Dermatology Practical & Conceptual

Long-Term Effectiveness of Brodalumab for the Treatment of Moderate-To-Severe Psoriasis: A Real-Life Multicenter Study of Up to 3 Years in a Real-Life Italian Cohort

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ABSTRACT

Introduction: Data about the long-term effectiveness of brodalumab could be valuable in assessing patient adherence to treatment and improving psoriasis management.

Objective: The aim of our study was to evaluate the drug survival of brodalumab and identify any predictive factors for discontinuation.

Methods: A multicenter retrospective study was conducted in patients with moderate-to-severe psoriasis who were treated for up to 3 years. We extracted data from patient files, related to the characteristics of the patients and the disease. Drug survival analysis was descriptively analyzed using Kaplan–Meier survival curves. Univariable and multivariable analyses were performed to assess baseline patient characteristics that predicted clinical response.

Results: The study included 90 patients. Among them, 28 (31.1%) suspended brodalumab through the observation period. At weeks 52, 104 and 156 the median PASI score were 0.0 [0.0 – 0.8], 0.0 [0.0 – 1.0] and 0.0 [0.0 – 0.0], respectively. The estimated cumulative survival rates at weeks 52 and 104 were 86.32% and 78.09%, respectively. In the multivariable survival analysis, predictor factors for overall discontinuation included body mass index (BMI) (OR 1.10, 95% CI 1.03 - 1.18), baseline PASI (OR 1.06, 95% CI 1.02 - 1.10), and psoriatic arthritis (OR 5.05, 95% CI 0.89 - 13.50).

Conclusions: Brodalumab has shown long-term effectiveness for up to 3 years. Considering baseline disease severity and patient characteristics could aid in optimizing the long-term management of psoriasis.

Introduction

The management of psoriasis has improved in recent years due to the expansion of available systemic therapies. Biologic drugs target specific immune system pathways involved in psoriasis, allowing for the optimization of clinical responses and the long-term management of patients. The remarkable pharmaceutical improvement in recent years has led to the development of new biologic therapies that target interleukins (IL) 17 and 23, allowing to achieve higher skin clearance with a good safety profile.

Brodalumab is a fully human monoclonal antibody that specifically targets the interleukin-17 receptor A (IL-17RA), inhibiting the signaling pathway of several IL-17 isoforms (instead of (IL-17isoforms) involved in psoriasis pathogenesis [1,2]. The rapid action and high efficacy of brodalumab have already been demonstrated in three phase 3 randomized double-blind trials (RCTs): AMAGINE-1, AMAGINE-2, and AMAGINE-3 [3, 4, 5], as well as in real-life settings [6, 7, 8, 9, 10]. For the long-term management of psoriasis, evaluating brodalumab's drug survival might help to assess its real-world success and patient's adherence to the treatment, but to date data in literature are scanty.

Herein we present a retrospective real-life multicenter study conducted in a real life Italian cohort, involving patients with moderate to severe psoriasis who were treated with brodalumab for a period up to 3 years.

Method

We conducted a multicenter, retrospective, observational study in patients with psoriasis who started brodalumab therapy between May 2019 and January 2021. We included patients of age >18 years from the following dermatology units in Italy: 'Tor Vergata' University of Rome, Catholic University of the Sacred Heart in Rome IRCCS, 'Daniele Innocenzi' of University of Rome 'La Sapienza,' Polo Pontino and Istituto Dermopatico dell'Immacolata – IRCCS, Rome.

Exclusion criteria were generalized, palmoplantar pustular psoriasis, use of additional systemic therapies for psoriasis, and participation in clinical trials. Patients were treated with brodalumab at the European Medicines Agency (EMA)-approved dosage.

We collected data related to the characteristics of the patients (age, sex, body mass index [BMI], comorbidities, smoking habits) and of the disease (age at onset, previous therapies, and special-site involvement). The severity of psoriasis was measured with the Psoriasis Area and Severity Index (PASI) score at baseline and after 4, 12, 24, 52, 104, and 156 weeks of treatment. Patients obtaining a PASI 90 improvement at week 4 were defined fast responders. Reasons for withdrawal of brodalumab and any adverse event that occurred during treatment were recorded. Discontinuation of therapy was defined as interruption of brodalumab administration for more than 90 days.

Descriptive statistics for continuous variables were reported as medians/means and interquartile ranges (IR)/ standard deviations (SD), dichotomous variables were described using absolute and relative (%) frequencies. The drug survival analysis was descriptively analyzed using

Kaplan–Meier survival curves. Three "events" for drug survival were defined and analyzed separately. (i.e. overall discontinuation; discontinuation because of brodalumab ineffectiveness; adverse events or other type of events other than ineffectiveness). Patients were censored when lost to follow-up, discontinued due to an event other than the events of interest, or when the database was extracted, and patients were actively undergoing their treatment with the drug of interest at that moment. Univariable and multivariable Cox regression analyses were carried out using variables considered of clinical importance. Statistical significance was set at p-value <0.05. Analyses were performed in May 2023 by using STATA 13.0 Software (StataCorp, Texas).

The protocol was reviewed and approved by Fondazione Policlinico Universitario Agostino Gemelli IRCCS - Università Cattolica del Sacro Cuore, Prot N.: 15188/23. All patients signed a hospital-based informed consent. The study was performed following the principles of the Declaration of Helsinki.

Results

Ninety patients with moderate- to- severe plaque psoriasis treated with brodalumab were included. Mean age of patients was 52.2 (SD 15.0) years, and the majority (67.8%) were males. Median PASI score at baseline was 15.0 (IR 10.0 - 22.0). Other baseline characteristics of patients are presented in Table 1. Data about the first 52 weeks of treatment have been already reported [11]. In particular, 29/90 (32.2%) patients achieved PASI 90 at week 4 and were considered fast responders.

Among 90 enrolled patients, 28 (31.1%) suspended brodalumab through the observation period. At weeks 52, 104, and 156 the median PASI score were 0.0 [0.0 – 0.8], 0.0 [0.0 – 1.0] and 0.0 [0.0 – 0.0], respectively. The reasons for discontinuation were adverse events in 8 patients (8.9%), ineffectiveness in 15 patients (16.7%) and loss to follow-up in 5 patient (5.6%). Discontinuation for adverse events were due to eczematous eruptions in 2 patients, and in singular cases to recurrent candidiasis, lower limb myalgia, myocardial infarction, cerebral ischemia, concomitant anemia and transaminase increase due to alcohol abuse, and to recurrent upper respiratory tract infection. Median time of observation among those who discontinued brodalumab was 62.5 (IR 32.0 – 111.0) weeks after the start of the drug.

The overall drug survival is reported in Figure 1A. Overall, a total of 86.32%, 78.09% of patients was under treatment at weeks 52 and 104 respectively. The drug survival rate for discontinuation due to adverse events was 93.69% (confidence interval [CI] 85.35-97.35), and 92.04% (CI 82.93-96.39) after 52 and 104 weeks, respectively (Figure 1B). The drug survival rate for discontinuation due to ineffectiveness was 93.44% (IC 84.81-97.24) and 87.94% (IC 76.95-93.90) after 52 and 104 weeks, respectively (Figure 1C). Data about 156 weeks were not reported because only 24 patients reached this timepoint.

Table 1. Clinical and Demographic Characteristics of the Study Population.

Demographic or Clinical Characteristic (total n = 90)	N (%); Mean (SD), Median [IQR]
Sex	
Males	29 (32.22)
Females	61 (67.78)
Age	52.22 (15.03)
Age of onset	29.45 (15.64)
Arthritic Psoriasis	
Yes	21 (23.33)
No	69 (76.67)
BMI	26.73 [24.10 – 29.41]
Scalp psoriasis	
Yes	44 (48.89)
No	46 (51.11)
Nail psoriasis	
Yes	23 (25.65)
No	67 (74.44)
Palmoplantar psoriasis	
Yes	12 (13.33)
No	78 (86.67)
Genital psoriasis	
Yes	25 (27.78)
No	65 (72.22)
Previous Biological Treatments	
Yes	47 (52.22)
No	43 (47.78)
Other anti IL17 use	
Yes	19 (21.11)
No	71 (78.89)
PASI at baseline	15.0 [10.0 – 22.0]
PASI week 12 (n=90)	0.0 [0.0 – 2.0]
PASI week 52 (n=85)	0.0 [0.0 – 0.8]
PASI week 104 (n=73)	0.0 [0.0 – 1.0]
PASI week 156 (n=24)	0.0 [0.0 – 0.0]
Fast Responder*	
No	61 (67.78)
Yes	29 (32.22)

*Patients achieving PASI 90 at week 4.
BMI = body mass index; IQR = interquartile range; PASI = Psoriasis Area and Severity Index; SD = standard deviation.

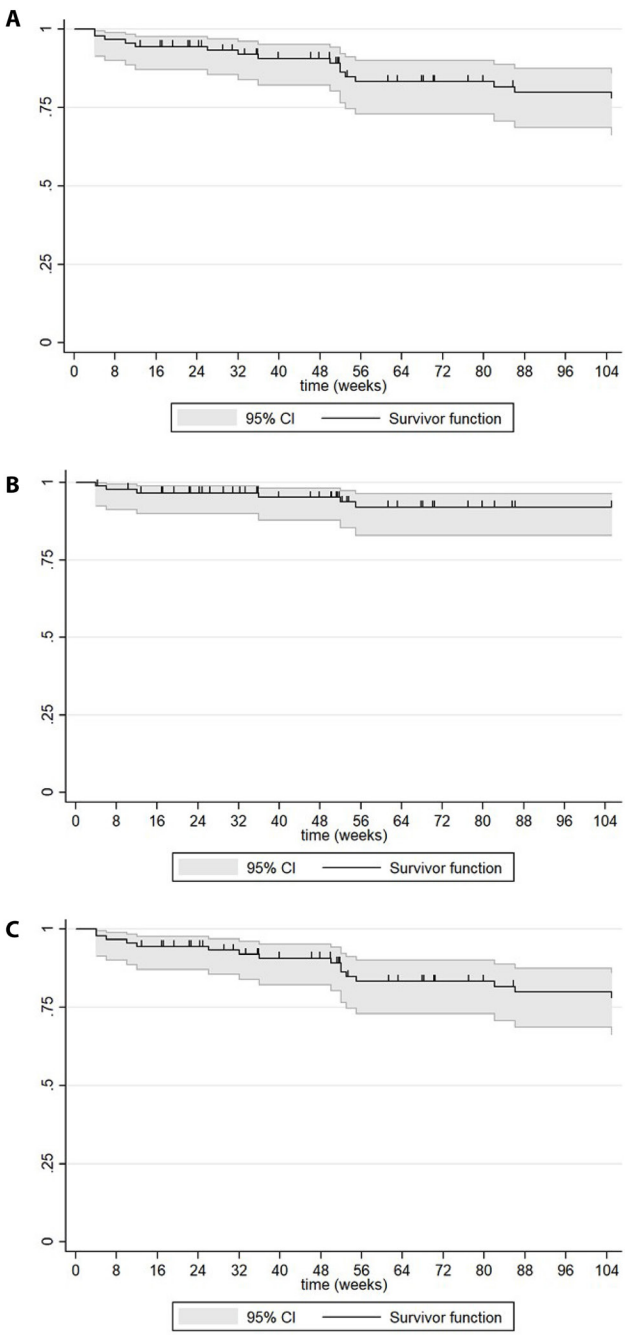

Figure 1. Kaplan–Meier curves of (A) overall drug survival; (B) discontinuation because of adverse events or other events; and (C) discontinuation because of a lack or loss of efficacy (confidence interval [CI] in light gray).

An univariable logistic regression was performed and results are reported in Table 2. In detail, predictive factors for overall drug discontinuation were psoriatic arthritis OR 2.93 (95% CI, 1.30 – 6.61), BMI with an OR of 1.07 (95% CI, 1.02 – 1.13) and baseline PASI OR 1.05 (95% CI, 1.02 – 1.09). At the multivariable survival analysis (Table 3), positive predictor factors for overall discontinuation resulted BMI OR 1.10 (1.03 – 1.18)), baseline PASI OR 1.06 (95% CI, 1.02 – 1.10) and psoriatic arthritis OR 5.05 (95% CI, .89 – 13.50). Factors associated with suspension for ineffectiveness were BMI OR 1.11 (95% CI, 1.01 – 1.23), baseline PASI OR 1.07 (95%CI, 1.02 – 1.13) and psoriatic arthritis OR 11.65 (95% CI, 2.92 – 46.46). No significant predictive factors emerged for discontinuation for adverse events.

Detailed Report of Cases of Special Interest

Patient #1: Patient with multi-drug resistance, comorbidities, and BMI ≥40. We present the case of a 56-year-old male, with class III obesity, arterial hypertension, hyperuricemia, type II diabetes, hypercholesterolemia and a history of psoriasis from the age of 32. He was in therapy from 2001 to 2002 with cyclosporine discontinued for inefficacy. Then, for more than 10 years he was treated only with topical treatments. In June 2016, ustekinumab was administered (PASI score=42), and then discontinued after 90 weeks for persistence of psoriasis (residual PASI=15). In May 2018, therapy with secukinumab was started, with a lack of response, and therefore switched to guselkumab after 42 weeks of treatment (March 2019, PASI score=15). Even with this last therapy, no improvement was observed after 108 weeks (PASI score=15). Finally, in April 2021, brodalumab treatment was started (Figure 2A), with a rapid improvement after 6 weeks (PASI score= 6, Figure 2B) and a complete remission after 12 weeks. Currently, the patient has reached the second year of treatment with brodalumab, maintaining a complete remission of the disease (Figure 2C).

Patient #2: A complex oncological history and multiple treatment suspensions without recurrences. A 48-year-old woman was affected by moderate-severe psoriasis for nearly 30 years and had undergone various therapies over time, including topical treatments, cyclosporine, and NB-UVB phototherapy, with partial benefit. Two years earlier the patient underwent a conization procedure for cervical intraepithelial neoplasia III (CIN III). However, she was in general good health. At the time of our observation, in December 2019, the patient presented a PASI score of 13 and DLQI of 12 (Figure 3A). She was prescribed brodalumab, which led to a complete remission of psoriasis (PASI 0) and pruritus after 4 weeks, along with a significant improvement in her quality of life (DLQI 4).

After 9 months of therapy, the patient was diagnosed with a right fronto-temporal meningioma. Consequently, she discontinued brodalumab and underwent neurosurgery to remove the tumor. Despite discontinuing the biological therapy, the patient did not experience a relapse of psoriasis until 3 months after the neurosurgical intervention, when she had a recurrence localized to the scalp (Figure 3B). Subsequently, the patient resumed brodalumab after consultation with the neurosurgeon, achieving again the remission of her psoriasis.

Table 2. Univariable Drug Survival Analysis.

		Overall		Ineffectiveness		Adverse Events	
		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Sex	Female	Ref		Ref		Ref	
	Males	1.43 (0.60 – 3.44)	0.419	1.15 (0.39 – 3.37)	0.802	1.59 (0.32 – 7.89)	0.571
Age		1.00 (0.97 – 1.03)	0.933	1.01 (0.97 – 1.04)	0.750	0.99 (0.94 – 1.04)	0.636
Arthritic psoriasis	No	Ref		Ref		Ref	
	Yes	**2.93 (1.30 – 6.61)**	**0.010**	**5.60 (1.94 – 16.17)**	**0.001**	1.29 (0.26 – 6.40)	0.756
BMI		**1.07 (1.02 – 1.13)**	**0.004**	1.07 (0.99 – 1.14)	0.056	**1.09 (1.00 – 1.18)**	**0.049**
Scalp psoriasis	No	Ref		Ref		Ref	
	Yes	3.27 (1.36 – 7.86)	0.080	1.96 (0.70 – 5.53)	0.203	**8.56 (1.05 – 69.76)**	**0.045**
Nail psoriasis: No	No	Ref		Ref		Ref	
	Yes	2.38 (0.95 – 5.96)	0.064	2.63 (0.78 – 8.80)	0.117	3.00 (0.67 – 13.57)	0.152
Palmoplantar psoriasis	No	Ref		Ref		Ref	
	Yes	0.40 (0.06 – 2.96)	0.368	0.75 (0.10 – 5.76)	0.781	n.c.	n.c.
Genital psoriasis	No	Ref		Ref		Ref	
	Yes	2.13 (0.95 – 4.81)	0.068	1.21 (0.38 – 3.87)	0.748	**4.94 (1.75 – 20.75)**	**0.029**
Other anti-IL-17 use	No	Ref		Ref		Ref	
	Yes	0.88 (0.30 – 2.59)	0.821	1.25 (0.35 – 4.48)	0.737	0.60 (0.07 – 4.91)	0.637
Previous biological drug	No	Ref		Ref		Ref	
	Yes	1.47 (0.65 – 3.30)	0.358	1.95 (0.65 – 5.83)	0.233	1.66 0.40 – 6.98()	0.487
Fast Responder	No	Ref		Ref		Ref	
	Yes	1.57 (0.71 – 3.48)	0.261	1.78 (0.61 – 4.73)	0.302	1.24 (0.30 – 5.21)	0.765
PASI at baseline		**1.05 (1.02 – 1.09)**	**0.003**	**1.05 (1.00 – 1.10)**	**0.036**	1.06 (0.99 – 1.11)	0.053

BMI = body mass index; CI = confidence interval; OR = odds ratio; n.c., non computable; PASI = Psoriasis Area and Severity Index.

Table 3. Multivariable Survival Analysis.

		Overall		Ineffectiveness		Adverse events	
		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Sex	Female	Ref		Ref		Ref	
	Males	0.70 (0.26 – 1.85)	0.466	0.46 (0.13 – 1.66)	0.237	0.87 (0.15 – 5.00)	0.878
Age		0.99 (0.95 – 1.02)	0.443	0.99 (0.94 – 1.03)	0.533	0.98 (0.93 – 1.04)	0.497
BMI		**1.10 (1.03 – 1.18)**	**0.003**	**1.11 (1.01 – 1.23)**	**0.032**	1.09(0.98 – 1.20)	0.106
Baseline PASI	No	**1.06 (1.02 – 1.10)**	**0.002**	**1.07 (1.02 – 1.13)**	**0.010**	1.06 (1.00 – 1.12)	0.046
Arthritic Psoriasis	No	**Ref**		**Ref**		Ref	
	Yes	**5.05 (1.89 – 13.50)**	**0.001**	**11.65 (2.92 – 46.46)**	**0.001**	1.71 (0.29 – 10.08)	0.554
Previous biological drug	No	Ref		Ref		Ref	
	Yes	0.88 (0.34 – 2.23)	0.791	0.87 (0.25 – 3.04)	0.957	1.67 (0.31 – 8.94)	0.552
Fast Responder	No	Ref		Ref		Ref	
	Yes	1.63 (0.71 – 3.74)	0.249	1.94 (0.65 – 5.78)	0.233	1.08 (0.23 – 5.06)	0.926

BMI = body mass index; CI = confidence interval; OR = odds ratio; PASI = Psoriasis Area and Severity Index.

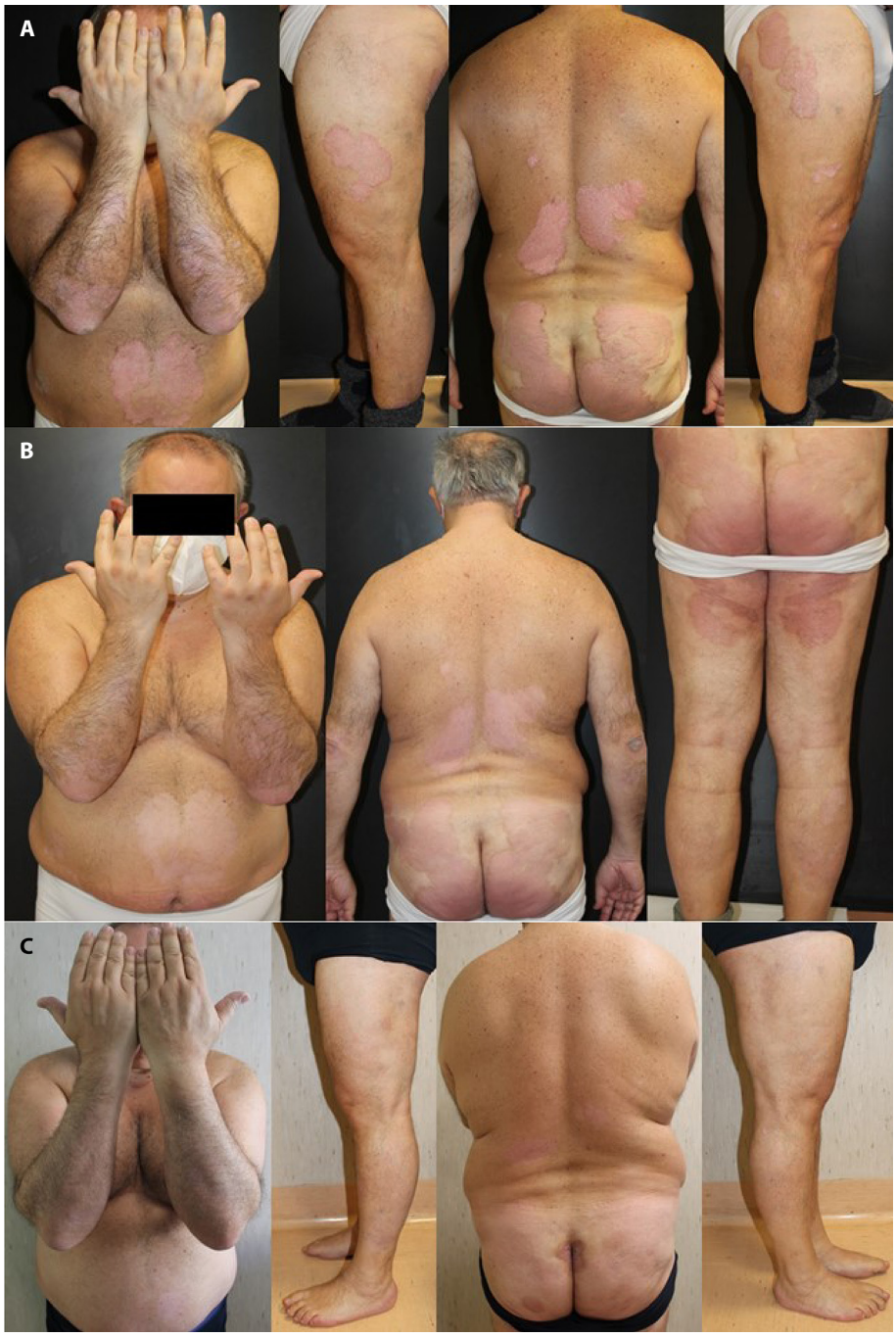

Figure 2. Patient #1. (A) At baseline. (B) At week 6. (C) At week 108.

Two years later, the patient received a diagnosis of left ovarian fibrothecoma and underwent bilateral ovariectomy and adnexectomy. Additionally, due to the detection of breast calcifications, multiple biopsies were performed, leading to a diagnosis of atypical ductal hyperplasia. As a result, the patient must undergo regular clinical and instrumental follow-ups. During these assessments and surgical procedures, the patient temporarily discontinued brodalumab therapy without experiencing a recurrence of psoriasis. Upon advice from oncology specialists, she resumed treatment with the maintenance dosage regimen. To date, the patient remains in clinical remission for psoriasis and has not experienced a recurrence of cervical intraepithelial neoplasia or meningioma (Figure 3C).

Patient #3: An obese patient with latent tuberculosis. We present the clinical case of a 52-year-old Caucasian male, a workman and habitual smoker with hypertension, dyslipidemia, and class II obesity (BMI 37.04). The patient had a positive family history of psoriasis and was affected from plaque psoriasis since the age of 16, and psoriatic arthritis for the last 20 years. His clinical presentation was characterized by psoriatic plaques mainly located on the trunk and hands, with a PASI of 36 and a DLQI score of 18 (Figure 4A). Due to the high PASI score and the presence of comorbidities,

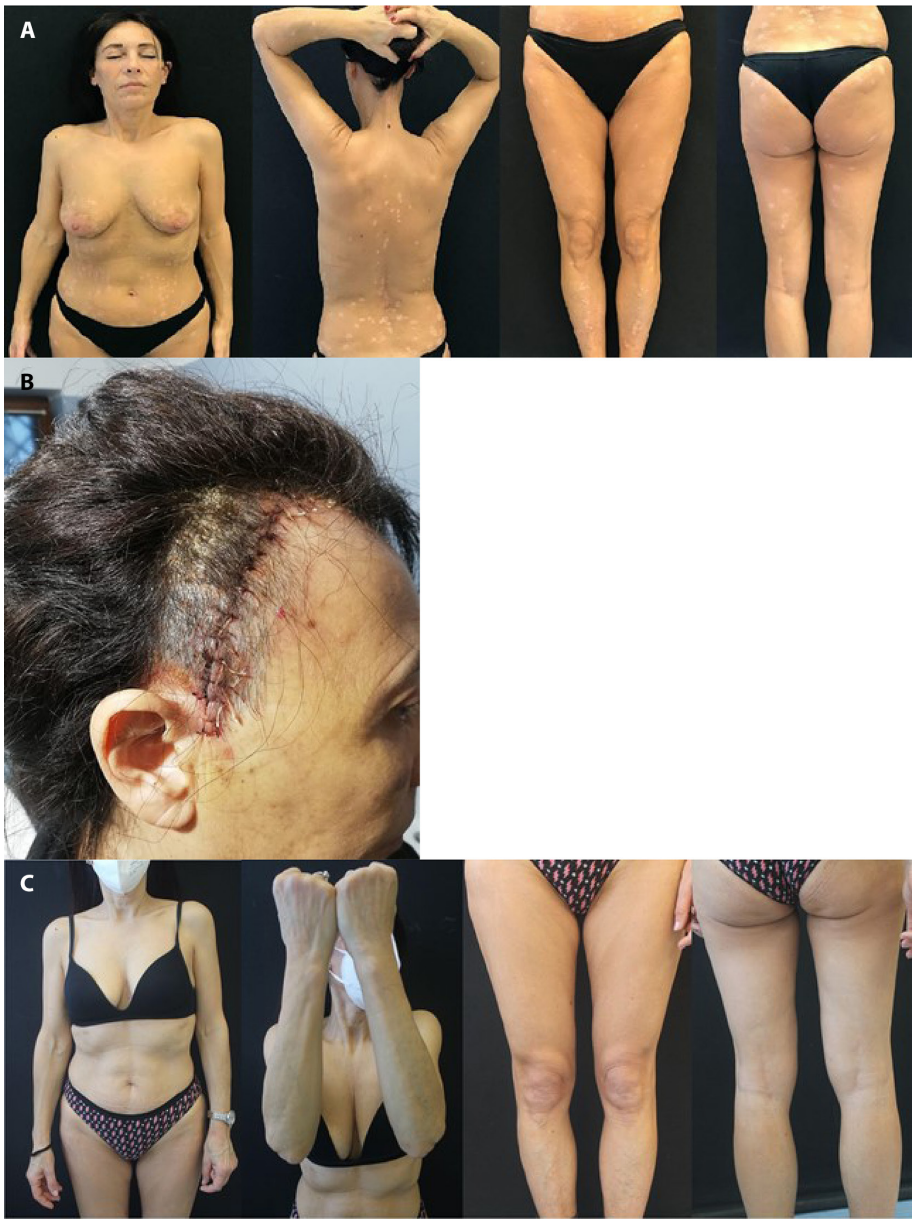

Figure 3. Patient #2. (A) At baseline. (B) Recurrence of psoriasis on the scalp after neurosurgical intervention and 3 months after brodalumab discontinuation. (C) At week 160.

the patient was screened to start biologic therapy. Infectious examinations revealed a positive result for Quantiferon TB Gold, indicating latent tuberculosis infection. Therefore, isoniazid prophylaxis was initiated, but after only 15 days, it induced an increase in liver enzymes. After an infectious disease consultation, the tuberculosis prophylaxis was switched to rifampicin. After 30 days of starting tuberculosis prophylaxis and after liver enzyme increase was resolved, the patient began treatment with brodalumab. 12 weeks later, patients achieved complete resolution of psoriasis, including the challenging lesions of the hands (Figure 4B). The patient has currently completed three years of brodalumab treatment, without any recurrence of psoriasis.

Patient #4: Brodalumab after failure of anti-IL-17 secukinumab. We present the case of a 38-year-old male patient with an 11-year history of psoriasis. The patient was obese (BMI 34.7), dyslipidemic and smoker (20 cigarettes per day). Previously, he had been unsuccessfully treated with ciclosporin (suspended due to hypertension), etanercept (suspended due to ineffectiveness), and secukinumab (suspended due to lack of efficacy after 2 years). After a partial remission with secukinumab, the patient experienced a recurrence of the disease in November 2019, localized on the legs, trunk, and scalp. Consequently, we decided to initiate brodalumab treatment, considering its rapid action. Remarkably, after only 4 weeks, we observed a near-complete resolution of the disease, with the PASI score decreasing from 10 (at baseline)

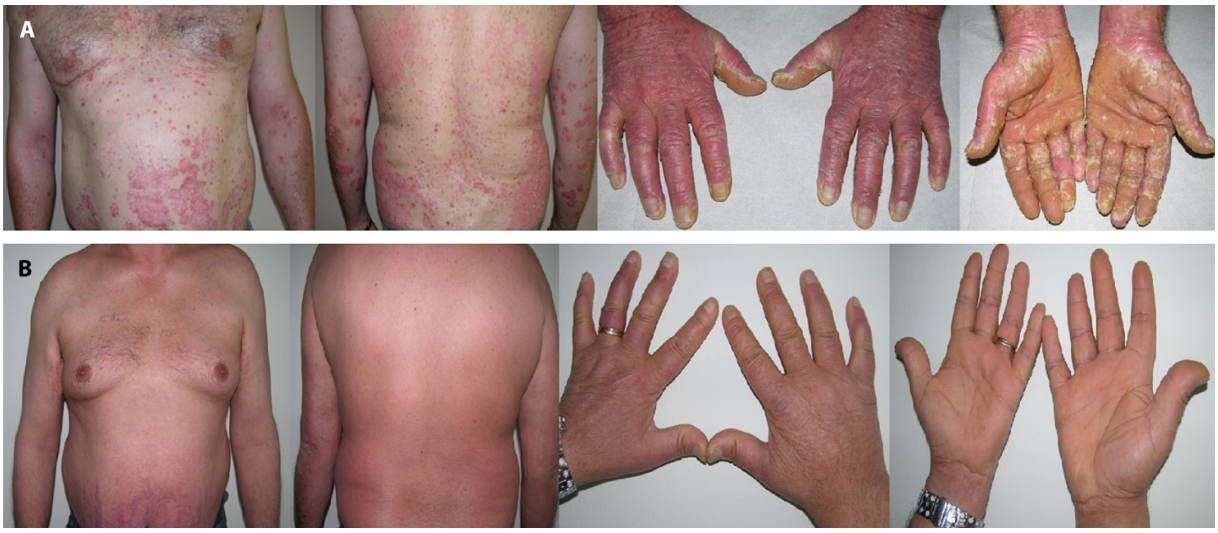

Figure 4. Patient #3. (A) At baseline. (B) At week 12.

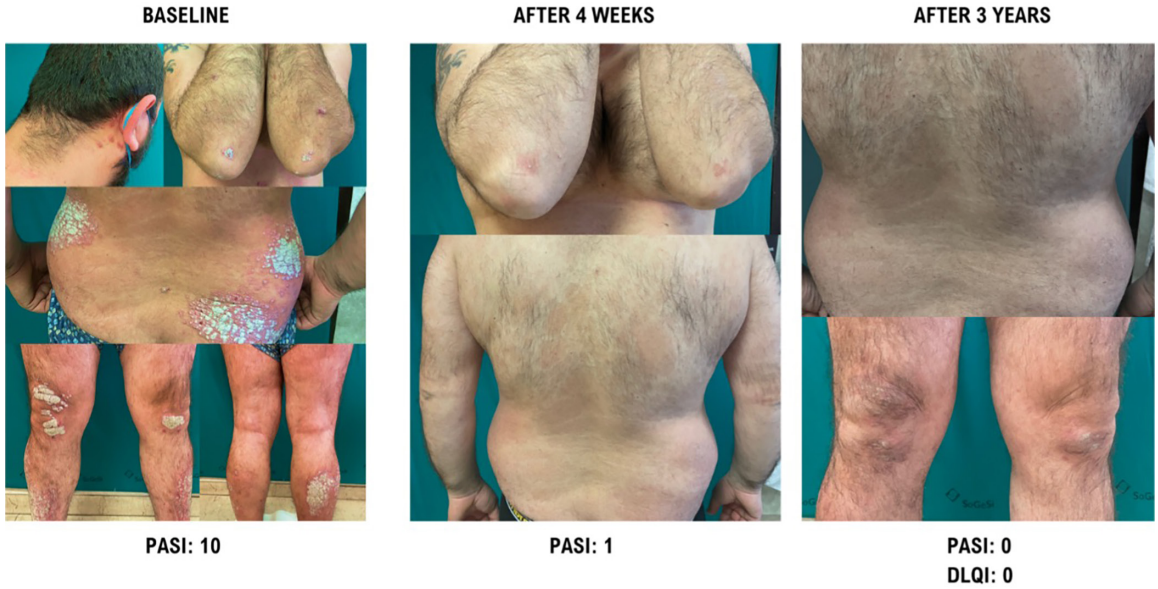

Figure 5. Patient #4, at baseline and after 4 weeks and 3 years of treatment with brodalumab. The hyperchromic patches can be attributed to post-inflammatory hyperpigmented outcomes.

to 1 (Figure 5). After 3 years, the patient continues to receive brodalumab treatment with complete clearance of psoriasis and no impact on his quality of life (PASI 0; DLQI 0) (Figure 5).

Drug survival is a real-life indicator of treatment success over the long-term, encompassing factors such as drug efficacy, safety and patient adherence. Considering the diverse range of systemic therapies available for psoriasis, drug survival plays a crucial role in guiding us in the selection of the most suitable treatment option for patients [12].

In this study we assessed the drug survival of brodalumab, a monoclonal antibody targeting the interleukin-17 receptor A (IL-17RA), in patients with moderate to severe psoriasis. The data collected over a 3-year period provided valuable insights into the long-term effectiveness of the drug. In detail, after 52 and 104 weeks, 86.32% and 78.09% of patients, respectively, were still receiving brodalumab. These results demonstrated a favorable drug survival rate, with a significant proportion of patients remaining on the treatment throughout the observation period.

There are currently limited studies available that report the long-term survival rate of brodalumab and they report conflicting data and differences between various anti IL-17 agents [7, 13, 14, 15, 16]. Elgaard et al. reported a low brodalumab survival rate, in detail 65.7% and 57.2% after 1 and 2 years respectively. However, this datum may be explained by the very high percentage of bio-experienced patients (>90%) and by the low number of patients followed

up for the whole period of the study. Moreover, Gaudet et al. reported similar results and, in particular, a 1-year survival rate of 70%, analyzing data collected through the brodalumab patient support program in Canada [11, 17]. Our results are in line with the studies by other authors that reported survival rates at 1 year ranging from 85 to 89.9% and at 2 years from 77.32 to 80.0%. In addition, Torres et al analyzed the drug survival of different IL-17 and IL-23 inhibitors, and brodalumab resulted the IL-17 inhibitor with the highest drug survival at 24 months (overall probability of drug survival of 0.80 compared to 0.79 for ixekizumab, and 0.75 for secukinumab). The higher drug survival of brodalumab compared to other IL-17 inhibitors, although with no statistical significance, appeared also in the recent real-world analysis conducted in the Czech Republic [18, 19].

Finally, Gargiulo et al. recently published an Italian study that involved 606 patients treated with brodalumab, out of which 115 completed a 3-year follow-up. The study confirmed the high persistence in treatment even at 36 months, with a notable survival rate of 85.64% [20].

Discontinuation of brodalumab in our study primarily occurred due to adverse events. The most frequent in our patients was the onset of an eczematous eruption, occurring in 2/90 patients (2.22%). This is a well-known adverse event which can occur during anti IL-17 treatments. Although the exact underlying pathogenetic mechanism is not yet fully understood, it has been hypothesized that the incidence of eczematous eruptions is mainly linked to the overexpression of IL-17 C. Brodalumab, acting on IL-17RA and blocking IL17A, IL-17 F, and IL-17 C, does not result in an increase of IL-17 C and this may explain the lower prevalence of this side effect in our population respect to what is reported for other anti IL17 agents (2.2% vs 5.8%) [21]. Several cases have been described that support this hypothesis. For instance, a patient with an eczematous eruption induced by ixekizumab was treated with brodalumab with success, and a patient with concurrent atopic dermatitis and psoriasis was managed with brodalumab achieving a complete clinical response [22, 23]. Otherwise, brodalumab was well tolerated in our population and only one patient (1/90) experienced another well-known IL17 agent side effect, such as recurrent candidiasis. This is in line with the role of IL-17 in host defence against mucocutaneous candidiasis [24].

Predictive factors associated with suspension due to adverse events in the univariable logistic regression were BMI, scalp psoriasis, and genital psoriasis. It's now well-established that a higher BMI is associated with increased comorbidities and adverse events, even not directly related to psoriatic therapy, while we do not clinically correlate scalp psoriasis and genital psoriasis with adverse events. These predictive factors were not confirmed in the multivariable analysis.

The optimal safety profile of brodalumab has been also confirmed by its successful use in our reported patients with a complex medical history, such as those with latent tuberculosis and multiple neoplasms (cases 2 and 3, respectively). Moreover, we analyzed predictive factors for drug survival. Psoriatic arthritis and PASI at baseline were identified as positive predictive factors for overall discontinuation and suspension due to ineffectiveness. Psoriatic arthritis affects approximately 30% of patients with psoriasis [25] and therefore the ability of a drug to manage the articular component is important when choosing among the available therapeutic options. Brodalumab showed good results in clinical trials for psoriatic arthritis [26], but evidence in real-world is currently limited [17]. In contrast to our result, in the study of Kojanova et al and of Gkanti et al, psoriatic arthritis resulted associated to a longer drug survival [18, 27].

PASI at baseline can have an impact on the efficacy of treatments for psoriasis [28]. Patients with higher baseline PASI may experience a reduced responsiveness or a loss of efficacy to biological treatments. In fact, although it has not yet been reported in drug survival analyses specific on brodalumab, higher baseline PASI was identified as a predictor of drug discontinuation in the drug survival analysis of Il 17 and Il 23 inhibitors by Torres et al [19]. This finding aligns with our result and confirms that patients with a more severe disease at baseline may have a lower drug survival. Moreover, although two of the reported cases showed a high effectiveness of brodalumab in very obese patients, at the multivariable analysis BMI resulted associated with a mild increase risk (OR 1.10) of discontinuation for all reasons and for ineffectiveness [29]. Although in the post hoc analysis of AMAGINE 2/3 trials BMI was not associated to a lower efficacy of brodalumab [30], in the real-world setting this finding is not always confirmed and obesity in some studies seems to be related to lower efficacy and drug survival [14, 17, 18]. For this reason, a trial is currently ongoing to investigate the administration of a higher dosage of brodalumab in patients with an increased BMI (NCT04306315).

Finally, we did not find significant difference in effectiveness between biologic-naive and bio-experienced patients. This datum is worthy of note since, in the real-world setting, bio-experienced patients represent a therapeutic challenge because they may have developed resistance or inefficacy to prior biologic treatments. In fact, therapies for psoriasis often have a faster, greater efficacy and longer drug survival in patients who are naive to biologics [31, 32, 33]. The efficacy of brodalumab in bio-experienced patients may be explained with its unique mechanism of action that inhibits the IL17-receptor. This is in line with our cases 1 and 4, pivotal trials and real-world studies showing that brodalumab resulted effective also in patients previously treated with other biologics anti IL-17A. (amagine1-2-3) [34, 35].

Limitations

The limitations of our study are the retrospective study design and the size of the study population. However, the long observation period provide important evidence in a real-world setting.

Conclusions

Brodalumab has shown promising long-term efficacy in the management of moderate to severe plaque psoriasis, in a period up to 3 years. The data presented in our study contribute to the better understanding of brodalumab's success in real world. Consideration of baseline disease severity, comorbidities, and BMI can help in predicting patient adherence and optimizing the long-term management of moderate to severe plaque psoriasis with brodalumab.

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