Clinical outcomes and response of patients applying topical therapy for pyoderma gangrenosum: A prospective cohort study

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Background: Pyoderma gangrenosum (PG) is an uncommon dermatosis with a limited evidence base for treatment.

Objective: We sought to estimate the effectiveness of topical therapies in the treatment of patients with PG.

Methods: This was a prospective cohort study of UK secondary care patients with a clinical diagnosis of PG that was suitable for topical treatment (recruited between July 2009 and June 2012). Participants received topical therapy after normal clinical practice (primarily topical corticosteroids [classes I-III] and tacrolimus 0.03% or 0.1%). The primary outcome was speed of healing at 6 weeks. Secondary outcomes included the following: proportion healed by 6 months; time to healing; global assessment; inflammation; pain; quality of life; treatment failure; and recurrence.

Results: Sixty-six patients (22-85 years of age) were enrolled. Clobetasol propionate 0.05% was the most commonly prescribed therapy. Overall, 28 of 66 (43.8%) ulcers healed by 6 months. The median time to healing was 145 days (95% confidence interval, 96 days to ∞). Initial ulcer size was a significant predictor of time to healing (hazard ratio, 0.94 [95% confidence interval, 0.88-1.00); $P = .043$). Four patients (15%) had a recurrence.

Limitations: Our study did not include a randomized comparator.

Conclusion: Topical therapy is potentially an effective first-line treatment for PG that avoids the possible side effects associated with systemic therapy. It remains unclear whether more severe disease will respond adequately to topical therapy alone. (J Am Acad Dermatol 2016;75:940-9.)

Key words: cohort; corticosteroid; pyoderma gangrenosum; side effects; tacrolimus; topical therapy.

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Conflicts of interest: None declared.

This study was conducted as part of a randomized controlled trial of systemic treatments for pyoderma gangrenosum (Controlled-Trials.com ISRCTN35898459 [registered April 20, 2009]). Ethics and regulatory approvals were obtained (ethics approval, 09/H0903/5; Medicines and Healthcare Products Regulatory Agency approval, 19162/0213/001).

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Pyoderma gangrenosum (PG) is an uncommon, painful ulcerative inflammatory dermatosis that is associated with considerable morbidity[1,2] and a reported 3-fold increased risk of death.[3]

The most commonly prescribed treatments for patients with PG are systemic therapies (eg, prednisolone, cyclosporine, intravenous immunoglobulin, or biologic therapies). Nevertheless, topical treatments (eg, corticosteroids and calcineurin inhibitors) have also been recommended for localized disease[4,5] and may be a useful first-line therapy for some patients.

We conducted a multicenter prospective cohort study to investigate the efficacy of topical therapy as a first-line treatment for PG. This cohort study was conducted alongside a randomized controlled trial (RCT) of systemic treatments for PG (ie, the *S*tudy of *T*reatments f*O*r *P*yoderma *GA*ngrenosum *P*atients [STOP GAP]), in which oral prednisolone was compared to cyclosporine.[6] Our objective was to provide prospectively collected estimates of treatment response for patients receiving topical therapy for PG.

CAPSULE SUMMARY

- Pyoderma gangrenosum is a painful ulcerating disease. The current evidence base for treatment is limited.
- In a large prospective study of topical treatments, 44% of patients were healed by 6 months. Ulcer size was a predictor of healing, and 15% of patients with pyoderma gangrenosum had a recurrence.
- Clobetasol propionate 0.05% is a potentially useful first-line therapy for patients with pyoderma gangrenosum, particularly for patients with small lesions.

METHODS

Ethics and regulatory approvals were obtained and participants gave written informed consent. The Independent Trial Steering Committee and Independent Data Monitoring Committee provided oversight as part of the STOP GAP group.

Study design

This was a prospective cohort study of patients with a clinical diagnosis of PG for whom topical therapy was indicated. Patients with more severe PG (ie, requiring systemic therapy) were enrolled into a parallel RCT[6] but were eligible for inclusion in the topical therapy cohort study if systemic therapy was contraindicated or if the patient preferred to receive topical treatment. Participants were enrolled for ≤6 months or until the target PG ulcer had healed. Medications were prescribed as per local practice at the recruiting hospital.

Research questions

This study sought to answer the following 4 questions:

1. What is the typical treatment response in patients for whom topical therapy is indicated?
2. What proportion of participants require escalation of treatment to systemic medication?
3. What is the impact of PG on patient-reported quality of life?
4. What factors predict treatment response?

Participants

Recruitment took place in 28 secondary care hospitals throughout the United Kingdom. Participants were identified from dermatology, rheumatology, gastroenterology, and general medicine clinics.

Participants were ≥18 years of age and had a clinical diagnosis of PG that was confirmed by the recruiting dermatologist—with a biopsy specimen obtained to exclude alternative etiologies if clinically indicated—and ≥1 measureable ulcer. The decision whether to treat with topical therapy or not was based on the views of the dermatologist in discussion with patients.

Patients were excluded if they had pustular or granulomatous PG variants, because they may have responded differently to therapy and because measurement of a single ulcer was not possible. Patients were also excluded if they had received oral prednisolone, cyclosporine, or intravenous immunoglobulin for the treatment of PG in the previous month or were participating in another clinical trial.

Ongoing treatment with systemic therapies for the management of underlying comorbidities (eg, rheumatoid arthritis) was permitted.

Interventions

Patients received topically applied interventions for the treatment of PG. The dermatologist was free to prescribe whichever therapy and dosage regimen they preferred according to local practice. In the United Kingdom, it was normal practice to apply topical interventions to the inflammatory edge of the ulcer. Systemic therapies for the treatment of PG were prohibited but were continued if they were taken for other conditions.

Abbreviations used:

DLQI:	Dermatology Life Quality Index
EQ-5D-3L:	EuroQol 5 dimensions, 3 levels
PG:	pyoderma gangrenosum
RCT:	randomized controlled trial
TNF:	tumor necrosis factor

Assessments and outcomes

Study visits took place at 2 weeks, 6 weeks, and 6 months—or at the time of healing, if sooner. Other unscheduled consultations took place as per normal practice.

A target lesion was used for outcome assessment. Lesion size was captured by the treating dermatologist based on maximal longitudinal length and maximum perpendicular length, converted to area by the formula (length × width × 0.785), which approximates an ellipse.

Outcomes included the following measures: 1) speed of healing at 6 weeks (primary outcome in-line with RCT primary outcome); 2) proportion healed by 6 months; 3) time to healing; 4) global assessment of improvement at 6 weeks and final visit; 5) inflammation assessment at 6 weeks and final visit[7]; 6) pain in the first 6 weeks (scored daily 0-4); and 7) quality of life measurements (ie, the European Quality of Life 5 dimensions, 3 levels[8] [EQ-5D-3L] and the Dermatology Life Quality Index[9] [DLQI]).

Healing was defined as the point at which dressings were no longer required. This was reported by the participants, and a clinic visit was arranged to confirm healing as soon as possible thereafter. In cases where the date on which dressings were stopped was unavailable, healing was assumed to have taken place on the day that the ulcer was confirmed as healed by the recruiting dermatologist. Pain scores and use of dressings were collected using daily diaries.

Measures taken to control bias

This was an open study, with no control group. In order to mitigate the risk of bias, consecutive participants were enrolled into the study and followed-up prospectively. Outcomes were assessed using standard methods, and clinicians' and patients' views were compared where appropriate. Every effort was made to maintain follow-up of all participants.

Sample size

This was a pragmatic cohort study. No formal sample size calculation was performed, because this was a descriptive study without formal between-treatment comparisons.

Statistical analysis

The primary analysis included all participants who received ≥1 topical medication and had available data at both the baseline and the 6-week visit. Predefined subgroups were as follows: 1) participants who received clobetasol propionate 0.05% and 2) participants who received a topical calcineurin inhibitor (ie, tacrolimus or pimecrolimus).

Data are presented descriptively, and data relating to participants of the STOP GAP RCT are included alongside those of the topical therapy cohort, but no formal comparisons have been made.

If a participant received >1 topical medication, they were included in all relevant study populations. Participants who withdrew because of a lack of treatment response or those who started a systemic medication during the study period were classified as treatment failures for the topical medication.

Exploratory analyses adjusting for lesion size at baseline, the presence of underlying autoimmune disease, age, weight, sex, and size of recruiting center were conducted to determine possible factors associated with treatment response. Linear regression models were used for continuous outcomes, logistic regression for binary outcomes, and Cox proportional hazards for time to event outcomes.

RESULTS

Participants and treatment allocation

Recruitment took place between July 2009 and June 2012. In total, 67 participants were enrolled in the study, but 1 was subsequently excluded from the analysis for having received oral prednisolone for PG (Fig 1).

Forty-nine (74.2%) participants received clobetasol propionate 0.05% (Dermovate; GlaxoSmithKline, London, UK); 10 (15.2%) received tacrolimus 0.03% or 0.1% (Protopic; Astellas Pharma, Northbroook, IL); and 8 received other topical interventions, including other topical corticosteroids (n = 6), fludroxycortide impregnated tape (n = 1; Haelan Tape [Typharm, Norwich, UK]), and lymecycline (n = 1; Tetralysal 300 [Galderma, Watford, UK]). One participant received both clobetasol propionate and tacrolimus and was therefore included in both subgroups. Five participants in the clobetasol propionate group were taking concurrent antiinflammatory/immune modifying medications for the treatment of other conditions, including azathioprine (n = 2), tetracyclines (n = 2), and anti—tumor necrosis factor (n = 1).

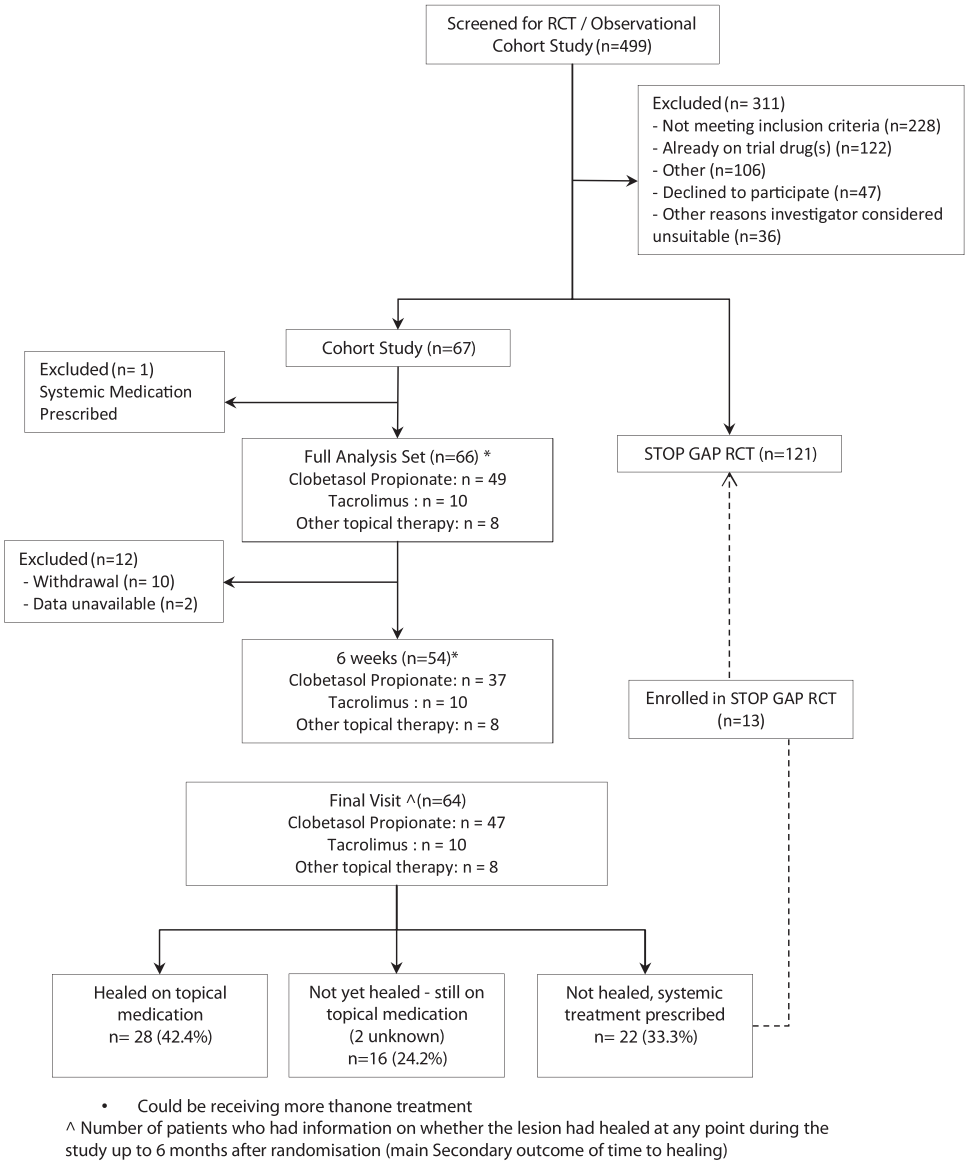

Fig 1. Participant flow.

The reason for choosing systemic or topical therapy (and therefore eligibility for the cohort study or the RCT) were as follows: 1) topical treatment failure (for those opting for systemic therapy; n = 47); 2) features of the disease (n = 43); and 3) patient preference (n = 6).

The details of both demographic and baseline characteristics are summarized in Table I. The majority of participants were identified through dermatology services (n = 47; 71.2%); others were identified from gastroenterology (n = 7; 10.6%), rheumatology (n = 1; 1.5%), general medicine (n = 2; 3%), and other sources (n = 9; 13.6%).

Baseline characteristics for participants in the cohort study were broadly similar to those enrolled in the parallel RCT, with the exception that the mean lesion size was smaller (4.7 cm^2 vs 9 cm^2), the mean number of ulcers was lower (1.6 vs 2.4), and fewer participants had had PG previously (18% vs 31%; Table I).

Adherence to medication

Only 12 of 66 (18.2%) participants provided data on adherence to their prescribed treatments at the end of the study. Nevertheless, the levels of treatment response achieved would suggest that the participants were using their medications broadly as prescribed. Nine participants in the clobetasol propionate group used systemic medication for comorbidities during the study (azathioprine

Table I. Baseline characteristics of participants in the Study of Treatments for Pyoderma Gangrenosum Patients randomized controlled trial and topical therapies cohort study

			Cohort subgroups	
	RCT (n = 112)	Cohort study (n = 66)	Clobetasol propionate (n = 49)	Tacrolimus (n = 10)
Demographics				
Mean age, y (SD)	54.4 (16.3)	57.3 (17.3)	57.5 (17.9)	53.0 (13.0)
Sex, n (%)				
Female	73 (65.2)	44 (66.7)	34 (69.4)	6 (60.0)
Ethnicity, n (%)				
White	108 (96.4)	64 (97.0)	47 (95.9)	10 (100.0)
Mean weight, kg (SD)	90.7 (25.8)	80.4 (20.3)	77.8 (17.2)	86.2 (29.7)
Medical history				
Underlying comorbidities, n (%)				
Crohn's disease	8 (7.1)	6 (9.1)	2 (4.1)	2 (20.0)
Ulcerative colitis	15 (13.4)	8 (12.1)	7 (14.3)	1 (10.0)
Rheumatoid arthritis	8 (7.1)	2 (3.0)	2 (4.1)	0 (0.0)
Other inflammatory arthritis	6 (5.4)	5 (7.6)	3 (6.1)	2 (20.0)
Monoclonal gammopathy	0 (0.0)	1 (1.5)	1 (2.0)	0 (0.0)
Myeloma	0 (0.0)	1 (1.5)	1 (2.0)	0 (0.0)
Hematologic malignancy	0 (0.0)	1 (1.5)	1 (2.0)	0 (0.0)
Other malignancy	4 (3.6)	6 (9.1)	5 (10.2)	0 (0.0)
Diabetes	13 (11.6)	7 (10.6)	5 (10.2)	2 (20.0)
Renal impairment	2 (1.8)	3 (4.5)	2 (4.1)	0 (0.0)
Epilepsy	1 (0.9)	1 (1.5)	1 (2.0)	0 (0.0)
Characteristics of PG				
Type of PG, n (%)				
Classical	97 (86.6)	55 (83.3)	43 (87.8)	9 (90.0)
Cribriform	6 (5.4)	1 (1.5)	0 (0.0)	0 (0.0)
Peristomal	4 (3.6)	6 (9.1)	3 (6.1)	1 (10.0)
Bullous	1 (0.9)	2 (3.0)	2 (4.1)	0 (0.0)
Unsure	4 (3.6)	2 (3.0)	1 (2.0)	0 (0.0)
Previous episode of PG				
Yes, n (%)	31 (27.7)	18 (27.3)	12 (24.5)	3 (30.0)
Area of target lesion, cm^2				
n	112	65	48	10
Median (Q1; Q3)	9.0 (3.2, 24.4)	4.7 (2.4; 11.0)	4.4 (1.6; 10.5)	6.8 (2.8, 11.0)
Location of lesion: n (%)				
Upper limb	3 (2.7)	7 (10.6)	6 (12.2)	0 (0.0)
Lower limb	75 (67.0)	39 (59.1)	29 (59.2)	6 (60.0)
Other	34 (30.4)	20 (30.3)	14 (28.6)	4 (40.0)
No. of lesions	n = 110	n = 65	n = 48	n = 10
Mean (SD)	2.4 (2.1)	1.6 (1.2)	1.6 (1.1)	1.8 (1.1)
n	112	66	49	10
Erythema, n (%)				
None	6 (5.4)	0 (0.0)	0 (0.0)	0 (0.0)
Slight	5 (4.5)	9 (13.6)	10 (20.4)	1 (10.0)
Moderate	36 (32.1)	10 (15.2)	15 (30.6)	8 (80.0)
Severe	39 (34.8)	32 (48.5)	16 (32.7)	1 (10.0)
Very severe	26 (23.2)	15 (22.7)	8 (16.3)	0 (0.0)
n	112	65	49	10
Border elevation, n (%)				
None	5 (4.5)	14 (21.5)	6 (12.2)	0 (0.0)
Slight	53 (47.3)	23 (35.4)	24 (49.0)	1 (10.0)
Moderate	36 (32.1)	23 (35.4)	17 (34.7)	8 (80.0)
Severe	13 (11.6)	4 (6.2)	1 (2.0)	1 (10.0)
Very severe	5 (4.5)	1 (1.5)	1 (2.0)	0 (0.0)

Continued

Table I. Cont'd

	RCT (n = 112)	Cohort study (n = 66)	Cohort subgroups	
			Clobetasol propionate (n = 49)	Tacrolimus (n = 10)
Exudate, n (%)				
n	112	66	49	10
None	4 (3.6)	8 (12.1)	9 (18.4)	0 (0.0)
Slight	16 (14.3)	13 (19.7)	12 (24.5)	1 (10.0)
Moderate	59 (52.7)	27 (40.9)	22 (44.9)	8 (80.0)
Severe	15 (13.4)	11 (16.7)	4 (8.2)	1 (10.0)
Very severe	18 (16.1)	7 (10.6)	2 (4.1)	0 (0.0)

PG, Pyoderma gangrenosum; *RCT*, randomized controlled trial; *SD*, standard deviation.

[n = 2], anti—tumor necrosis factor [n = 1], and tetracyclines [n = 2]).

Treatment response

Details of the clinical outcomes are summarized in Table II.

The mean speed of healing was -0.1 cm^2 per day (standard deviation [SD], 0.3 cm^2). This is approximately half that observed in the RCT patients receiving systemic therapy, but the method of assessment was different for the 2 studies (eg, physical measurements by a clinician vs planimetry from digital images), and so direct comparison is difficult. The mean change from baseline in area of the lesion at the final visit was -4.2 cm^2 (SD, 11.5 cm^2), with similar changes reported in the clobetasol and tacrolimus subgroups (-4.0 [SD, 11.9 cm^2] and -3.9 [SD, 6.0], respectively).

Overall, 28 (43.8%) participants healed on topical therapy alone within the 6-month study period. Twenty-two (33.3%) required systemic therapy, and of these 13 (59.1%) went on to be enrolled into the RCT (Fig 1). For those that entered the RCT, 8 (61.5%) healed by 6 months, with 3 of the 13 (23.1%) healing by 6 weeks.

Ulcers healed in a median duration of 145 days (95% confidence interval [CI], 96 days to ∞; Fig 2; Table II). The Cox proportional hazards model suggested that the size of initial lesion was an important predictive factor in determining time to healing (hazard ratio [HR], 0.94 [95% CI, 0.88-1.00]; P = .043). The presence of an underlying autoimmune disease was not predictive (HR, 0.90 [95% CI, 0.41-1.95]; P = .786).

Global disease severity as reported by both clinicians and patients is summarized in Figs 3 and 4. Self-reported pain gradually reduced during the first 6 weeks of treatment, and quality of life scores improved for both disease-specific (DLQI) and general health status (EQ-5D-3L) questionnaires (Table II). No covariates were predictive of the scores at final visit for any of these outcomes other than baseline scores for DLQI and EQ-5D (DLQI estimate, -0.47 [95% CI, -0.77 to -0.17]; P = .003; EQ-5D visual analog scale estimate, -0.40 [95% CI, -0.65 to -0.15]; P = .003).

Recurrence

Of the 28 participants with a healed ulcer, 27 had recurrence data available (minimum follow-up from time of healing, 5.5 months; maximum follow-up, 37.2 months). Overall, 4 of 27 (14.8%) participants had a recurrence after their initial episode.

DISCUSSION

Main findings

This prospective cohort study of patients receiving topical therapy for the treatment of PG suggests that many patients with limited PG can be managed effectively with topical therapy alone. For almost half of the participants, healing was achieved within the 6-month study window, and most of these patients healed within 2 months. This is similar to the proportions healed in the STOP GAP RCT, where again roughly half of the ulcers had healed by 6 months. Care should be taken when comparing healing rates between the RCT and the cohort study because participants in the RCT had more severe disease, as shown by the increased number of ulcers, larger ulcer size at baseline, and greater impact on quality of life. Of those who failed to heal while undergoing topical therapy, one third subsequently received systemic therapy—suggesting that not all patients can be adequately treated with topical therapy alone.

The most important predictor of time to healing was size of the ulcer at presentation. This is consistent with previous findings.[10]

Given the increased mortality risk for patients with PG compared to patients with inflammatory bowel disease and apparently healthy individuals,[3] it is important to evaluate the role of topical therapies

Table II. Treatment response (randomized controlled trial participants and cohort participants)

			Cohort subgroups	
	RCT participants (n = 112)	All cohort participants (n = 66)	Clobetasol propionate (n = 49)	Tacrolimus (n = 10)
Speed of healing	n = 108	n = 54	n = 37	n = 10
Mean cm^2/day (SD)	-0.2 (0.8)	-0.1 (0.3)	-0.1 (0.2)	-0.1 (0.1)
Percent healed by final visit (≤6 months)	n = 112	n = 64	n = 47	n = 10
n (%)	53 (47.3)	28 (43.8)	20 (42.6)	5 (50.0)
Time to healing (days)	n = 112	n = 64	n = 47	n = 10
Median (95% CI)	169 days (113; ∞)	145 days (96; ∞)	136 days (46; ∞)	161 days (13; ∞)
Area of lesion (cm^2)*	n = 108	n = 55	n = 38	n = 10
Median baseline (Q1; Q3)	9.0 (3.2; 24.8)	5.9 (1.8; 13.6)	6.4 (1.6; 14.0)	6.8 (2.8; 11.0)
Median final visit (Q1; Q3)	0.0 (0.0; 8.1)	0.0 (0.0; 9.0)	0.0 (0.0; 9.0)	1.2 (0.0; 3.5)
Mean change from baseline at final visit (SD)	-9.1 (51.1)	-4.2 (11.5)	-4.0 (11.9)	-3.9 (6.0)
Median change (Q1; Q3)	-5.0 (-15.8; -1.5)	-3.4 (-8.7; -0.3)	-1.7 (-7.4; -0.2)	-3.3 (-8.5; -0.3)
Resolution of inflammation†	n = 107	n = 54	n = 49	n = 10
6 weeks, n (%)	11 (10.3)	8 (14.8)	6 (16.2)	0 (0.0)
	n = 108	n = 55	n = 38	n = 10
Final visit, n (%)	20 (18.5)	12 (21.8)	10 (26.3)	1 (10.0)
AUC for weekly pain in first 6 weeks (range, 0-20 weeks); high score = worse	n = 77	n = 37	n = 24	n = 7
Mean (SD)	7.6 (5.2)	5.4 (5.2)	5.6 (5.2)	7.3 (6.3)
DLQI (range, 0-30); high score = worse	n = 111	n = 66	n = 49	n = 10
Mean baseline (SD)	11.7 (8.2)	8.4 (6.0)	8.5 (6.0)	8.8 (4.6)
	n = 66	n = 49	n = 32	n = 10
Mean final (SD)	5.5 (7.2)	6.2 (6.8)	7.6 (7.5)	4.6 (5.4)
EQ-5D* (range, 0-1); high score = better	n = 108	n = 66	n = 49	n = 10
Mean baseline (SD)	0.48 (0.4)	0.59 (0.3)	0.60 (0.3)	0.51 (0.3)
	n = 69	n = 51	n = 34	n = 10
Mean final visit (SD)	0.71 (0.4)	0.69 (0.3)	0.65 (0.3)	0.73 (0.3)
EQ-5D VAS (range, 0-100); high score = better	n = 110	n = 66	n = 49	n = 10
Mean baseline (SD)	62.0 (21.8)	67.0 (20.4)	65.6 (21.9)	64.4 (15.9)
	n = 70	n = 50	n = 33	n = 10
Mean final visit (SD)	72.1 (21.2)	73.6 (20.5)	69.3 (22.2)	78.2 (13.1)
Recurrence (in those who had healed by 6 months)‡	n = 52	n = 27	n = 19	n = 5
n (%)	15 (28.8)	4 (14.8)	4 (21.1)	0 (0.0)

AUC, Area under the curve; *CI*, confidence interval; *DLQI*, Dermatology Life Quality Index; *EQ-5D VAS*, European Quality of Life − 5 dimensions visual analog scale; *SD*, standard deviation.

*Captures health utility based on responses (0-2) for mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.

†Assessed by clinician, resolution of inflammation defined as erythema and border elevation reduced to "none" (per Foss et al[7]).

‡Minimum follow-up after healing: RCT (0-40.3 months); cohort (5.5-37.2 months), depending on when recruited.

for the management of PG. Similar concerns about increased mortality and morbidity in bullous pemphigoid patients (that could be partly caused by systemic therapies, such as prednisolone), led to an RCT by Joly et al,[11] who found that mortality was reduced in patients who were treated with potent topical steroids compared to those receiving systemic steroids.

The potential impact of PG on patients' quality of life is high. Baseline EQ-5D-3L scores of 0.59 (cohort study) and 0.48 (RCT) are comparable to patients with mild to severe heart failure, where EQ-5D-3L scores of 0.78 (SD, 0.18) to 0.51 (SD, 0.21), respectively, have been reported.[12] One of the objectives of this study was to maintain contact with potential trial participants in order to improve recruitment into the RCT. In this regard, the cohort study was extremely effective, and resulted in an additional 13 of 121 (11%) patients being enrolled in the RCT. For trials of rare conditions, where the evidence base is limited, the added complexities and expense of running a parallel study of this kind can often be warranted.[13]

Strengths and limitations

This multicenter study is much larger than any of the previously published prospective cohort studies of patients with PG.[4,5,14] Clinicians prescribed topical medication in line with local practice, but treatment

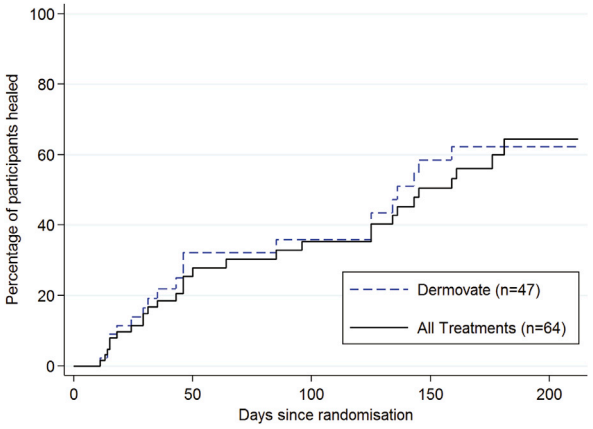

Fig 2. Kaplan–Meier plot of time to healing.

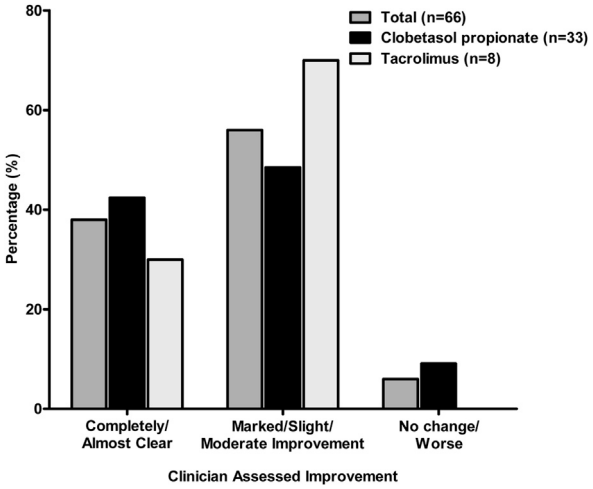

Fig 3. Global treatment response at final visit (clinician assessed).

allocations were not randomized. As a result, it is not possible to make a formal comparison of different topical treatments, such as corticosteroids versus tacrolimus. Data on subgroups of patients are presented for interest, but should be interpreted cautiously. Tacrolimus may be an effective treatment for PG, but further evaluation in comparison to topical corticosteroids is required. Little is known about the natural history of PG if left untreated. In the absence of a placebo control arm, it is not possible to say whether or not the lesions would have healed without intervention—although clinical experience would suggest that this is unlikely.

Generalizability

This was a pragmatic study that reflected current practice. For an uncommon condition such as PG, it was necessary to recruit across many hospitals, which aids the generalizabilty of the results. Nevertheless, this cohort of patients was recruited

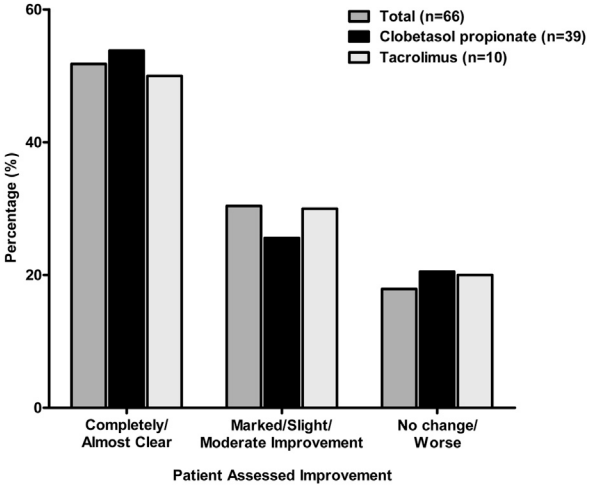

Fig 4. Global treatment response at final visit (patient assessed).

alongside an RCT of systemic treatments for PG, and this may have impacted the type of patients agreeing to take part. Patients with more severe disease were randomized into the RCT; those with milder or more localized disease entered the cohort study.

In conclusion, mild PG may be controlled effectively using topical agents without incurring the side effects associated with systemic treatments. The importance of ulcer size on presentation in determining treatment response and the relatively high recurrence rates are findings that will assist clinicians in optimizing the management of patients with PG, and in managing patients' expectations with regard to the potential effectiveness of treatments.

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