

Supplementary Material

Current treatments for generalized pustular psoriasis: A narrative summary of a systematic literature search

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Table S1: Search strategy

Parameter	#	Query
Disease	#1	Ti,AB((pustular OR pustulous OR pustulosa) NEAR/1 (psoriasis OR psoriatic OR psoriaform)) OR Ti,AB("Von Zumbusch") OR EMB.EXACT("pustular psoriasis")
Treatment patterns	#2	Ti,AB((treatment OR treatments OR therapy OR therapies OR clinical OR care OR consensus OR dose OR doses OR dosing) NEAR/3 (pattern OR patterns OR duration OR utilization OR utilisation OR time OR management)) OR Ti,AB(retreat* OR "disease management" OR standard OR practice)
Treatment guidelines	#3	Ti,AB((clinical OR practice OR treatment OR treatments OR care) NEAR/3 (guideline* OR guidance OR pathway* OR consensus)) OR EMB.EXACT.EXPLODE("Practice Guideline") OR MESH.EXACT("Guideline" OR "Critical Pathways" OR "Standard of Care") OR DTYPE("Practice Guideline")
Clinical outcomes/ safety	#4	Ti,AB(efficacy OR effectiveness OR response OR responded OR responses OR outcome OR outcomes) OR EMB.EXACT("clinical effectiveness") OR EMB.EXACT("treatment response") OR MESH.EXACT.EXPLODE("Treatment Outcome")
	#5	Ti,AB(safety OR adverse OR complications OR "side effect" OR "side effects") OR EMB.EXACT.EXPLODE("adverse event") OR MESH.EXACT.EXPLODE("Drug-Related Side Effects and Adverse Reactions")
	#6	#4 OR #5
Clinical burden	#7	Ti,AB((symptom OR symptoms OR clinical OR treatment OR disease) NEAR/3 burden) OR Ti,AB((functioning OR function) AND (reduce OR reduced OR impair OR impaired OR decrease OR decreased OR impact OR impacted)) OR Ti,AB((daily OR day) NEAR/3 activit*) OR Ti,AB(sequelae OR sequela OR consequence OR consequences OR dysfunction* OR impairment OR impairments OR deficit OR deficits OR disability OR disabilities) OR EMB.EXACT("International Classification of Functioning, Disability and Health") OR MESH.EXACT("International Classification of Functioning, Disability and Health")
QoL	#8	EMB.EXACT("International Classification of Functioning, Disability and Health" OR "Dermatology Life Quality Index" OR "quality of life" OR "short form 36" OR "patient-reported outcome" OR "patient preference" OR "questionnaire" OR "quality adjusted life years") OR EMB.EXACT.EXPLODE("health status indicator") OR MESH.EXACT("International Classification of Functioning, Disability and Health" OR "Quality of Life" OR "Value of Life" OR "Patient Reported Outcome Measures" OR "Patient Preference" OR Questionnaires OR "Quality-Adjusted Life Years") OR MESH.EXACT.EXPLODE("Health Status Indicators") OR Ti,AB(burden OR (impact NEAR/3 (caregiver OR family OR families OR society OR societal or patient OR person)) OR "unmet need" OR "disability adjusted" OR "disability-

Parameter	#	Query
		adjusted" OR DALY* OR "dartmouth coop" OR "Duke health profile" OR EQ5D OR "EQ 5D" OR EQ OR EUROQOL OR "EURO QOL" OR EUROQUAL OR "EURO QUAL" OR ((daily OR day) NEAR/3 activit*) OR "functional status" OR FSQ OR (function* NEAR/5 (reduc* OR impair* OR decrease* OR impact*)) OR "quality of life" OR hrqol OR hrql OR hql OR hqol OR "hr qol" OR "h qol" OR "health stat*" OR "life quality" OR (health NEAR/3 (status OR indicator*)) OR "Nottingham health" OR NHP OR PQOL OR "perceived quality" OR QLS OR "quality of life scale" OR wellbeing OR "well being" OR "well-being" OR QWB OR rosser OR SF OR "short form" OR "short-form*" OR "shortform*" OR SF6 OR SF8 OR SF12 OR SF20 OR SF36 OR "sickness impact" OR SIP OR "patient reported" OR "patient-reported" OR "self reported" OR "self-reported" OR QALY* OR QALD* OR QALE* OR QTIME* OR (utilit* NEAR/3 (valu* OR measur* OR health OR life OR estimat* OR elicit* OR disease OR score* OR weight OR instrument OR instruments OR index)) OR "quality adjusted" OR "quality-adjusted" OR "life year*" OR "life-year*" OR "health year*" OR "health-year*" OR disutilit* OR "willingness to pay" OR "willingness-to-pay" OR WTP OR (preference* NEAR/3 (valu* OR measur* OR health OR life OR estimat* OR elicit* OR disease OR score* OR instrument OR instruments OR index)) OR "healthy utility index" OR hui OR hui1 OR hui2 OR hui3 OR "standard gamble" OR "time trade off" OR "time tradeoff" OR TTO OR QOL OR "health assessment questionnaire" OR "health assessment questionnaires" OR HAQ)
Economic burden	#9	MESH.EXACT("Cost of Illness" OR "Economics, Hospital" OR "Economics, Nursing" OR "Economics, Pharmaceutical" OR "Fees and Charges" OR "Economics, Dental" OR "Employer Health Costs" OR "Efficiency" OR "Presenteeism" OR "Absenteeism") OR MESH.EXACT.EXPLODE("Health Care Costs" OR "Health Expenditures" OR "Economics, Medical" OR "Salaries and Fringe Benefits") OR EMB.EXACT("cost of illness" OR "drug cost" OR "productivity" OR "medical leave" OR "presenteeism" OR "absenteeism") OR EMB.EXACT.EXPLODE("health care cost" OR "salary and fringe benefit") OR TI,AB(presenteeism OR absenteeism OR (cost* NEAR/3 (medical OR direct OR indirect OR drug OR pharmaceutical OR hospital OR emergency OR outpatient OR inpatient OR ambulatory OR "primary care" OR practitioner OR device OR informal OR economic OR societal OR intangible OR caregiver OR physician OR specialist OR healthcare OR "health care" OR annual* OR clinic)) OR ((burden OR impact) NEAR/3 (cost OR costs OR economic OR economics OR caregiver OR caregivers OR family OR families OR society OR societal OR employee OR employer)) OR (los* AND work AND day*) OR "sick day" OR "sick leave" OR "sickness absence" OR "work absence" OR "work incapacity" OR "work leave" OR "disability absence" OR ((resource OR healthcare OR "health care") NEAR/5 (use OR utilization OR utilisation)) OR ((visit* OR admission* OR readmission* OR re-admission* OR stay* OR day*) NEAR/3 (physician OR emergency OR specialist OR outpatient OR inpatient OR "primary care" OR practitioner OR hospital OR clinic)) OR hospitalization OR hospitalisation OR "length of stay" OR "LOS")
Disease and treatment patterns	#10	#1 AND #2

Parameter	#	Query
Disease and treatment guidelines	#11	#1 AND #3
Disease and efficacy/safety	#12	#1 AND #6
Disease and burden	#13	#1 AND (#7 OR #8 OR #9)
Combined search	#14	#10 OR #11 OR #12 OR #13
Limit publication date	#15	#14 AND PD(>1979)
Exclude conference abstracts	#16	#15 NOT DTYPE("Conference abstract")

Table S2: Inclusion and exclusion criteria

Category	Inclusion/exclusion criteria	
	Inclusion	Exclusion
Population	Age: any Gender: any Ethnicity: any Studies which enrol a mixed population of patients (i.e. studies where generalized pustular psoriasis [GPP] is a sub-population within a larger psoriasis group and there is clear distinction of the GPP population)	Disease: other forms of psoriasis where no sub-group analysis is provided for patients with GPP
Intervention/comparator	Any interventions/comparators to be included	Not applicable
	Efficacy	
	Relapse rate (relapse of skin lesions) Flares: number of flares, flare recurrences Treatment failure Treatment response: complete response, marked response, improvement, no response, partial response • Clinical Global Impression of Improvement (CGI) • Body surface area (BSA) • Pustule count • Psoriasis Area and Severity Index (PASI) • Physician Global Assessment (PGA) • Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) rate following treatment • Generalized Pustular Psoriasis Area and Severity Index (GPPASI) score • Duration of response	

Category	Inclusion/exclusion criteria	
	Inclusion	Exclusion
Outcomes	• Hospitalization • Duration of hospitalization • Remission	• Studies that do not have any extractable data
	Safety • Any adverse event (AE) • Any grade 3/4 AE • Any serious AE • Any treatment-related AE • All treatment withdrawals (including due to AEs) • Mortality due to treatment or other causes	
	Patient-reported outcomes/QoL • Qualitative data on patient experience/disease impact and symptoms/quality of life (QoL) • EQ-5D, SF-36, Pain [including Visual Analogue Scale (VAS)], FACIT-Fatigue Scale, Dermatology Life Quality Index (DLQI) • Indirect burden/caregiver QoL including any qualitative data on caregiver experience/QoL	
	Economic Treatment costs, AE costs, hospitalization costs, per patient costs, resource utilization, indirect costs	
Study	All randomized controlled clinical trials (irrespective of blinding status) Non-randomized controlled trials Single-arm trials	Clinical guidelines, review articles

Category	Inclusion/exclusion criteria	
	Inclusion	Exclusion
	Observational studies (non-interventional studies, retrospective analysis, prospective studies, case studies, cohort studies, case control studies, case series, case reports) Editorials, letters, notes or comments to the editor Cost analysis, budget impact analysis, cost of illness, cost minimization, cost effectiveness and cost-benefit studies	
Other	Countries No restriction Language No restriction Time frame Studies published between 1980–September 2023	Studies not published between 1980–September 2023

Table S3: Characteristics of included studies

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
1	Adachi <i>et al.</i> (2016) [1]	GMA	Japan	Case report	NA	NA	1	18/16 years	Female	Japanese
2	Albela <i>et al.</i> (2022) [2]	Acitretin; Secukinumab	Malaysia	Case series	NA	NA	4	Case 1: 4/0 years Case 2: 11/0 years Case 3: 8/0 years Case 4: 10/0 years	Male: 2 Female: 2	Chinese: 1 Malay: 2 Orang Asli: 1
3	Alvarez <i>et al.</i> (2011) [3]	Adalimumab	Spain	Case report	NA	15 months	1	13 years/6 months	Female	NA
4	Arakawa <i>et al.</i> (2016) [4]	Ustekinumab; Anakinra	Germany	Case series	NA	NA	4	Case 1: 20s Case 2: 50s Case 3: 20s Case 4: 50s	Female: 4	NA
5	Bachelez <i>et al.</i> (2019) [5]	Spesolimab	France, Malaysia, Republic of Korea, Taiwan, Tunisia	Multicentre, single-arm, open-label, proof-of-concept study (NCT02978690)	20 weeks	NA	7	Mean (SD): 38.6 (13.8) years	Male: 3 Female: 4	White: 2 Asian: 4 NA: 1
6	Bachelez <i>et al.</i> (2021) [6]	Spesolimab	Multicentre	Multicentre, randomized, double blind, placebo-controlled trial (Effisayil™ 1; NCT03782792)	12 weeks	NA	53 (35 treated)	Mean (SD): 43.2 (12.1) years [treatment arm]	Treatment arm Male: 14 Female: 21	White: 24 Asian: 29
7	Braun-Falco <i>et al.</i> (1987) [7]	Etretinate; PUVA	Germany	Retrospective case series	Patients treated between 1969 and 1981	12 years	7	Case 1: 57 years Case 2: 60 years Case 3: 69 years Case 4: 19 years Case 5: 19 years Case 6: 4 years Case 7: 25 years	Female: 5 Male: 2	NA

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
8	Burden <i>et al.</i> (2023) [8]	Spesolimab	Multicentre	Multicentre, randomized, double-blind, placebo-controlled trial (Effisayil™ 1; NCT03782792)	12 weeks	NA	53 (35 treated)	Mean (SD): 43.2 (12.1) years [treatment arm]	Treatment arm Male: 14 Female: 21	White: 24 Asian: 29
9	Burlando <i>et al.</i> (2022) [9]	Ixekizumab	Italy	Case study	NA	2 years	1	51 years	Male	NA
10	Chandran <i>et al.</i> (2010) [10]	Infliximab	Singapore	Case report	NA	NA	1	48/16 years	Female	Chinese
11	Chen <i>et al.</i> (2018) [11]	Acitretin	China	Retrospective study and literature review	10–32 months	4–6 weeks in the first half year then every eight weeks in the second half year, and finally every 3 months in the following year	10	Age at onset: 0.3–7 years	Female: 4 Male: 6	NA
12	Chen <i>et al.</i> (2019) [12]	Infliximab	China	Case report	NA	NA	1	12 years	Male	Chinese
13	Cherqaoui <i>et al.</i> (2018) [13]	Ustekinumab; Anakinra	France	Case report	NA	15 months	1	1 month	Male	Tunisian parents
14	Choon <i>et al.</i> (2014) [14]	Cyclosporine; Retinoids; Methotrexate; Adalimumab; Doxycycline; Dapsone; Prednisolone; Supportive	Malaysia	Retrospective chart review	Between 1989 and November 2011	From first clinic visiting ranging from Nov 1972–Nov 30, 2011, mean: 2895 days (approx. 8 years), range 26 days–39 years. After first episode of GPP Sept 1989–Aug 2011, mean:	102	Mean (range): 48.1 years (22–89)/40.9 years (21–81)	Female: 68 Male: 34	Malay: 57% Chinese: 29% Indian: 11% Other: 3%

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
						1838 days (approx. 5 years) range 22 days–22 years				
15	Cohen Barak <i>et al.</i> (2015) [15]	Cyclosporine	Israel	Retrospective chart review	7 months	NA	1	NA	NA	NA
16	Collins <i>et al.</i> (1992) [16]	Methotrexate	Ireland	Retrospective review	NA	NA	6	NA	NA	NA
17	Cordoro <i>et al.</i> (2017) [17]	Infliximab; Secukinumab; Anakinra	USA	Case report	NA	1 year	1	NA	Male	NA
18	Das <i>et al.</i> (2013) [18]	Hydroxyurea	India	Prospective, non-randomized study	6 months	6 months	6	NA	NA	NA
19	Daudén <i>et al.</i> (2010) [19]	Ustekinumab	Spain	Case report	NA	16 months	1	47 years/14 years	Male	NA
20	Dogra <i>et al.</i> (2017) [20]	Cyclosporine	India	Retrospective chart review	8 weeks	NA	1	10 years	Male	NA
21	Du <i>et al.</i> (2022) [21]	Adalimumab	China	Case series + literature review	Between 2019 and 2021	1 month	7	Mean age: 8.71 years	Male: 3 Female: 4	NA
22	Ekinci <i>et al.</i> (2021) [22]	Acitretin; Secukinumab; Ustekinumab	Turkey	Case series	NA	Case 1: 6 months Case 2: 1 year Case 3: 1 year	3	Case 1: 64 years Case 2: 37 years Case 3: 76 years	Male: 2 Female: 1	NA
23	Esposito <i>et al.</i> (2008) [23]	Etanercept	Italy	Case series	NA	48 weeks	6	Mean age: 53.1 years	Female: 5 Male: 1	NA
24	Fradin <i>et al.</i> (1990) [24]	Cyclosporine	USA	Case report	NA	NA	1	49 years/19 years	Male	NA
25	Fujii <i>et al.</i> (2018) [25]	GMA	Japan	Case report	NA	NA	1	79 years	Female	NA
26	Fujisawa <i>et al.</i> (2011) [26]	GMA	Japan	Case series	NA	NA	3	Case 1: 61 years Case 2: 64 years Case 3: 63 years	Female: 1 Male: 2	NA
27	Fujisawa <i>et al.</i> (2015) [27]	GMA	Japan	Case series	NA	NA	3	Case 1: 31 years Case 2: 61 years Case 3: 63 years	Female: 2 Male: 1	NA

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
28	Gabeff <i>et al.</i> (2019) [28]	Secukinumab	France	Case report	NA	6 months	1	32 years	Female	Syrian
29	Gowda <i>et al.</i> (2020) [29]	Acitretin	India	Case report and literature review	NA	NA	1	42 years	Female	NA
30	Gu <i>et al.</i> (2011) [30]	Acitretin	China	Case report	NA	NA	1	23 years/14 years	Male	Chinese
31	Guerra <i>et al.</i> (2023) [31]	Brodalumab	Italy	Case series	NA	NA	1	91 years	Female	NA
32	Haustein & Rytter (2000) [32]	Methotrexate	Germany	26-year retrospective single-centre study	January 1972 to December 1998	NA	24	NA	NA	NA
33	Heyer <i>et al.</i> (2022) [33]	Risankizumab	Germany	Case report	NA	6 months	1	70 years	Female	Caucasian
34	Ho <i>et al.</i> (2018) [34]	Secukinumab	Taiwan	Case report	NA	NA	1	6 years	Male	Taiwanese
35	Ichiyama <i>et al.</i> (2021) [35]	Corticosteroids ; Brodalumab; Vitamin D3	Japan	Case report	3 years	NA	1	35 years/0 years	Male	Japanese
36	Ikeda <i>et al.</i> (2013) [36]	GMA	Japan	Single-arm, unblinded study	5 weeks	NA	15 (1 patient did not complete the first GMA session and was withdrawn from the study)	Average: 50.3 ± 12.9 years (range 31–71 years)	Male: 11 Female: 4	NA
37	Imafuku <i>et al.</i> (2016) [37]	Secukinumab	Japan	Interventional, multicentre, single-arm, open-label study (NCT01952015; JAPIC JapicCTI-132305)	52 weeks	NA	12, only 11 completed induction period	Mean: 56.3 years	Male: 8 Female: 4	Japanese
38	Isse Ali <i>et al.</i> (2022) [38]	Prednisolone	Somalia	Case report	NA	8 months	1	26 years	Female	NA

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
39	Jing <i>et al.</i> (2021) [39]	Secukinumab	China	Case report	NA	4 months	1	5 years	Female	NA
40	Juanqin <i>et al.</i> (1998) [40]	Lei-Gong-teng (Chinese herb) + dapsone + erythromycin; Etretinate + prednisone/erythromycin; Methotrexate; Hydroxyurea; Thiamphenicol	China	Retrospective analysis	Patients treated between 1985 and 1996	NA	30	2–12 years with an average of 7 years; 22 patients were <10 years	Males: 21 Females: 9	NA
41	Kamata <i>et al.</i> (2021) [41]	GMA	Japan	Case series	NA	NA	14	64.5 ± 12.6 years	NA	NA
42	Kawakami <i>et al.</i> (2015) [42]	Infliximab; Adalimumab	Japan	Case series	NA	Case 1: 97 weeks Case 2: 64 weeks	2	Case 1: 43 years Case 2: 30 years	Case 1: male Case 2: Female	NA
43	Kořt-Kamińska <i>et al.</i> (2021) [43]	Acitretin; Infliximab	Poland	Case reports and literature review	NA	NA	2	Case 1: 73 years Case 2: 60 years	Case 1: Female Case 2: Male	NA
44	Kowalzik <i>et al.</i> (2003) [44]	Infliximab	Germany	Case report	NA	NA	1	46 years/ First developed psoriasis 7 years prior	Male	NA
45	Kromer <i>et al.</i> (2021) [45]	Methotrexate; Apremilast; Cyclosporine; Acitretin; Fumaric acid ester; Infliximab; Adalimumab; Etanercept; Secukinumab; Ixekizumab; Ustekinumab;	Germany	Non-interventional retrospective patient chart review	Patients treated between January 2005 and May 2019	NA	86	Age at symptom onset, mean (SD): 51.2 (19.2)	Female: 56 Male: 30	NA

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
		Guselkumab; PUVA								
46	Kura <i>et al.</i> 2022 [46]	Itolizumab	India	Case series	24 weeks	Regular follow-up (timeframe not specified)	3	Case 1: 12/5 years Case 2: 30/5 years Case 3: 54/54 years	Female: 3	NA
47	Lau <i>et al.</i> (2017) [47]	Acitretin	Malaysia	Retrospective chart review	Data collection November 2015 to April 2016	Median duration of follow-up after onset of GPP was 8.8 years (IQR: 4.3, 22.8 years)	27	Median: 16.3 years (IQR: 11.5, 24.9)/ 6.5 years (IQR: 2.0, 11.5)	Female: 16 Male: 11	74% Malay 22.2% Chinese 3.7% Indian Patient 18: Chinese
48	Lee <i>et al.</i> (2018) [48]	Acitretin; NB-UVB	Korea	Case report	NA	>1 year	1	22 months/4 months	Male	NA
49	Li <i>et al.</i> (2023) [49]	Secukinumab	China	Case report	NA	6 months	1	31 years/~21 years	Female	NA
50	Lorand <i>et al.</i> (1983) [50]	Etretinate	Belgium	Case series	NA	NA	4	45–74 years	Male: 2 Female: 2	NA
51	Lu <i>et al.</i> (2020) [51]	Infliximab	China	Case series	NA	12 months	2	Case 1: 7/3 years Case 2: 12/5 years	Male: 2	Chinese
52	Lu <i>et al.</i> (2022) [52]	Acitretin	China	Prospective comparative study	52 weeks	NA	54	Mean: 52.6 ± 4.4 years [treatment arm]	Treatment arm Male: 21 Female: 19	Chinese
53	Mansouri <i>et al.</i> (2015) [53]	Gevokizumab	USA	Patient cases from an open-label, expanded-access study	12 weeks	4 weeks	2	Case 1: 35 years Case 2: 59 years	Male: 1 Female: 1	White: 2
54	Mazzotta <i>et al.</i> (2011) [54]	Etanercept	Italy	Case report	NA	2 years' follow-up after 5 years of treatment	1	11 years/3 months	Male	NA

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
55	Miao <i>et al.</i> (2022) [55]	Acitretin; Secukinumab	China	Retrospective study	Patients treated between January 2019 and January 2022	NA	36	6–12 years	Male: 29 Female: 7	NA
56	Minai <i>et al.</i> (2022) [56]	Secukinumab	Japan	Case report	NA	NA	1	72 years	Female	NA
57	Miyachi <i>et al.</i> (2022) [57]	Corticosteroids ; Biologics; Oral agents	Japan	Retrospective cohort study	Patients treated between July 2020 and March 2019	NA	274	NA	Male: 143 Female: 131	NA
58	Miyamoto <i>et al.</i> (2020) [58]	Infliximab; GMA	Japan	Case series	NA	NA	3	Case 1: 54 years Case 2: 36 years Case 3: 66 years	Female: 2 Male: 1	Japanese: 3
59	Mizutani <i>et al.</i> (2020) [59]	GMA	Japan	Case series	NA	NA	2	Case 1: 31 years Case 2: 77 years	Female: 2	NA
60	Morita <i>et al.</i> (2018) [60]	Adalimumab	Japan	Multicentre, open-label, 52-week study (NCT02533375)	52 weeks	70 days	10	Mean $\pm$ SD: 49.8 $\pm$ 13.3 years	Male: 7 Female: 3	Japanese
61	Morita <i>et al.</i> (2022) [61]	Ixekizumab	Japan	Multicentre, open-label clinical trial (UNCOVER-J2; NCT03942042)	20 weeks	NA	7	Mean: 45 years	Male: 3 Female: 4	Japanese
62	Morita <i>et al.</i> (2022) [62]	Spesolimab	Multicentre	Multicentre, randomized, double-blind, placebo-controlled trial (Effisayil™ 1; NCT03782792)	12 weeks	NA	29 (16 treated)	Mean (SD): 42.2 (11.6) years [treatment arm]	Treatment arm Female: 10 Male: 6	Asian
63	Morita <i>et al.</i> (2023) [63]	Spesolimab	Multicentre	Multicentre, randomized, double-blind, placebo-controlled trial	44 weeks (last treatment)	4 weeks (follow up for 4 weeks)	123 (92 treated over 3 arms)	Years, mean (SD) Placebo: 39.5 (14.0)	Female: 76 Male: 47	Asian: 79 White: 44

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
				(Effisayil™ 2; NCT04399837)	t at week 44)	following last treatment)		Low dose: 38.9 (16.5) Medium dose: 42.9 (16.7) High dose: 40.2 (16.4)		
64	Mugheddu <i>et al.</i> (2017) [64]	Secukinumab	Italy	Case report	NA	NA	1	66 years	Male	Caucasian
65	Navarini <i>et al.</i> (2023) [65]	Spesolimab	Multicentre	Multicentre, randomized, double-blind, placebo-controlled trial (Effisayil™ 1; NCT03782792)	12 weeks	NA	53 (35 treated)	NA	NA	NA
66	Newland <i>et al.</i> (2002) [66]	Infliximab	USA	Case report	NA	NA	1	44 years	Female	Caucasian
67	Novotny <i>et al.</i> (1988) [67]	Dapsone	NA	Case series	NA	NA	3	NA	NA	NA
68	Ohnishi <i>et al.</i> (2018) [68]	GMA	Japan	Case series	NA	NA	22	32–78 years	Female: 13 Male: 9	Japanese
69	Okubo <i>et al.</i> (2019) [69]	Ixekizumab	Japan	Multicentre, single-arm, open-label study (UNCOVER-J; NCT01624233)	244 weeks	24 weeks after last regular visit	5	29–67 years	Female: 3 Male: 2	Japanese
70	Okubo <i>et al.</i> (2022) [70]	Certolizumab	Japan	Exploratory analysis of open-label randomized trial	52 weeks	8 weeks after treatment stopped	7	Mean (SD) years 400 mg group: 44.7 (8.3) 200 mg group: 51.0 (14.6)	400 mg group Male: 1 Female: 2 200 mg group Male: 2 Female: 2	Japanese
71	Osmola-Mańkowska <i>et al.</i> (2014) [71]	Cyclosporine; Acitretin; PUVA	Poland	Case report	NA	NA	1	31 years	Male	NA
72	Ozawa <i>et al.</i> (1999) [72]	Methotrexate; Etretinate;	Japan	Retrospective, multicentre study	Patients treated	NA	385	Mean age at onset	Male: 167 Female:	Japanese

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
		PUVA; Cyclosporine			between 1987 and 1996			Without any previous history of PV (N=244): 38.2 years With previous history of PV (N=103): 41.0 years	190 Unknown: 1	
73	Park <i>et al.</i> (2016) [73]	Corticosteroids ; Acitretin	Korea	Case report	NA	6 months	1	60 years	Female	NA
74	Posso-De Los Rios <i>et al.</i> (2014) [74]	Methotrexate; Cyclosporine; Acitretin; Infliximab	NA	Case series and literature review	NA	Acitretin: 21 (2–74) months CyA: 11 (0.75–36) months MTX: 6 (0.16–22) months Infliximab: 4 (0.06–10) months	22	NA	NA	NA
75	Poulalhon <i>et al.</i> (2007) [75]	Infliximab	France	Prospective follow-up study	September 2001 to February 2005	Median: 78 weeks	3	NA	NA	NA
76	Prasertyothin <i>et al.</i> (2017) [76]	Infliximab	Thailand	Retrospective chart review	Patients treated between July 2002 and October 2014	NA	1	NA	Female	NA
77	Reymundo <i>et al.</i> (2022) [77]	Secukinumab	Spain	Case series	Between January 2014 and July 2020	12–36 months	5	Mean (SD): 45.1 (16.8) years	Female: 2 Male: 3	NA
78	Rosinska <i>et al.</i> (1988) [78]	Etretinate	Poland	Case series	NA	NA	5	Case 1: 9 years Case 2: 11 years Case 3: 3 years	Female: 2 Male: 3	NA

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
								Case 4: 14 years Case 5: 5 years		
79	Ruan <i>et al.</i> (2023) [79]	Secukinumab	China	Case series	July 2019–August 2020	48 weeks	18	Mean: 7.9 ± 2.3 years	Male: 10 Female: 8	NA
80	Rubin <i>et al.</i> (1985) [80]	Etretinate	USA	Case report	NA	4 months	1	44 years	Male	NA
81	Ruggiero <i>et al.</i> (2022) [81]	Risankizumab	Italy	Case report	NA	24 weeks	1	38 years	Male	NA
82	Saeki <i>et al.</i> (2015) [82]	Ixekizumab	Japan	Multicentre, single-arm, open-label study (NCT01624233)	52 weeks	NA	5	Mean ± SD: 48.2 ± 15.6 years	Male: 2 Female: 3	Japanese
83	Saeki <i>et al.</i> (2017) [83]	Ixekizumab	Japan	Multicentre, single-arm, open-label study (NCT01624233)	52 weeks	NA	5	Mean ± SD: 48.2 ± 15.6 years	Male: 2 Female: 3	Japanese
84	Samotij <i>et al.</i> (2021) [84]	Acitretin; Infliximab;	Poland	Case report	NA	NA	1	72 years	Female	NA
85	Sano <i>et al.</i> (2018) [85]	Guselkumab	Japan	Single-arm, open-label, multicentre study	52 weeks	NA	10	Mean (SD): 42.6 (8.97) years	Male: 6 Female: 4	NA
86	Skrabl-Baumgartner <i>et al.</i> (2015) [86]	Methotrexate; Infliximab	Austria	Case report	NA	NA	1	8 years	Male	NA
87	Storan <i>et al.</i> (2016) [87]	Ustekinumab	Ireland	Case report	NA	2.5 years	1	90 years	Female	NA
88	Sugiura <i>et al.</i> (2015) [88]	Infliximab	Japan	Case series	NA	NA	4	Case 1: 39 years Case 2: 36 years Case 3: 29 years Case 4: 65 years	Female: 2 Male: 2	Japanese
89	Suzuki <i>et al.</i> (2012) [89]	GMA	Japan	Case series	NA	NA	3	Case 1: 65 years Case 2: 36 years Case 3: 71 years	Female: 1 Male: 2	NA
90	Takahashi <i>et al.</i> (2015) [90]	Cyclosporine	Japan	Case report	NA	NA	1	3 months	Female	NA
91	Tariq <i>et al.</i> (2022) [91]	Secukinumab	Pakistan	Prospective study	5 months	NA	2	NA	NA	NA

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
92	Torii <i>et al.</i> (2011) [92]	Infliximab	Japan	Multicentre, open-label, uncontrolled study	62 weeks	NA	7	Mean $\pm$ SD: 41.7 $\pm$ 17.3 years	Male: 2 Female: 5	Japanese
93	Torii <i>et al.</i> (2017) [93]	Infliximab	Japan	Multicentre, single-arm, open-label trial	40 weeks	NA	7	Mean (SD): 36.7 (9.7) years	Male: 4 Female: 3	Japanese
94	Trent & Kerdel (2004) [94]	Infliximab	USA	Retrospective study	NA	NA	4	Average (range): 40 years (17–52)	Female: 4	NA
95	Uçmak <i>et al.</i> (2014) [95]	Acitretin	Turkey	Case series	NA	NA	2	Case 1: 2 years Case 2: 3 years	Female: 1 Male: 1	NA
96	Verma <i>et al.</i> (2012) [96]	Zinc acetate	India	Case report	NA	NA	1	67 years	Female	NA
97	Viguier <i>et al.</i> (2012) [97]	Infliximab; Adalimumab; Etanercept	France	Retrospective chart review	NA	NA	11	NA	Female: 8 Male: 3	NA
98	Warren <i>et al.</i> (2023) [98]	Imsidolimab	UK and Poland	Open-label, single-arm, multiple-dose study (GALLOP; NCT03619902)	12 weeks	12 weeks	8	Mean (SD): 51.3 (14.9)/Years since diagnosis, mean (SD): 4.0 (6.5)	Female: 4 Male: 4	White: 8 Asian: 1
99	Weishaupt <i>et al.</i> (2007) [99]	Infliximab	Germany	Case report	NA	NA	1	24 years/7 months	Female	NA
100	Wilsmann-Theis <i>et al.</i> (2018) [100]	Secukinumab; Ixekizumab	Germany	Case series	NA	NA	7	Mean (SD): 56.9 ($\pm$ 13.9) years	Female: 5 Male: 2	NA
101	Wollina <i>et al.</i> (2001) [101]	Cyclosporine	Germany	Case report	NA	15 months	1	17 years	Male	NA
102	Wolska <i>et al.</i> (1983) [102]	Etretinate	Poland	Randomized, double-blind study	NA	Up to 3 years	N=10 (4 in double-blind study; 6 additional, subsequent cases)	NA	NA	NA
103	Wolska <i>et al.</i> (1985) [103]	Etretinate	Poland	Case series	NA	5 years	18	24–67 years	Male: 9 Female: 9	NA
104	Wu <i>et al.</i> (2017) [104]	Topical steroids	China	Case series	Patients treated	NA	82	Age of onset With history of	Male: 39	Chinese

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
					between July 2010 and July 2016			psoriasis vulgaris: 32.7 ± 18.0 years Without history of psoriasis vulgaris: 25.5 ± 21.2 years	Female: 43	
105	Wu <i>et al.</i> (2022) [105]	Secukinumab	China	Prospective study	May 2020–September 2021	NA	13	5–90 years	Male: 9 Female: 4	NA
106	Xue <i>et al.</i> (2022) [106]	Secukinumab	China	Case study	NA	8 months	1	27 years	Female	NA
107	Yamanaka <i>et al.</i> (2022) [107]	Risankizumab	Japan	Randomized, open-label, multicentre study (NCT03022045)	160 weeks	20 weeks after last administration of study drug	8	Mean (SD): 57.5 (18.7) years	Male: 6 Female: 2	Japanese
108	Yamasaki <i>et al.</i> (2017) [108]	Brodalumab	Japan	Open-label, multicentre study (NCT01782937)	52 weeks	NA	12	Mean (± SD) 43.1 (± 16.8) years	Male: 3 Female: 9	Japanese
109	Yang <i>et al.</i> (2020) [109]	Acitretin	China	Case series	NA	1-month	24	Mean ± SD: 6.92 ± 3.48 years	Male: 10 Female: 14	NA
110	Yang <i>et al.</i> (2022) [110]	Acitretin; NB-UVB	China	Case report	NA	1 year	1	14 years	Female	Chinese
111	Youshou <i>et al.</i> (1994) [111]	Hydroxyurea; PUVA; Dapsone; Thiamphenicol; Etretinate; Prednisone; Lei-Gong-teng (Chinese herb) + dapsone + erythromycin/tetracycline	China	Case series	NA	NA	78	NA	Male: 51 Female: 27	NA
112	Yu <i>et al.</i> (2020) [112]	Acitretin; Glycyrrhizin	China	Retrospective case series	NA	12 months	9	46.0 ± 16.2 years	Male: 5 Female: 4	Chinese

No.	Study reference	Treatment	Country	Study type	Study duration	Follow-up duration	GPP population/ sample size (N)	Age/age at diagnosis	Gender	Ethnicity (%)
113	Zachariae <i>et al.</i> (1982) [113]	Colchicine	Denmark	Case series	NA	NA	4	12–74 years	Male: 2 Female: 2	NA
114	Zangrilli <i>et al.</i> (2008) [114]	Adalimumab	Italy	Case report	NA	72 weeks	1	50 years	Female	NA
111 5	Zheng <i>et al.</i> (2021) [115]	Corticosteroids ; Methotrexate; Acitretin; Infliximab; Adalimumab; Etanercept	China	Retrospective study	Patients treated between 2014 to 2019	NA	110	34.1 ± 18.1 years	Male: 80 Female: 30	Chinese
116	Zheng <i>et al.</i> (2022) [116]	Ixekizumab	China	Prospective study	≥16 weeks	52 weeks	1	11 years/8 years	Male	Chinese
117	Zhu <i>et al.</i> (2018) [117]	Acitretin	China	Retrospective cohort study	Patients treated between 2012 and 2014	2–4 years	61 with GPP: HOMG: n=25 HEMG: n=7 NMG: n=29	Mean (SD) years: HOMG: 22.44 ± 16.90 HEMG: 26.57 ± 16.05 NMG: 35.45 ± 20.15	HOMG: male/female=13/12 HEMG: male/female=4/3 NMG: male/female=16/13	NA
118	Zhu <i>et al.</i> (2021) [118]	Acitretin; Secukinumab	China	Case report	4 months	11 months	1	3 years	Female	Chinese

CyA, cyclosporine; GMA, granulocyte and monocyte adsorption; GPP, generalized pustular psoriasis; HEMG, heterozygous mutation group; HOMG, homozygous mutation group; IQR, interquartile range; MTX, methotrexate; NA, not available; NMG, non-mutation group; PUVA, psoralen and UV-A; SD, standard deviation

Table S4: Criteria for assigning evidence level

Level	Description
A	Strong research-based evidence, e.g., two or more randomized controlled trials or a systematic review with clearly positive results
B	Moderate evidence, e.g., one randomized controlled trial or multiple adequate studies
C	Limited research-based evidence, e.g., controlled prospective studies
D	No evidence, e.g., retrospective studies or consensus reached in the absence of good quality evidence

Table S5: Levels of evidence by treatment

Treatment	Citation	Study type	Level of evidence*
Biologic therapies			
Spesolimab	Bachelez <i>et al.</i> (2019) [5]	Multicentre, single-arm, open-label, proof-of-concept study (NCT02978690)	A
	Bachelez <i>et al.</i> (2021) [6] Navarini <i>et al.</i> (2023) [65] Burden <i>et al.</i> (2023) [8] Morita <i>et al.</i> (2023) [119]	Multicentre, randomized, double-blind, placebo-controlled trial (Effisayil™ 1; NCT03782792)	
	Morita <i>et al.</i> (2023) [63]	Multicentre, randomized, double-blind, placebo-controlled trial (Effisayil™ 2; NCT04399837)	
Imsidolimab	Warren <i>et al.</i> (2023) [98]	Open-label, single-arm, multiple-dose study (GALLOP; NCT03619902)	C
Certolizumab	Okubo <i>et al.</i> (2022) [70]	Exploratory analysis of open-label randomized trial	C
Infliximab	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	C
	Poulalhon <i>et al.</i> (2007) [75]	Prospective follow-up study	
	Torii <i>et al.</i> (2011) [92]	Multicentre, open-label, uncontrolled study	
	Torii <i>et al.</i> (2017) [93]	Multicentre, single-arm, open-label trial	
	Trent & Kerdel (2004) [94]	Retrospective study	
	Viguier <i>et al.</i> [97]	Retrospective chart review	
	Zheng <i>et al.</i> (2021) [115]	Retrospective study	
Adalimumab	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	C
	Morita <i>et al.</i> (2018) [60]	Multicentre, open-label, 52-week study (NCT02533375)	
	Viguier <i>et al.</i> (2012) [97]	Retrospective chart review	
	Zheng <i>et al.</i> (2021) [115]	Retrospective study	
Etanercept	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	D
	Viguier <i>et al.</i> (2012) [97]	Retrospective chart review	
	Zheng <i>et al.</i> (2021) [115]	Retrospective study	
Ixekizumab	Kromer <i>et al.</i> (2017) [45]	Non-interventional retrospective patient chart review	C
	Morita <i>et al.</i> (2022) [61]	Multicentre, open-label clinical trial (UNCOVER-J2; NCT03942042)	
	Okubo <i>et al.</i> (2019) [69]	Multicentre, single-arm, open-label study (UNCOVER-J; NCT01624233)	

	Saeki <i>et al.</i> (2015) [82] Saeki <i>et al.</i> (2017) [83]		
	Zheng <i>et al.</i> (2022) [116]	Prospective study	
Secukinumab	Imafuku <i>et al.</i> (2016) [37]	Interventional, multicentre, single-arm, open-label study (NCT01952015; JAPIC JapicCTI-132305)	C
	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	
	Miao <i>et al.</i> (2023) [55]	Retrospective study	
	Tariq <i>et al.</i> 2022 [91]	Prospective study	
	Wu <i>et al.</i> (2023) [105]	Prospective study	
Brodalumab	Yamasaki <i>et al.</i> (2017) [108]	Open-label, multicentre study (NCT01782937)	C
Guselkumab	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	C
	Sano <i>et al.</i> (2018) [85]	Single-arm, open-label, multicentre study	
Risankizumab	Yamanaka <i>et al.</i> (2023) [107]	Randomized, open-label, multicentre study (NCT03022045)	C
Gevokizumab	Mansouri <i>et al.</i> (2015) [53]	Patient cases from an open-label, expanded-access study	C
Ustekinumab	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	D
Non-biologic systemic therapies			
Etretinate	Ozawa <i>et al.</i> (1999) [72]	Retrospective multicentre study	B
	Wolska <i>et al.</i> (1983) [102]	Randomized, double-blind study	
Acitretin	Chen <i>et al.</i> (2018) [11]	Retrospective study and literature review	C
	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	
	Lau <i>et al.</i> (2017) [47]	Retrospective chart review	
	Lu <i>et al.</i> (2022) [52]	Prospective comparative study	
	Miao <i>et al.</i> (2023) [55]	Retrospective study	
	Zheng <i>et al.</i> (2021) [115]	Retrospective study	
	Zhu <i>et al.</i> (2018) [117]	Retrospective cohort study	
Hydroxyurea	Das <i>et al.</i> (2013) [18]	Prospective, non-randomized study	C
	Juanqin <i>et al.</i> (1998) [40]	Retrospective analysis	
Methotrexate	Collins <i>et al.</i> (1992) [16]	Retrospective review	D

	Haustein & Rytter (2000) [32]	26-year retrospective single-centre study	
	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	
	Ozawa <i>et al.</i> (1999) [72]	Retrospective study	
	Zheng <i>et al.</i> (2021) [115]	Retrospective study	
Cyclosporine	Cohen Barak <i>et al.</i> (2015) [15]	Retrospective chart review	D
	Choon <i>et al.</i> (2014) [14]	Retrospective chart review	
	Dogra <i>et al.</i> (2017) [20]	Retrospective chart review	
	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	
Corticosteroids	Miyachi <i>et al.</i> (2022) [57]	Retrospective cohort study	D
	Zheng <i>et al.</i> (2021) [115]	Retrospective study	
Fumaric acid ester	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	D
Apremilast	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	D
Other therapies			
GMA	Ikeda <i>et al.</i> (2013) [36]	Single-arm, unblinded study	C
PUVA	Braun-Falco <i>et al.</i> (1987) [7]	Retrospective case series	D
	Kromer <i>et al.</i> (2021) [45]	Non-interventional retrospective patient chart review	
	Ozawa <i>et al.</i> (1999) [72]	Retrospective, multicentre study	
Glycyrrhizin	Yu <i>et al.</i> (2020) [112]	Retrospective case series	D
Dapsone	Juanqin <i>et al.</i> (1998) [40]	Retrospective analysis	D
Thiamphenicol	Juanqin <i>et al.</i> (1998) [40]	Retrospective analysis	D

*Level of evidence definitions are provided in Table S4

GMA, granulocyte and monocyte adsorption; PUVA, psoralen and UV-A

Figure S1: Levels of evidence available for non-biologic systemic therapies

Treatment	Approved for use in GPP	No. of GPP patients in study (range)	Population type*	Efficacy	Safety	PRO/QoL	Level of evidence†	
Etretinate	-	10–188		✓	✓	⊗		Retinoids
Acitretin	-	10–98		✓	✓	✓		
Hydroxyurea	-	6–30‡		✓	✓	⊗		Conventional immunosuppressant agents
Methotrexate	-	6–42**		✓	✓	⊗		
Cyclosporine	-	1–17**		✓	✓	⊗		Calcineurin inhibitor
Corticosteroids	-	8–274		✓	✓	⊗		Corticosteroids
Fumaric acid ester	-	19**		✓	✓	⊗		Fumarates
Apremilast	-	2**		✓	✓	⊗		PDE-4 inhibitor

 Adults
  Children
  Relevant outcomes reported
  No relevant outcomes reported

*Where patient age was not specified for the relevant treatment patients are assumed to be adult

†Level of evidence definitions are provided in Table S4

‡ 30 patients included in the study, the number receiving hydroxyurea was not specified

**Study specified treatment courses rather than patient numbers

GPP, generalized pustular psoriasis; PRO, patient-reported outcome; QoL, quality of life

*Where patient age was not specified for the relevant treatment patients are assumed to be adult

†Level of evidence definitions are provided in Table S4

‡ 30 patients included in the study, the number receiving hydroxyurea was not specified

**Study specified treatment courses rather than patient numbers

Figure S2: Levels of evidence available for other therapies

Treatment	Approved for use in GPP	No. of GPP patients in study (range)	Population type*	Efficacy	Safety	PRO/QoL	Level of evidence†	
GMA	-	15						Apheresis
PUVA	-	1–89						Phototherapy
Glycyrrhizin	-	9						Other
Dapsone	-	26						Antibiotics
Thiamphenicol	-	2						

 Adults
  Children
  Relevant outcomes reported
  No relevant outcomes reported

GMA, granulocyte and monocyte adsorption; GPP, generalized pustular psoriasis; PRO, patient-reported outcome; PUVA, psoralen and UV-A; QoL, quality of life

*Where patient age was not specified for the relevant treatment patients are assumed to be adult

†Level of evidence definitions are provided in Table S4

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