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Research Article

Effectiveness of Brodalumab on Scalp, Palmoplantar, and Genital Psoriasis: A Descriptive Pilot Study

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Introduction. Psoriasis of the scalp, genital areas, and palms and soles represents a treatment challenge in clinical practice. Randomized clinical trials and real-life studies investigating the efficacy of biological drugs in these sites are scarce. The present is a descriptive retrospective real-life study with the aim to evaluate the efficacy and safety of brodalumab in these difficult-to-treat areas. *Materials and Methods*. 158 psoriatic patients with scalp involvement, 69 with genital involvement, and 54 with palmoplantar involvement being treated with brodalumab were assessed at weeks 16, 28, and 48 using PSSI (Psoriasis Scalp Severity Index), sPGA-G (Physician Global Assessment of Genitalia), and ppPASI (Palmoplantar Psoriasis Area and Severity Index). *Results*. The achievement of relative PSSIs (75%, 90%, and 100%) was already observed in week 16. 86% achieved PSSI75, 80% PSSI90, and 75% PSSI100. The sPGA-g 0/1 was achieved by 83% of patients at week 16 and 100% at week 24 and 48. At week 16 ppPASI75, 90, and 100 were all reached by 76.9% of patients; at week 24, 84.6% of patients reached all relative ppPASI. *Conclusions*. Brodalumab proved to be effective and safe in the treatment of scalp, genital, and palmoplantar regions.

1. Introduction

The frequent psoriatic involvement of certain areas of the body such as the scalp (43%–65% of patients), palms and soles (12–16% of patients), and genital area (14–43% of patients) is associated with a greater reduction in quality of life and pruritus than other areas of the body [1–3]. These sites tend to be recalcitrant to conventional therapies and are predisposed to koebnerisation [1]. These areas are traditionally described as difficult-to-treat that often lead to therapeutic failure and drug switches [1]. Frequently, a difficult site involvement is related to another; for example, in patients with palmoplantar psoriasis, the risk of nail involvement is 91% higher [4]. Lesions are difficult to control with topical therapies due to insufficient penetration of active components and inadequate cosmetic characteristics of the vehicles used [5].

Recent work has shown that the involvement of sites such as the scalp and nails is associated with a higher risk of developing concomitant psoriatic arthritis [6], confirming the urgency of systemic treatment of these forms, even though they are not particularly extensive. Despite numerous scores proposed in the literature in the evaluation of these areas, such as Physician's Global Assessment of Genitalia (sPGA-G) for genital, Psoriasis Scalp Severity Index (PSSI) for the scalp, and Palmoplantar Psoriasis Area and Severity Index (ppPASI) for palmoplantar psoriasis, their diffusion and sharing are still scarce at clinical level [2]. Although numerous studies have demonstrated the efficacy of biological drugs in psoriasis patients, randomized studies are needed to better investigate the efficacy of these drugs in the scalp, extremities, and genital regions [1]. Brodalumab is a fully human IL-17 receptor A monoclonal antibody that has shown good efficacy in both registration and real-life

studies [7–9]. Efficacy data on hard-to-treat areas are currently scarce, limited to a few case series and post hoc analyses of registration trials [1].

2. Materials and Methods

We conducted a 48-week retrospective descriptive study with the objective to evaluate the safety and effectiveness of brodalumab on psoriatic patients with involvement of the scalp, genitals, and palmoplantar regions. We analyzed all patients treated with brodalumab at a dosage of 210 mg subcutaneously every 14 days (after a run-in period of injection once a week for three weeks) with retrievable medical records from January 2020 to June 2022, followed at the Dermatologic Clinic of the University of Turin. According to our national drug agency, patients must have a history of treatment failure or an experience of an adverse event to a previous conventional systemic therapy (such as methotrexate) and present PASI ≥ 10, or involvement of sensitive sites such as face, hands, and genitalia before starting any biological drugs. Bio-experienced patients were switched to brodalumab after primary failure (not achieving satisfactory PASI by patients or clinicians after 16 weeks) or loss of efficacy (PASI > 5 at follow-up visit after initial response), or adverse event. The effectiveness of brodalumab was analyzed at 0, 16, 24, and 48 weeks using sPGA-G, PSSI, and ppPASI. Compliance was assessed with a clinical follow-up visit every 4 months. Safety and tolerability of brodalumab were analyzed across different timepoints, assessing mild, moderate, and severe adverse events (AE) reported at visits. Data are presented as mean ± standard deviation (SD) for continuous variables and as percentage numbers for categorical variables. We analyzed only the observed case without imputation of failure. For this pilot study, no control group was considered, so no blinding investigation was conducted. No survival analysis was conducted due to the short follow-up. Pictures were taken by the clinicians at the moment of the visits after signed informed consent. All patients signed informed consent, and the study complies with the ethical standards of the 1975 Helsinki Declaration.

3. Results

As of 1st June 2022, a total of 201 patients have been treated with brodalumab at the Dermatology Unit of the University of Turin. Analyzing the medical records, 183 patients were observed with at least one involvement of the so-called difficult sites: of these, 158 had scalp psoriasis involvement, 69 genital involvement, and 54 palmoplantar involvement. Seventeen had both palmoplantar and genital areas involved (9.3%), 44 had both palmoplantar and scalp (24%), 65 had both genital and palmoplantar (35.5%), and 16 patients presented all three areas involved (8.7%).

The mean age of patients with scalp involvement was 52 years (SD ± 15), 73% of patients were male, and the mean age of psoriasis onset was 31 years (SD ± 15). Sixty percent of the patients were biologically naive, 25% had joint involvement, 24% were obese, and 31% complained of cardiovascular comorbidity. The mean PSSI fell from a baseline of 18.6 (SD ± 11.4) to 1.9 (SD 4.6) at week 16, and the reduction was maintained at the subsequent timepoints of week 24 and 48 (1.26, SD ± 4.4 and 1.1, SD ± 3.9, respectively). Regarding the achievement of relative PSSIs (75%, 90%, and 100%), a rapid response was observed already at week 16. 86% achieved PSSI75, 80% PSSI90, and 75% PSSI100. At week 24 and 48, there was a further improvement in response with an achievement of PSSI 75, 90, and 100 by 94%, 89%, and 88% of patients, respectively (Figure 1). 23 patients discontinued treatment (15%), 8 patients for primary inefficacy (no achievement of response), 6 for secondary inefficacy, 5 for AE (1 case of dizziness, 1 for oral candidiasis, 1 for acne, and 2 for arthralgias), and 4 for logistical problems. 39 patients reported at least one AE, the most common being arthralgias (14 patients), followed by asthenia (9 patients) (Table 1). Patients with genital involvement had a mean age of 48 years (SD ± 14), 70% were male, and the mean age of patients at the onset of psoriasis was 29 years (SD ± 12). Sixty-six percent of the patients had not experienced previous biological therapy, 26% complained of joint involvement, 24% were obese, and 30% reported cardiovascular comorbidity. At baseline, the mean severity of psoriatic lesions was 2.2 sPGA-G (SD 0.9), and at week 16, it was 0.2 (SD 0.8) with further decline at week 24 and 48 (0.2, SD 0.4, and 0.1, SD 0.3). The sPGA-g 0/1 was achieved by 83% of patients at week 16 and 100% of patients at week 24 and 48 (Figure 1). 13% of patients discontinued treatment: 6 patients due to primary inefficacy, 2 due to secondary inefficacy, 1 due to AE (arthralgias), and 1 due to logistical problems. Seventeen patients reported AEs, again arthralgias being the main reported side effect (Table 1). The 54 patients with palmoplantar involvement had a mean age of 54 years (SD ± 16), 58% were male, and the mean age of onset was 30 years (SD16). All patients had joint involvement, 44% were bio-naive, 25% were obese, and 31% reported cardiovascular comorbidities. The mean ppPASI decreased from a mean of 3.5 (SD 1.9) to 0.2 (SD 0.6) at week 48, with a rapid response as early as week 16 0.4 (SD 0.8) and week 24 0.2 (SD 0.6). At week 16, 76.9% of patients reached all the relative ppPASIs: ppPASI75, 90, and 100; and at week 24 and 48, 84.6% of patients reached all relative ppPASIs (Figure 1). In Figure 2, we report a case of rapid resolution of palmar psoriasis in a psoriatic patient on treatment with brodalumab. In this case, the ppPASI fell from 7 to 0 within 12 weeks from baseline. Eleven patients discontinued treatment: 5 for primary inefficacy, 1 for secondary inefficacy, 4 for AE (2 cases of arthralgias, 1 of acne, and 1 of skin ulcers), and 1 for logistical reasons. 17 patients experienced AEs as in the previous difficult sites, with arthralgias being the most common one (Table 1).

4. Discussion

Brodalumab is proven to be rapid, effective, and safe in the so-called difficult-to-treat areas: scalp, genital, and palmoplantar regions. The patient population with the involvement of the palmoplantar regions is markedly different from the other two with a higher frequency of female population, bio-experienced patients, and especially

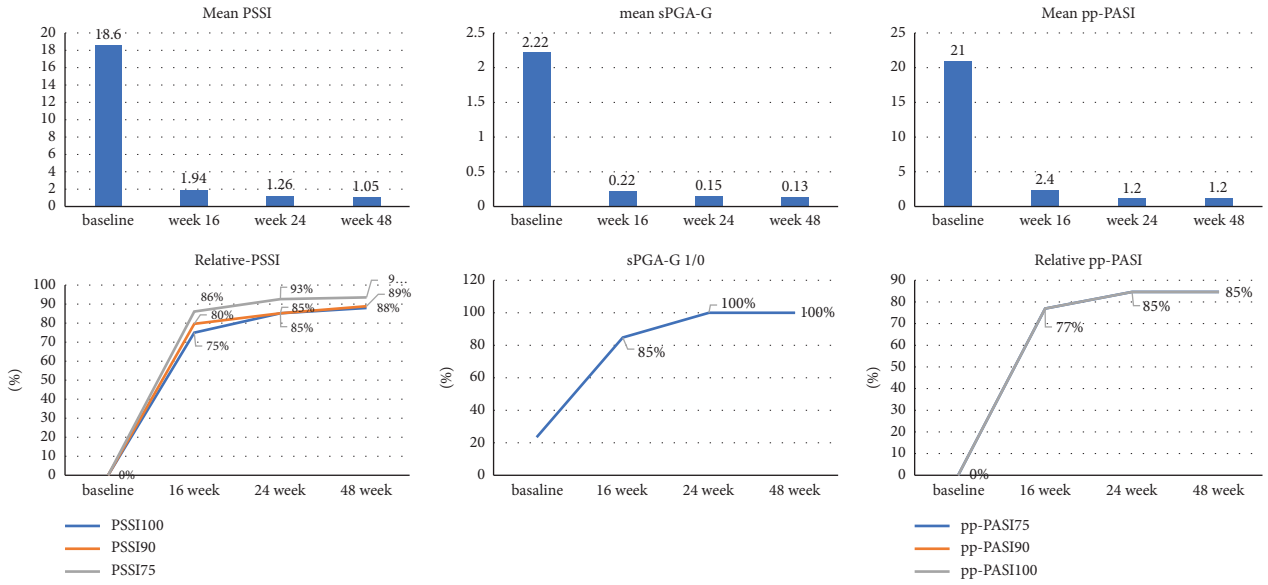

Figure 1: (a) Mean PSSI reduction (18.6 SD ± 11.4, 1.94 SD ± 4.55, 1.26 SD ± 4.4, and 1.05 SD ± 3.9, at each timepoints) (in the *y*-axis, the absolute values and in the *x*-axis, the timepoints) and percentual achievement of relative PSSI 75, 90, and 100 from baseline to 48 weeks (in the *y*-axis, the percentage values expressed in decimals and in the *x*-axis, the timepoints). (b) Mean sPGA-G reduction (2.2 SD ± 1.5, 0.2 SD ± 0.8, 0.2 SD ± 0.9, and 0.1 SD ± 0.8, at each timepoints) (in the *y*-axis, the absolute values and in the *x*-axis, the timepoints) and percentual achievement of sPGA-g 0/1 from baseline to 48 weeks (in the *y*-axis, the percentage values expressed in decimals and in the *x*-axis, the timepoints). (c) Mean ppPASI reduction (3.5 SD ± 1.9, 0.4 SD ± 0.8, 0.2 SD ± 4.4, and 0.6 SD ± 0.6, at each timepoints) (in the *y*-axis, the absolute values and in the *x*-axis, the timepoints) and percentual achievement of ppPASI 75, 90, and 100 from baseline to 48 weeks (in the *y*-axis, the percentage values expressed in decimals and in the *x*-axis, the timepoints). PSSI: Psoriasis Scalp Severity Index, sPGA-G: Genital Physician Global Assessment, ppPASI: Palmoplantar Psoriasis Area Severity Index, SD: standard deviation.

Table 1: General characteristics of the population and adverse events. N: absolute number, M: male, F: female, % percentage, SD: standard deviation.

Scalp involvement		Genital involvement		Palms and soles involvement	
N	158	*N*	69	*N*	54
Age (mean, SD)	52 (SD ± 15)	Age (mean, SD)	48 (SD ± 14)	Age (mean, SD)	54 (SD ± 16)
Age of onset (mean, SD)	31 (SD ± 15)	Age of onset (mean, SD)	29 (SD ± 12)	Age of onset (mean, SD)	30 (SD ± 16)
Gender M/F (%)	73%	Gender M/F (%)	70%	Gender M/F (%)	58%
Bio-naïve (%)	60%	Bio-naïve (%)	66%	Bio-naïve (%)	44%
Joint involvement (5)	25%	Joint involvement (5)	26%	Joint involvement (5)	100%
Obesity (%)	24%	Obesity (%)	24%	Obesity (%)	25%
Cardiovascular disease (%)	31%	Cardiovascular disease (%)	30%	Cardiovascular disease (%)	31%
Adverse events	39	Adverse events	17	Adverse events	17
(i) Arthralgia	14	(i) Arthralgia	9	(i) Arthralgia	7
(ii) Asthenia	9	(ii) Asthenia	3	(ii) Asthenia	3
(iii) Acne	2	(iii) Tinea cruris	1	(iii) Xerosis	1
(iv) Oral candidiasis	2	(iv) Oral candidiasis	1	(iv) Skin ulcer	1
(v) Globus pharingeus	1	(v) Cefalea	2	(v) Leg oedema	1
(vi) Leg oedema	1	(vi) Diarrhea	1	(vi) Diarrhea	2
(vii) Cefalea	3	(vii) Wearing off	1	(vii) Wearing off	1
(viii) Site of injection skin reaction	1	(viii) Humour deflexion	1	(viii) Alopecia	1
(ix) Blefaritis	1	(ix) Dizziness	1	(ix) Acne	1
(x) Diarrhea	2				
(xi) Rhinitis	1				
(xii) Wearing off	1				
(xiii) Xerosis	1				
(xiv) Dizziness	1				
(xv) Alopecia	1				
(xvi) Acne	1				

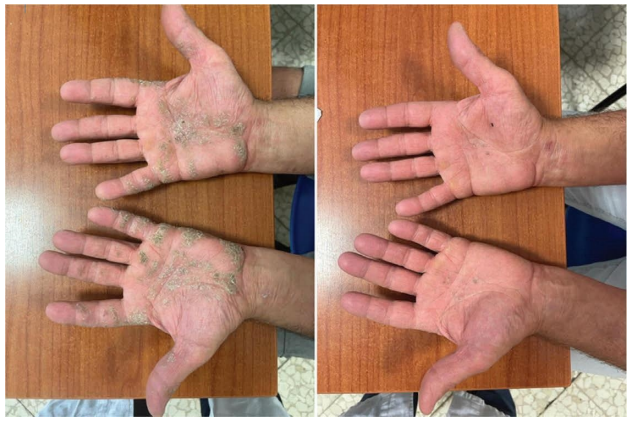

Figure 2: A palmar psoriasis improvement in male patients after 12 weeks of brodalumab, and a clear reduction of PASI is appreciable. PASI: Psoriasis Area Severity Index.

widespread joint involvement. However, different characteristics do not seem to compromise the rapid response to treatment in this population as well. The scalp is the most frequently difficult area affected in psoriatic patients [2]. Guselkumab, infliximab, ixekizumab, and brodalumab demonstrated high efficacy in the treatment of scalp psoriasis in a review of RCTs (randomized clinical trials) [10]. In the post hoc analysis of the phase 3 study, AMAGINE-1, brodalumab, in patients with scalp psoriasis showed rapid efficacy, superior to placebo, already at week 12 in achieving PSSI 75 and 100 (89% and 63.4%, respectively) [11]. Narcisi et al. in a real-life study showed a slower achievement of sc-PGA 0/1 in patients treated with brodalumab compared to other IL-17 inhibitors (55% at week 16) [12]. Although the timepoints analyzed were different (12 weeks in the studies described and 16 weeks in ours), a faster response occurred in our population: 86%, 80%, and 75% of patients achieved PSSI 75, 90, or 100, respectively. Regarding the genital area, no studies are available on the efficacy of brodalumab. Ixekizumab was investigated for efficacy and safety in this specific body region in the GenPs clinical trial [1]. A Greek comparative study observed no significant differences between risankizumab and ixekizumab at weeks 16 and 24 in the achievement of sPGA-G 0/1 (68.8% vs. 70.0% and 89.8% vs. 93.8%) [13]. In a case series, 10 patients showed the efficacy of tildrakizumab in this specific body region [14]. Similarly, Galluzzo et al. showed a reduction from 3.3 to 0.2 at 28 weeks of sPGA-G in 7 patients treated with tildrakizumab [2]. In our population, patients treated with brodalumab showed a reduction in mean sPGA-G from 2.2 to 0.1 at week 48. The response considering sPGA-G 0/1 was complete at week 24 and 48 with 100% of patients achieving the outcome. In our population, the results are similar to the other treatments described. Palmoplantar psoriasis is plagued by high resistance to treatment, traditionally topical steroids, and acitretin as systemic therapy [1]. Resistance to biological treatment is described in only one-third of patients achieving a complete or near complete response to secukinumab at 16 weeks in the main randomized trial on this specific site [15]. Similar results regarding secukinumab are reported by Galluzzo et al. in a real-life multicentre study. Guselkumab was superior to placebo in reaching ppPASI 50 and PGA 0/1 at 16 weeks (60% vs. 21% and 24% vs. 8%, respectively) [16]. In a real-life study including 7 patients treated with tildrakizumab, a ppPASI reduction of 75.5% occurred at week 16 and 100% occurred at week 24 [2]. Concerning brodalumab, Politou et al.showed the achievement of ppPGA 0 at week 16 in 4 out of 4 patients with palmoplantar involvement after secukinumab failure [1]. In contrast, Pinter et al. showed a therapeutic failure of brodalumab in 4 patients with the same involvement [17]. In our population, a steep reduction in mean ppPASI occurred from 3.5 to 0.4 at week 16, and relative ppPASI 75, 90, and 100 reached 84.6% at weeks 24 and 48. At an indirect comparison, brodalumab seems to better perform than other biological investigations so far in the literature, according to the above-mentioned study, but possibly randomized comparative studies are needed to confirm this observation. Regarding safety, most adverse events were mild and not directly related to treatment, rarely leading to discontinuation. Concerning arthralgias, most cases referred to worsening of preexisting joint involvement. The limitations of this study are the low sample size, which limited further statistical investigation, and the retrospective nature.

5. Conclusion

Brodalumab proved to be effective and safe in the treatment of difficult scalp, genital, and palmoplantar regions. The data are in line with those currently reported in the literature, albeit scarce. Multicentric blinded RCT is needed to validate the newer findings to optimize the treatment option in difficult-to-treat areas of psoriasis.

Data Availability

Data are available upon reasonable request.

Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of AOU città della Salute e della Scienza di Torino(ss-dermo-20).

Consent

Patients signed informed consent.

Disclosure

Luca Mastorino, Caterina Cariti, Pietro Quaglino, Simone Ribero, and Paolo Dapavo shared senior authorship.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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