency department (57%), to the general practitioner (34%), a dermatologist (26%), an expert of infectious diseases (20%) or of internal medicine (11%). The second question was focused on the subsequent step, i.e., “Which specialist is involved in patient care, after first encounter?” Agreement emerged between experts that in most cases, a dermatologist is involved in the second step of the clinical care journey (74%). Experts of infectious diseases were also cited by 43% of panelists, while other answers were reported by less than 20% of participants. The third question was focused on the management of a patient hospitalized due to an acute flare: 89% of experts consistently indicated that dermatologists take charge of the patient during hospital stay. Similarly, most experts (94%) agreed that outpatient management after an acute flare is taken charge by a dermatologist. Only the first question required analysis in a second round. The following statement, based on first round replies and a 4-level Likert scale, was proposed: “First encounter of the GPP patient in the healthcare journey most frequently involves emergency department clinicians, general practitioners, and dermatologists,” and most participants agreed (41%) or completely agreed (52%; total agreement, 93%).

Clinicians were further asked which are, in their experience, the healthcare resources most impacted by GPP patients’ needs. The majority of panelists reported the need for hospitalization (82%), access to the emergency department (82%), and specialists visits (74%) among the most impacted resources.

Unmet Needs and Quality of Life of GPP Patients

Both clinical and general patient needs were investigated. During the first round, various clinical needs were reported by the panelists. According to those replies, in the second round, we proposed the following statement: “The main clinical unmet needs of GPP are an in-depth disease knowledge and availability of rapid and effective treatments.” This statement achieved full consensus (52% of panelists agreed, and 48% fully agreed). Also, from the patient perspective, several needs emerged during the first Delphi round, particularly the need for a prompt and correct diagnosis and the availability of rapid and effective treatments (both reported by more than three-fourths of experts). When, during round 2, we proposed those points as the main patient needs, full consensus was found.

Questions were focused on the quality of life of both patients and their caregivers. As concerns the patients, an impact of GPP on the psychological/emotional (94%),

physical (91%), and relational areas (77%) was most frequently indicated by the experts. With reference to caregivers, the psychological/emotional (86%) and familial areas (77%) were most frequently reported as affected. According to the panelists, the daily activities of patients that are impacted most by the disease are intimacy with a partner (87%); physical activity (80%); and socializing with relatives, friends, and other people (80%). Most experts (88%) agreed that the burden of GPP is higher than that of plaque psoriasis. Those who disagreed noted that plaque psoriasis, in its severe form, has a high disease burden, too.

Discussion

This eDelphi study provided a large number of cues aimed to improve patient management and the understanding of the burden of GPP in Italy, useful to fill the gap of knowledge on this rare disease. Although an increasing interest in the study of GPP has emerged during the last few years, there is still a scarcity of data from observational and other types of studies in Italy [27–30]. We reported a high agreement in responses from Italian experts on various aspects of GPP, including its epidemiology, specific disease characteristics (e.g., flare frequency and duration), diagnostic and care pathway of Italian patients, unmet needs, and quality of life. Concurrence between most clinicians (i.e., about three-fourths of them) was also found on the use of ERASPEN criteria for GPP diagnosis. On the other hand, a broad spectrum of treatments of different drug classes are used both in the acute and chronic phases of the disease, i.e., to manage and prevent flares, and no consensus on the issue was thus achieved.

Data on the epidemiology of GPP in Europe are scanty, and information on disease prevalence and incidence is limited [6, 8]. GPP prevalence was estimated to vary between 0.6% and 2.4% among patients with psoriasis [31] which, in turn, affects 1.1–1.9% of the general population in Western, high-income countries [32]. Notwithstanding the poor and heterogeneous evidence available, consensus was rapidly achieved that GPP is rare in Italy, with experts estimating the prevalence ranging between 1 and 3 cases per million inhabitants and the incidence between 0.5 and 1 new case per million person-years. The OrphaNet website (<https://www.orpha.net/>, last accessed on January 10, 2024) includes GPP among rare diseases, and recently – through a Delphi approach – clear consensus emerged among an international group of experts that GPP is a rare life-threatening or chronically debilitating condition with prevalence below 50 per 100,000 in the EU [14].

A consensus on the main characteristics of GPP flares, including their frequency, duration, and severity, was achieved in this study, thus providing a detailed description of the acute phase of disease. In broad agreement with other expert surveys and (sparse) real-world data [5, 9, 26], an average of 0.4 flares per patient per year and a mean duration of a treated flare in a comprehensive range of 2–8 weeks were considered appropriate by the Italian panelists. With specific reference to disease severity and management in the Italian setting, it emerged that disease flares lead to hospitalization – generally in the internal medicine or dermatology departments – in about half of patients and that a small proportion of them also require ICU stay for an average of 2–3 weeks.

The treatment approach was heterogeneous between clinicians, both in the acute and quiescent phases of disease, and no clear pattern of care emerged in the Italian context. Current treatment of flares is also divided between the use of non-biological agents only (34% of panelists), biological agents only (14%), or both types of drugs (52%). Among biological drugs, anti-IL-17 drugs were most frequently used by the panelists during a GPP flare, with anti-IL23 agents being an alternative therapy for some clinicians [2, 33]. The ample heterogeneity in the therapeutic approach is explained by the lack of specific treatments approved for GPP and of clinical guidelines on disease treatment in Europe, as well as by several other specific factors, including the variability of GPP severity, the presence/absence of comorbidities, patient characteristics, and preferences. The paucity of original studies on the efficacy/effectiveness and safety of different therapies for GPP is also a major issue [2, 3].

A high burden of disease and several clinical and patient unmet needs were highlighted since the first round of the eDelphi study. A prompt disease diagnosis (facilitated by improved knowledge of GPP among general practitioners and ED physicians and by a correct diagnostic pathway) and the availability of rapid and effective treatments emerged as the most important unmet needs in GPP. Besides clinicians, a member of patients' associations participated to the eDelphi study. The long diagnostic pathway was highlighted by the latter as particularly frustrating for the patient. Experts agreed that GPP impacts both the psychological and physical matters of the patients, limiting several common activities, and the psychological and familial matters of their caregivers. Previous surveys conducted in other countries in GPP patients reported results on the impact of specific symptoms of disease [34] and on daily activities affected [10].

A number of findings of this Delphi consensus were consistent with those reported in a recent international Delphi study of GPP involving 21 expert dermatologists worldwide [15]. In particular, the appropriateness of

ERASPEN criteria for the diagnosis of GPP achieved majority of agreement in both analyses. In consideration of the different settings and specific aims of the investigations, the topics examined in the two consensuses were, in any case, largely heterogeneous.

Delphi surveys are subject to several limitations: they rely on expert opinions rather than on evidence-based methods; their quality is difficult to assess as there are no commonly accepted quality criteria; and their results may vary according to different groups of experts involved [23]. Therefore, our results may not reflect the opinions of all Italian specialists of GPP. We tried to reduce this weakness by inviting a large number of expert dermatologists, and in fact, the number of panelists was higher in this as compared to most common Delphi surveys [35].

In conclusion, given the current rarity of (Italian) evidence on GPP, we provided urgently needed information on this disease from a panel of specialists, with a specific focus on the Italian situation. A clear need for additional research to guide treatment during both the acute and chronic phases of GPP emerged. Through the availability of collective expert indications, our results may help disease management at both a clinical and public health level.

Key Message

A high agreement of Italian experts emerged in this eDelphi study on several GPP-related topics.

Acknowledgment

The Italian Delphi GPP Group (for the members, see online suppl material; for all online suppl. material, see <https://doi.org/10.1159/000538072>). contributed substantially to this work by participating in the Delphi survey and by discussing the main study results during the final Web meeting of the project.

Statement of Ethics

This work is based on a survey of disease experts, and no patient was involved. No sensitive data were collected. All disease experts provided written informed consent by electronic means before participation.

Conflict of Interest Statement

Laura Atzori served as an advisory board member; as a consultant for AbbVie, Novartis, Janssen, Leo pharma, Ely-lilly; and received congress hospitality from AbbVie, Almirall, Pfizer,

Novartis, Bristol-Myers Squibb, Ely-lilly, Leo Pharma, UCB. Giovanni Damiani received grants from AbbVie, Almirall, Pfizer, Novartis and was the speaker for AbbVie, Almirall, Pfizer, Novartis, Bristol-Myers Squibb, Leo Pharma.

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Author Contributions

C.G. and P.M. designed the study and provided methodological and technical support to conduct the Delphi survey; L.A., F.B., G.D., G.F., C.P., F.P., and S.P., as part of the Executive Board, revised the clinical/scientific topics to be examined and overviewed the project; A.S. contributed to the finalization of the Delphi study with her expertise in rare diseases and patient support. All the authors revised and approved the manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available due to privacy reasons but are available from Dr. Carlotta Galeone upon reasonable request.

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