Clinical, Cosmetic and Investigational Dermatology

Dovepress

open access to scientific and medical research

Open Access Full Text Article

COMMENTARY

Exploring the Clinical Presentation, Course, and Burden of Disease in Generalized Pustular Psoriasis [Podcast]

Joseph F Merola[1],*, Ahmad Z Amin[2],*

[1]Brigham and Women's Hospital, Boston, Massachusetts, USA; [2]Northwestern University Feinberg, School of Medicine, Chicago, Illinois, USA

*These authors contributed equally to this work

Correspondence: Dr Joseph F Merola, Email jfmerola@bwh.harvard.edu

Abstract: Generalized pustular psoriasis (GPP) is the most severe form of pustular psoriasis and affects large areas of the body. GPP is a rare disease, and has a variable presentation; thus, its diagnosis is challenging. The onset of symptoms is rapid, with the appearance of painful skin erythema, followed by the widespread eruption of sterile pustules. Acute GPP (called a flare) is often accompanied by systemic symptoms, including high fever, pain in skin lesions, malaise, and fatigue. Approximately half of GPP flares require hospitalization, with an average inpatient duration of 10–14 days. GPP prevalence estimates range from approximately 2–124 cases per million persons, with a female predominance. The most common age of onset of GPP is 40–60 years, although cases have been described in younger adults and children. GPP affects every aspect of patients' lives and has a high physical and psycho-social impact. Recent research on the interleukin-36 pathway associated with GPP led to the development of a GPP-specific treatment, spesolimab, which was approved by the US FDA in September 2022. This podcast explores the clinical presentation, disease course, and burden of disease in GPP, including differential diagnosis and common triggers of an acute flare.

Keywords: generalized pustular psoriasis, interleukin-36 pathway, clinical presentation, disease burden, diagnosis

Moderator: Dr Uwe Wollina

Guests: Dr Joseph F Merola, Dr Ahmad Z Amin

This Podcast was sponsored by Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI).

Dr. Uwe Wollina: Hello and welcome to the podcast series on generalized pustular psoriasis (GPP). This is episode one in a series of four podcasts on different aspects of GPP, and listeners can obtain further information on this condition in the subsequent episodes.

My name is Uwe Wollina. I am former head of the department of Dermatology and Allergology at the Academic Teaching Hospital Dresden, Germany. I have the pleasure of moderating today's podcast where we will be talking about the clinical presentation, disease course, and burden of disease in GPP with our guest speakers, Dr. Joseph Merola and Dr. Ahmed Amin. Dr. Merola and then Dr. Amin, would you like to share some details regarding your clinical background? Thank you.

Dr. Joseph F. Merola: Thanks for having me. I'm an Associate Professor at Harvard Medical School and the Director for the Center for Skin and Related Musculoskeletal Diseases at The Brigham and Women's Hospital here in Boston.

Dr. Ahmad Z Amin: Hello and thanks for having me. I'm an Associate Professor of Dermatology at Northwestern University in Chicago, Illinois. I also serve as the Director of our psoriasis program.

Dr. Uwe Wollina: Thanks for your introductions. It's a pleasure to join you today. Today we are going to discuss the clinical presentation and disease course of GPP, as well as discussing the potential triggers

Received: 11 October 2023
Accepted: 11 October 2023
Published: 5 March 2024

of an acute GPP flare. GPP can be debilitating for our patients, and we will discuss the different aspects of the burden of disease for patients with GPP.

To start us off, could you provide an overview of generalized pustular psoriasis and tell us how common it is and who it affects?

[00:01:52]

Dr. Joseph F. Merola: So, generalized pustular psoriasis, which is often abbreviated as GPP, is one of several pustular psoriasis conditions that form a heterogeneous group of autoinflammatory diseases, typically characterized by sudden and painful skin inflammation, along with these small, sterile pustules.

Widespread pustular psoriasis can affect large areas of the body, and we typically call that generalized pustular psoriasis. There are also localized variants that can affect palms and soles, known as palmoplantar pustulosis. Also, disease can be confined to the fingers, toes, and/or nail, typically for example, the nail bed, and is known as acrodermatitis continua of Hallopeau.

GPP was first described in 1910 by a German dermatologist called Leopold von Zumbusch who reported repeated pustular eruptions occurring in a patient with plaque psoriasis. And although GPP can present in patients with plaque psoriasis, they are two distinct conditions in terms of their clinical characteristics, pathology and, we know more recently, genetic background.

The current diagnostic definition of GPP was developed by the European Rare and Severe Psoriasis Expert Network in 2017, and this group described GPP as the occurrence of primary sterile, macroscopically visible epidermal pustules on non-acral skin, with or without systemic inflammation, with or without plaque psoriasis, that is either relapsing, meaning more than one episode, or persisting, lasting more than three months.[1] This differs from current Japanese guidelines on GPP, which specify systemic involvement must be present.[2]

Regarding the epidemiology of the disease, pustular psoriasis as a group is rare and represents only about 1% of all cases of psoriasis.[3] Estimating accurate prevalence information for GPP is difficult due to the rarity of the disease, its variation in presentation, and a lack of consistent diagnostic criteria. The way disease estimates are measured really can vary across countries. Therefore, published data show wide variations by geographical region, for example. Asian populations appear to be affected more by GPP than White populations. For example, about seven out of one million people have GPP in Japan versus two out of one million in France.[4,5]

[00:04:09]

Dr. Uwe Wollina: Thanks for explaining how the presentation of GPP differs. Can you please describe how GPP manifests? Does it affect one population more than others?

Dr. Joseph F. Merola: So that's a great question. GPP shows a female predominance, with two to three cases in women for each case in a man,[6,7] and the most common age of onset is between 40 and 60 years, although cases have been described in younger adults and children.[5,7]

Dr. Uwe Wollina: Could you briefly summarize the courses of GPP and talk about how the disease presents?

Dr. Ahmad Z Amin: Sure, absolutely. Let's talk a little bit about the etiology and pathophysiology. Pathogenesis of GPP appears to be caused by the effects of genes that activate inflammatory signaling pathways, especially those involving interleukin-36.[8] This results in recruitment and activation of various immune cells in the epidermis, particularly neutrophils and macrophages.

Now, what this means is that part of the immune system malfunctions and results in uncontrolled signaling that leads to swelling and redness in the skin, and also attracts certain types of white blood cells that release chemicals that cause more swelling and redness in the skin.

Environmental risk factors include viral or bacterial infections, use of certain medications, and discontinuation of corticosteroids.[9]

Let's talk a little bit about the presentation. GPP is the most severe form of pustular psoriasis. The onset of symptoms occurs rapidly, with painful, fiery skin erythema, followed by widespread appearance of pustules. The trunk and limbs are frequently affected but disease rarely arises on the face. Mucosal involvement may also occur, affecting the mouth, tongue, and genitals.[9] The

pustules often merge to form bigger lesions, sometimes resulting in "lakes of pus". The presentation of GPP in children can be similar to adult disease with diffuse generalized pustules, but more commonly presents in an annular, or ring-shaped, pattern with lesions confined to the trunk.

[0:06:04]

An acute episode of GPP, called a flare, is often accompanied by systemic symptoms, including high fever, pain in skin lesions, malaise, fatigue, and edema.[9] Patients have described a flare as feeling on fire and reported experiencing significant pain from the pustules. Other symptoms associated with flares include itching, skin dryness and scaling, general discomfort, and headache.

Now, as we mentioned earlier, GPP is a disease that relapses and remits and has a highly variable clinical course even within the same patient.[10] Flares may recur several times in a year or not return until many years after the initial diagnosis. The duration of a flare is also unpredictable, and it may last several weeks to several months. Also, previous episodes of a flare are not indicative of future disease severity.

Now, it's worth emphasizing that onset of GPP flares can be very sudden and rapid. Severe flares constitute a medical emergency due to the potentially life-threatening complications that may follow.[9,11] These include sepsis, respiratory distress, high output heart failure, and other conditions that may lead to multiorgan failure.

Skin symptoms can be assessed using a special scoring tool called the Generalized Pustular Psoriasis Physician Global Assessment, or GPPGA.[12,13] This tool assesses and grades the pustules, redness, and skin scaling to give a composite score and can be reapplied at regular intervals to monitor disease status over time.

To summarize then, GPP should be suspected in an individual presenting with sudden onset of inflamed painful skin with pustulosis, even if systemic symptoms are absent. In such cases, it is vital to determine if that individual needs immediate hospitalization. We talk more about this topic in episode 2.

[00:07:51]

Dr. Uwe Wollina: What might cause a GPP flare? What are the triggers?

Dr. Joseph F. Merola: For many patients, there's often no obvious cause for a GPP flare, while in others a flare may be triggered by various internal or external factors, and we mentioned some of these earlier. Triggers can include exposure to certain medications, commonly antimicrobials and corticosteroids. In fact, systemic corticosteroids should be used with care in patients with any type of psoriasis, as their use may precipitate pustular flares in susceptible individuals.[14]

GPP flares may also be induced by exposure to sunlight, viral upper respiratory tract infection, bacterial skin infection, pregnancy, and during periods of extreme stress.[9] In some cases, the trigger is just not known.[14]

Dr. Uwe Wollina: Could you tell us how GPP affects pregnant women?

Dr. Joseph F. Merola: So, pustular psoriasis occurring during pregnancy has been classified as a variant of GPP by many, but this is somewhat controversial. GPP in pregnancy usually presents during the third trimester and resolves after birth, but may recur with subsequent pregnancies.[15] Without early diagnosis and treatment, it's associated with poor or even fatal neonatal outcomes, including placental insufficiency, fetal abnormalities, and stillbirth.[15]

And the pathogenesis of GPP in pregnancy is not fully understood, and may be due to pregnancy-specific changes in immune function and/or hormone levels that contribute to skin pustule formation.[16]

Given the sex and age predilection in patients with GPP, it might be expected that a significant proportion of women affected would be of childbearing potential. However, there's data regarding treatment of GPP in pregnancy and lactation that's scarce, and there are no safety data from well-controlled studies in this population. Consequently, treatment options are limited and have mainly been confined to reduced dose cyclosporin, topical agents, corticosteroids, and phototherapy, typically with narrowband UVB.

I'd like to share a case of GPP that occurred during pregnancy when I was the treating physician many years ago. It was in 2008. It was a 28-year-old woman in her first pregnancy at 38 weeks gestation, who presented with fevers, chills and elevated sedimentation rate to 45, hypoalbuminemia to 2.6, and hypocalcemia of 7.7, and presented with a pustular skin eruption.

This patient was treated with high-dose steroids and cyclosporin. She was induced for concern of fetal safety and then received post-partum treatment with methotrexate and a TNF inhibitor. The mother was treated again with cyclosporin post-partum, since acitretin was not ideal given her age. She improved, but was seen for intermittent flares over the next few years.

[00:10:42]

Dr. Uwe Wollina: Are there any skin conditions that may be mistaken for GPP?

Dr. Ahmad Z Amin: Diagnosing GPP may be challenging as it's a rare disease with variable symptoms, and there are several other conditions with a similar presentation. The main diagnosis to exclude is acute generalized exanthematous pustulosis, or AGEP. This condition is strongly associated with recent exposure to medication, commonly antibiotics or calcium channel blockers.[17]

Although AGEP may look similar to GPP, the pustules are often smaller and usually occur on skin folds. Also, AGEP has a shorter duration, one to two weeks, and does not recur unless the patient is exposed to the same trigger again.[9] However, a skin biopsy may be needed to distinguish AGEP from GPP, as the histopathologic features of each are different.[10]

Other differential diagnoses for GPP include the types of localized pustular psoriasis we mentioned earlier, as well as IgA pemphigus and subcorneal pustular dermatosis.[14]

Dr. Uwe Wollina: Could you explain about the impact GPP has on the people who have this disease? For example, how often might they need hospital treatment? How does GPP affect their quality of life?

[00:11:53]

Dr. Ahmad Z Amin: GPP affects every aspect of a patient's life physically, economically, emotionally, and socially.

A misdiagnosis is common before patients are diagnosed with GPP. This process requires having to see several healthcare providers, including specialists, for diagnostic testing.[18] Navigating the healthcare system to get diagnosed with GPP adds to the patient burden.

Regarding the clinical burden, approximately half of GPP flares require inpatient treatment,[19] with an average duration of 10 to 14 days stay in a hospital.[7,11] As long as a diagnosis is prompt and treatment is initiated quickly, the prognosis for most patients with GPP is good, although elderly individuals may have worse outcomes.[20] Similarly, children with GPP have a favorable prognosis, providing there are no serious secondary infections.[20]

Patients with GPP often experience comorbidities, including arthritis, psoriatic arthritis, hypertension, and diabetes.[21] Comorbidities contribute to the complexity of treating GPP and may increase the risk for complications and mortality.

Now, in terms of mortality, a recent Japanese study reported an overall inpatient mortality rate of 4% (among 1513 patients with GPP). Mortality was much higher in patients receiving only systemic corticosteroids versus those receiving biologic agents, at approximately 9% and 1%, respectively.[19]

Dr. Joseph F. Merola: So, we know that patients with GPP have higher healthcare resource utilization needs than those with plaque psoriasis or matched controls (without either GPP or plaque psoriasis). Rates of inpatient visits were four times higher in patients with GPP than matched controls.[22] This may be due to increased disease severity in the GPP group, evidenced by a greater proportion of them receiving systemic treatment than patients with plaque psoriasis, at 75% versus 28%, respectively.[23]

Real-world evidence from patients such as those in the CorEvitas Psoriasis Registry revealed that individuals with GPP had more severe symptoms than those with plaque psoriasis, resulting in a greater impact on quality of life.[24] Pain, fatigue, and itch were particular issues in the GPP group, and the higher proportion of them reported anxiety and depression versus the plaque psoriasis group, at 38% and 26%, respectively.

The economic burden for patients with GPP is also higher than for those with plaque psoriasis or the general population. This is mainly due to inpatient stays and the cost of biologic drug treatments.[25] Interestingly, only about 10% of the costs appear to be directly attributable to GPP-specific problems, indicating a high economic burden is caused indirectly due to other consequences and complications of GPP.

[00:14:38]

Dr. Ahmad Z Amin: The physical and psychosocial impact of GPP flares was revealed in a recent survey of 60 patients with GPP.[18] In the survey, more than 80% of the survey participants said that

emotional stress was the most common cause of their GPP flares, 70% had a fear of flares occurring, and only one third felt their symptoms were well controlled.

GPP had a significant impact on daily activities, even in the absence of flares. During a flare, more than half of participants were unable to be intimate with their partner, carry out exercise, or even wear shoes, and 40% or more were unable to socialize, run errands, or do household chores. Importantly, these issues continued in up to 25% of participants, even when GPP symptoms were not present.

Many participants had experienced a delay in receiving their diagnosis of GPP, commonly due to misdiagnosis or having to consult multiple healthcare professionals. Around one third of participants had experienced GPP symptoms for several years before the diagnosis was made. Unfortunately, half of participants felt their doctor did not understand the impact of GPP on their lives.

Dr. Uwe Wollina: And very briefly, what treatment options are available to patients with GPP? (This is covered in detail in a separate episode.)

[00:15:54]

Dr. Ahmad Z Amin: Until recently, there were no GPP-specific treatments approved for flares in the US, EU, and China, and nor were there treatments for the improvements of acute symptoms of GPP in Japan.[26]

At that point in time the main systemic treatment options for patients with GPP flares in the US included non-biologic therapies used in plaque psoriasis, such as retinoids, cyclosporine, and methotrexate.[10] These are older types of drugs that are used in plaque psoriasis to dampen down the immune system, and to reduce redness and swelling in the skin. Newer drugs, such as biologic agents, had gained approval for GPP treatment in Japan.[26]

Recent research on the interleukin-36 pathway associated with GPP led to the development of a specific treatment, spesolimab, which was approved by the FDA in the US in September 2022 for the treatment of GPP flares in adults.[27] Spesolimab was also approved by regulatory agencies in the EU,[28] Japan, and China. Spesolimab is the first approval of a class of drugs called interleukin-36 receptor inhibitors. Another agent in this drug class, imsidolimab, is in the latter stages of clinical development.[29] Hopefully, these innovations mark the beginning of a new era of targeted therapy for individuals with GPP.

Dr. Uwe Wollina: To conclude this session, based on your clinical experience, what are the main takeaways for healthcare providers?

Dr. Joseph F. Merola: So, a lack of awareness about GPP contributes to misdiagnoses and creates delays in treating GPP, therefore, the true burden of GPP is not fully realized. Given that it's a rare disease and a potentially serious condition, prompt diagnosis and initiation of effective treatment are crucial. GPP should be suspected in someone presenting with acute onset painful skin inflammation with pustules.

Dr. Ahmad Z Amin: As we discussed, GPP impacts every aspect of a patient's life. Healthcare providers should not underestimate the emotional and social burden of the disease. We have an opportunity to recognize the disease, especially now that an approved drug is available for patients.

[00:17:57]

Dr. Uwe Wollina: Thank you both for taking the time to speak with us today and for providing such valuable information on GPP. I hope listeners can join us for the next podcast in the series, where we will discuss the immunopathogenesis, or in other words, what really causes and leads to disease, in addition to a diagnostic approach in GPP.

Acknowledgments

This podcast was sponsored by Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI).

The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors received no direct compensation related to the development of the manuscript. Editorial support was provided by Katie Crosslin, PhD, and Debra Brocksmith, MB ChB, PhD, both of Envision Pharma Group, which was contracted and compensated by BIPI for this service. BIPI was given the opportunity to review the discussion points

for medical and scientific accuracy as well as intellectual property considerations. The authors thank Dr. Uwe Wollina for serving as the moderator, and for reviewing the transcript prior to journal submission.

Funding

Medical writing support, which was provided by Envision Pharma Group, was contracted and funded by Boehringer Ingelheim Pharmaceuticals, Inc.

Disclosure

JFM is a consultant and/or investigator for Amgen, AstraZeneca, Boehringer-Ingelheim, Bristol Myers Squibb, AbbVie, Dermavant, Eli Lilly, Incyte, Moonlake, Novartis, Janssen, UCB, Sanofi, Regeneron, Sun Pharma, Biogen, Pfizer, and LEO Pharma. AZA participates in activities such as speaking, advising, consulting, or providing educational programs for the following companies or other entities: AbbVie, Inc., Amgen, Inc., BMS, Dermavant, Eli Lilly and Company, Great Lakes Clinical Trials, Incyte, Janssen Biotech, Inc., (formerly Centocor Biotech, Inc.), Regeneron Pharmaceuticals, Inc., Sanofi-aventis US, LLC, and UCB Pharma (UCB S.A., Belgium).

References

1. Navarini AA, Burden AD, Capon F, et al. European consensus statement on phenotypes of pustular psoriasis. *J Eur Acad Dermatol Venereol*. 2017;31(11):1792–1799. doi:10.1111/jdv.14386
2. Fujita H, Terui T, Hayama K, et al. Japanese guidelines for the management and treatment of generalized pustular psoriasis: The new pathogenesis and treatment of GPP. *J Dermatol*. 2018;45(11):1235–1270. doi:10.1111/1346-8138.14523
3. Zheng M, Jullien D, Eyerich K. The prevalence and disease characteristics of generalized pustular psoriasis. *Am J Clin Dermatol*. 2022;23(Suppl 1):5–12. doi:10.1007/s40257-021-00664-x
4. Ohkawara A, Yasuda H, Kobayashi H, et al. Generalized pustular psoriasis in Japan: two distinct groups formed by differences in symptoms and genetic background. *Acta Derm Venereol*. 1996;76(1):68–71. doi:10.2340/00015555766871
5. Augey F, Renaudier P, Nicolas JF. Generalized pustular psoriasis (Zumbusch): a French epidemiological survey. *Eur J Dermatol*. 2006;16 (6):669–673.
6. Tosukhowong T, Kiratikanon S, Wonglamsam P, et al. Epidemiology and clinical features of pustular psoriasis: A 15-year retrospective cohort. *J Dermatol*. 2021;48(12):1931–1935.
7. Choon SE, Lai NM, Mohammad NA, Nanu NM, Tey KE, Chew SF. Clinical profile, morbidity, and outcome of adult-onset generalized pustular psoriasis: analysis of 102 cases seen in a tertiary hospital in Johor, Malaysia. *Int J Dermatol*. 2014;53(6):676–684. doi:10.1111/ijd.12070
8. Marrakchi S, Puig L. Pathophysiology of generalized pustular psoriasis. *Am J Clin Dermatol*. 2022;23(Suppl 1):13–19. doi:10.1007/s40257-021-00655-y
9. Choon SE, Navarini AA, Pinter A. Clinical course and characteristics of generalized pustular psoriasis. *Am J Clin Dermatol*. 2022;23(Suppl 1):21–29. doi:10.1007/s40257-021-00654-z
10. Gooderham MJ, Van Voorhees AS, Lebwohl MG. An update on generalized pustular psoriasis. *Expert Rev Clin Immunol*. 2019;15(9):907–919. doi:10.1080/1744666X.2019.1648209
11. Kharawala S, Golembesky AK, Bohn RL, Esser D. The clinical, humanistic, and economic burden of generalized pustular psoriasis: a structured review. *Expert Rev Clin Immunol*. 2020;16(3):239–252. doi:10.1080/1744666X.2019.1708193
12. Bachelez H, Choon SE, Marrakchi S, et al. Inhibition of the interleukin-36 pathway for the treatment of generalized pustular psoriasis. *N Engl J Med*. 2019;380(10):981–983. doi:10.1056/NEJMc1811317
13. Burden AD, Choon SE, Gottlieb AB, Navarini AA, Warren RB. Clinical disease measures in generalized pustular psoriasis. *Am J Clin Dermatol*. 2022;23(Suppl 1):39–50. doi:10.1007/s40257-021-00653-0
14. Crowley JJ, Pariser DM, Yamauchi PS. A brief guide to pustular psoriasis for primary care providers. *Postgrad Med*. 2021;133(3):330–344. doi:10.1080/00325481.2020.1831315
15. Trivedi MK, Vaughn AR, Murase JE. Pustular psoriasis of pregnancy: current perspectives. *Int J Womens Health*. 2018;10:109–115. doi:10.2147/IJWH.S125784
16. Seishima M, Fujii K, Mizutani Y. Generalized pustular psoriasis in pregnancy: current and future treatments. *Am J Clin Dermatol*. 2022;23 (5):661–671. doi:10.1007/s40257-022-00698-9
17. Stadler PC, Oschmann A, Kerl-French K, et al. Acute generalized exanthematous pustulosis: clinical characteristics, pathogenesis, and management. *Dermatology*. 2023;239(3):328–333. doi:10.1159/000529218
18. Reisner DV, Johnsson FD, Kotowsky N, Brunette S, Valdecantos W, Eyerich K. Impact of generalized pustular psoriasis from the perspective of people living with the condition: results of an online survey. *Am J Clin Dermatol*. 2022;23(Suppl 1):65–71. doi:10.1007/s40257-021-00663-y
19. Miyachi H, Konishi T, Kumazawa R, et al. Treatments and outcomes of generalized pustular psoriasis: A cohort of 1516 patients in a nationwide inpatient database in Japan. *J Am Acad Dermatol*. 2022;86(6):1266–1274. doi:10.1016/j.jaad.2021.06.008
20. Cockerill C. Pustular psoriasis. Medscape; 2021. Available from: https://emedicine.medscape.com/article/1108220-overview. Accessed July 17, 2023.
21. Prinz JC, Choon SE, Griffiths CEM, et al. Prevalence, comorbidities and mortality of generalized pustular psoriasis: A literature review. *J Eur Acad Dermatol Venereol*. 2023;37(2):256–273. doi:10.1111/jdv.18720
22. Hanna ML, Singer D, Valdecantos WC. Economic burden of generalized pustular psoriasis and palmoplantar pustulosis in the United States. *Curr Med Res Opin*. 2021;37(5):735–742. doi:10.1080/03007995.2021.1894108

23. Okubo Y, Kotowsky N, Gao R, Saito K, Morita A. Clinical characteristics and health-care resource utilization in patients with generalized pustular psoriasis using real-world evidence from the Japanese Medical Data Center database. *J Dermatol*. 2021;48(11):1675–1687. doi:10.1111/1346-8138.16084
24. Lebwohl M, Medeiros RA, Mackey RH, et al. The disease burden of generalized pustular psoriasis: real-world evidence from CorEvitas' Psoriasis Registry. *J Psoriasis Psoriatic Arthritis*. 2022;7(2):71–78. doi:10.1177/24755303221079814
25. Lofvendahl S, Norlin JM, Schmitt-Egenolf M. Economic burden of generalized pustular psoriasis In Sweden: a population-based register study. *Psoriasis*. 2022;12:89–98. doi:10.2147/PTT.S359011
26. Krueger J, Puig L, Thaçi D. Treatment options and goals for patients with generalized pustular psoriasis. *Am J Clin Dermatol*. 2022;23(Suppl 1):51–64. doi:10.1007/s40257-021-00658-9
27. Boehringer Ingelheim. FDA approves the first treatment option for generalized pustular psoriasis flares in adults; 2022. Available from: https://www.boehringer-ingelheim.us/press-release/fda-approves-first-treatment-option-generalized-pustular-psoriasis-flares-adults. Accessed September 28, 2022.
28. Boehringer Ingelheim. European Commission approves SPEVIGO® (spesolimab) for generalized pustular psoriasis flares; 2022. Available from: https://www.boehringer-ingelheim.com/human-health/skin-diseases/gpp/european-commission-approves-spevigo-spesolimab-generalized. Accessed January 24, 2023.
29. AnaptysBio. Long-Term Safety and Efficacy of Imsidolimab (ANB019) in Subjects With Generalized Pustular Psoriasis (GEMINI 2); 2022. Available from: https://clinicaltrials.gov/study/NCT05366855?tab=table. Accessed July 18, 2023.