



Gender Influence on Bimekizumab Response in Patients with Psoriasis: Results of a Real-World Multicenter Retrospective Study—IL PSO (Italian Landscape PSOriasis)

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ABSTRACT

Helena Gioacchini and Agnese Rossi equally contributed to the manuscript.

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Introduction: Several studies have demonstrated that psoriasis severity is generally greater in male patients, but it is unclear whether this gender difference may affect short-term therapeutic response. Notably, no studies have specifically investigated bimekizumab, a humanized, full-length IgG1 monoclonal antibody that acts as a dual inhibitor of interleukin (IL)-17A and IL-17F. **Methods:** This was a cross-sectional, observational, retrospective, multicenter analysis. A cohort of 318 patients with moderate to severe psoriasis, 229 male patients (median [IQR] age 35 [23–67] years) and 89 female patients (median [IQR] age 33 [20–68] years), were retrospectively evaluated for short-term response (16 weeks) to bimekizumab according to standard dosage (320 mg at weeks 0, 4, 8, 12, and 16, and every 8 weeks thereafter).

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Patients were assessed to evaluate whether gender differences in demographic and clinical characteristics can affect treatment response to standard dose of bimekizumab, during the first 16 weeks of treatment. Therapeutic outcomes were evaluated

by analyzing Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI) scores recorded in each patient at three consecutive time points: baseline (T0), after 4 weeks (T4), and after 16 weeks of treatment (T16).

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Results: Male patients showed more severe disease at baseline, compared to female patients ($p=0.01$). A significant reduction in disease severity was observed in both male and female patients after 16 weeks of treatment, but male patients showed a faster decrease in PASI score between baseline and week 4 of treatment compared to female patients ($p<0.001$). Nevertheless, by week 16, difference in PASI response and DLQI reduction between genders became less pronounced.

Conclusion: Although male patients exhibit greater disease severity at baseline compared to female patients, this does not result in a differential response to bimekizumab over the short term. Both male and female patients had equal probability of achieving complete or near-complete disease remission within the first 4 weeks of treatment, and both maintain this response status through week 16. The therapeutic benefit of bimekizumab may be due to the rapid dual inhibition of IL-17A and IL-17F, which may lead to consistent and robust clinical response across genders, regardless of baseline disease severity. Our results suggest a “gender severity-invariant effect” of bimekizumab, highlighting the treatment as rapidly effective in both genders, despite initial differences in disease severity.

Keywords: Psoriasis; Bimekizumab; Gender; Treatment; Real world evidence

Key Summary Points

Why carry out this study?

Psoriasis is an inflammatory and immune-mediated disease that is characterized by gender differences, with male individuals having more severe forms.

Literature data on gender differences in response to biological therapies are still pending and completely lacking in regard to bimekizumab.

Starting from the evidence that psoriasis is more severe in male patients, the study was conducted to evaluate whether this sex difference could penalize male patients in the clinical response to the standard dose of bimekizumab during the first 16 weeks of treatment.

What has been learned from the study?

Although male patients show greater disease severity at baseline compared to female patients, no differences in short-term response to bimekizumab have been detected.

Bimekizumab shows a “gender severity-invariant effect” on psoriasis, thus the treatment is equally effective in both genders over the short term, despite initial differences in disease severity.

INTRODUCTION

Psoriasis is a chronic, multifactorial skin disorder characterized by sharply demarcated erythematous plaques with micaceous scaling, typically located on extensor surfaces, the scalp, and the lumbosacral region [1]. Although prevalence estimates vary across studies, psoriasis affects both male and female patients at a similar rate, with an overall prevalence of around 4% [2].

Regarding the location of psoriatic lesions, some studies have identified gender differences, with nail psoriasis being more common in male patients, while palm-plantar pustulosis shows a distinct female predominance [3–6].

In terms of disease expression, female patients generally exhibit lower disease severity as measured by the Psoriasis Area Severity Index (PASI), but experience greater impairment in quality of life, as assessed by the Dermatology Life Quality Index (DLQI), compared to male patients [6–9].

The differences in disease severity between male and female patients may explain the ongoing disparity in the prescription of molecularly targeted drugs, which still tends to favor male patients. However greater disease severity could also represent a potential disadvantage for male patients, who may require more time to achieve a clinically satisfactory response compared to female patients.

However, conflicting results have been reported regarding treatment response based on gender [10, 11]. Specifically, no data are available on bimekizumab (BMK), a humanized, full-length IgG1 monoclonal antibody that acts as a dual inhibitor of interleukin (IL)-17A and IL-17F [12]. Therefore, the aim of our study is to evaluate whether sex differences in the demographic and clinical characteristics of patients with psoriasis may influence clinical response to a standard dose of BMK during the first 16 weeks of treatment.

METHODS

Study Design

The study is a cross-sectional, observational, retrospective, multicenter analysis conducted in accordance with the most recent revision of the

Declaration of Helsinki (2009/58). All enrolled patients had signed an informed consent to make their clinical data available for research purposes.

The study collected data from 318 patients with psoriasis currently undergoing treatment at several major Italian dermatological clinical centers: Ancona, Bari, Benevento, Bergamo, Brescia, Genova, Jesi, L'Aquila, Milano, Napoli, Roma, Torino, and Verona. Data were retrospectively collected from outpatients' and inpatients' medical records from September 2023 to September 2024 and recorded in an electronic medical record.

Ethical Approval

The study was approved by local ethical committees of each center, after first approval of the master ethics committee Campania 2 (see supplementary material).

Patient Population and Inclusion Criteria

Patients were included in the study if they were over 18 years of age, had moderate or severe psoriasis (PASI > 10 and/or body surface area (BSA) > 10 and/or DLQI > 10), had not responded to conventional topical and/or systemic treatments, and had received BMK for at least 16 weeks.

Patients who had received systemic treatments were included in the study only if they were re-treated after a washout period corresponding to 5 half-lives of the previously administered drug (for biologics, small molecules, and conventional systemic treatments). The decision to favor broad inclusion criteria responded to the need to identify a patient population as close as possible to that encountered in "real life" and representative of the entire spectrum of moderate to severe psoriasis.

At baseline, demographic (age, sex assigned at birth, as reported by physicians) and clinical data [age of psoriasis onset, body mass index (BMI), presence of psoriatic arthritis (PsA), metabolic comorbidities, previous systemic conventional and biological treatments for psoriasis, involvement of special areas (nails,

scalp, genital, face, and palmoplantar regions)] were assessed.

Treatment and Clinical Evaluation of Included Patients

Patients with psoriasis received BMK at standard doses (320 mg at week 0, 4, 8, 12, 16, and every 8 weeks thereafter). Therapeutic outcomes were evaluated by analyzing PASI and DLQI scores recorded in each patient at three consecutive time points: baseline (T0), after 4 weeks (T4), and after 16 weeks of treatment (T16).

Data about potential safety issues and adverse events (AEs) as well as reasons for possible discontinuation of BMK were recorded at each follow-up visit as well.

Statistical Analysis

Qualitative variables were summarized using absolute and percentage frequencies, while quantitative variables were reported as the median and interquartile range (1st and 3rd quartile). Comparisons were made respectively through the Wilcoxon sum-rank test for quantitative variables and the chi-square test or Fisher's exact test for qualitative variables, if the number was less than 5 units. The *p* values were adjusted for multiple tests with the Benjamini–Hochberg method.

Areas of special involvement such as nails, scalp, genital, face, and palmoplantar regions were categorized as special areas. A mixed-effects model for repeated measures was used, with PASI and DLQI scores as dependent variables, and time, gender, and BMI as explanatory variables.

The model was adjusted for the initial disease manifestation (arthritis, special areas), presence of metabolic syndromes, and number of previous systemic/biological treatments.

The model analyzed interactions with gender and time to evaluate the possibility of a different effect between male and female patients, types of psoriasis of first manifestation, presence of metabolic syndrome, presence of a new systemic treatment, and presence of a new biological

treatment; to account for repeated measures over time, patient identifier was used as a random effect in the model.

RESULTS

A total of 318 patients, 229 male patients (median [IQR] age 35 [23–67] years) and 89 female patients (median [IQR] age 33 [20–68] years) were treated for 16 weeks.

Although the proportion between the different psoriasis severity classes (mild, moderate, severe) was comparable between genders, male patients had higher PASI ($p=0.01$) with more severe psoriasis than female patients at baseline (Table 1).

Statistically significant difference in BMI ($p<0.01$) was evident at baseline between male and female patients, as expected (Table 1). No other significant differences were evident at baseline between male and female patients for age, arthritis, involvement of special areas, prevalence of metabolic comorbidities, previous exposure to systemic and biologics treatments, failure to previous biologic treatments, and impact on quality of life (Table 1). BMK resulted in significant reductions in PASI and DLQI scores over 16 weeks of treatment in the entire patient population (Fig. 1), both in male and female patients (Figs. 2 and 3).

An average PASI reduction of 12 ($p<0.001$) and 14 points ($p<0.001$), at 4 and 16 weeks, from baseline respectively, was observed. Gender, previous exposure to other biologics, and arthritis were factors associated with treatment response (Table 2).

Similarly, at 4 weeks, DLQI improved by 14 points ($p<0.001$) and by 16 points ($p<0.001$) after 16 weeks. Metabolic syndrome and involvement of special area were the only factors associated with therapeutic response to BMK at week 4 and 16 (Table 3).

A notable decrease was found in disease severity for both male and female patients over time, but it seems that male patients experienced a faster reduction in PASI score between baseline and 4 weeks of treatment, compared to female

Table 1 Demographic and clinical characteristics of treated patients at baseline

Variable	Total (<i>n</i> = 318)	Female (<i>n</i> = 89)	Male (<i>n</i> = 229)	<i>p</i> value (adj)
BMI, kg/cm ² , median (IQR)	22.7 (20.2; 25.4)	19.7 (18.2; 23.3)	23.1 (21.6; 26.4)	< 0.001
Age, years, median (IQR)	35 (23; 68)	33 (20; 68)	35 (23; 67)	0.999
Clinical manifestations, <i>n</i> (%)				
Arthritis	39 (12.3)	12 (13.5)	27 (11.8)	0.999
Nail involvement	58 (18.2)	11 (12.4)	47 (20.5)	0.999
Scalp	128 (40.3)	38 (42.7)	90 (39.3)	0.999
Genital	59 (18.6)	17 (19.1)	42 (18.3)	0.999
Face	8 (2.5)	1 (1.1)	7 (3.1)	0.999
Palm-plantar	16 (5.0)	8 (9.0)	8 (3.5)	0.999
Comorbidities, <i>n</i> (%)				
Hypertension	94 (29.6)	21 (23.6)	73 (31.9)	0.999
Hyperlipidemia	45 (14.2)	14 (15.7)	31 (13.5)	0.999
Diabetes	24 (7.6)	7 (7.9)	17 (7.4)	0.999
Neoplastic disease history	11 (3.6)	5 (5.6)	6 (2.6)	0.999
Liver steatosis	8 (2.5)	2 (2.2)	6 (2.6)	0.999
None	181 (56.9)	52 (58.4)	129 (56.3)	0.999
Naive to systemic treatments, yes, <i>n</i> (%)	69 (21.7)	15 (16.9)	54 (23.6)	0.999
Cyclosporine, yes, <i>n</i> (%)	135 (42.5)	41 (46.1)	94 (41.1)	0.999
Methotrexate, yes, <i>n</i> (%)	111 (34.9)	34 (38.2)	77 (33.6)	0.999
PUVA, yes, <i>n</i> (%)	78 (24.5)	23 (25.8)	55 (24.0)	0.999
Acitretin, yes, <i>n</i> (%)	39 (12.3)	10 (11.2)	29 (12.7)	0.999
Naive biologic treatments, yes, <i>n</i> (%)	183 (57.6)	44 (49.5)	139 (60.3)	0.999
Biologics failure, yes, <i>n</i> (%)	142 (44.7)	50 (56.2)	92 (40.2)	0.299
PASI at baseline, median (IQR)	15 (11.2; 20.0)	13.0 (10.0; 18.0)	16.0 (12.0; 22.0)	0.019
PASI baseline stratified, <i>n</i> (%)				
≤ 10	70 (22.0)	28 (31.5)	42 (18.3)	0.150
11–19	136 (42.8)	40 (44.9)	96 (41.9)	
≥ 20	112 (35.2)	21 (23.6)	91 (39.8)	
DLQI baseline, median (IQR)	18.0 (11.0; 23.0)	18.0 (13.0; 22.0)	18.0 (10.0; 23.0)	0.999
DLQI baseline stratified, <i>n</i> (%)				
≤ 5	48 (15.1)	7 (7.9)	41 (17.9)	0.999
6–9	11 (3.5)	3 (3.4)	8 (3.5)	
≥ 10	259 (81.4)	79 (88.7)	180 (78.6)	

Data are presented as median (IQR) for continuous variables and number (percentage) for categorical variables. *p* values were adjusted for multiple comparisons

BMI body mass index, *PASI* Psoriasis Area and Severity Index, *DLQI* Dermatology Life Quality Index, *IQR* interquartile range (1st–3rd quartile)

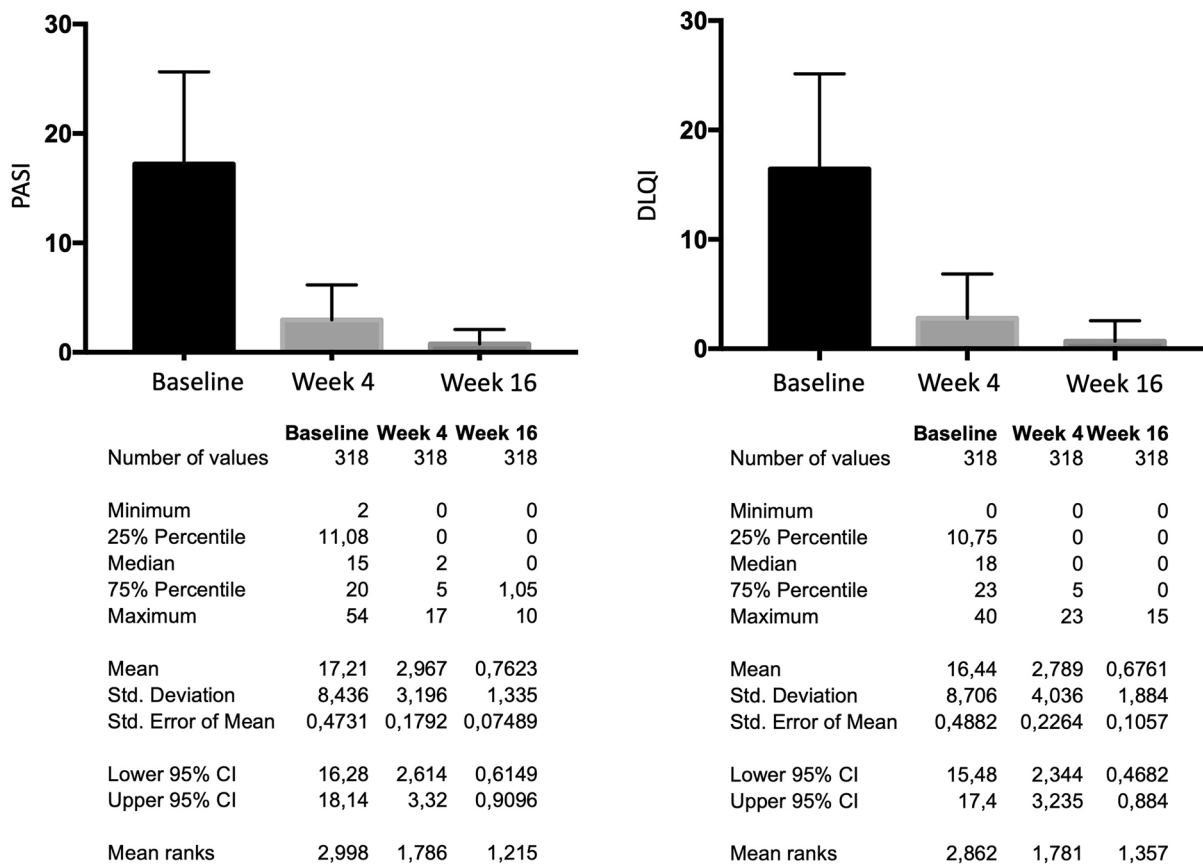


Fig. 1 PASI (Psoriasis Area and Severity Index) and DLQI (Dermatology Life Quality Index) reduction in whole group of patients, according to time endpoints (week 4 and week 16)

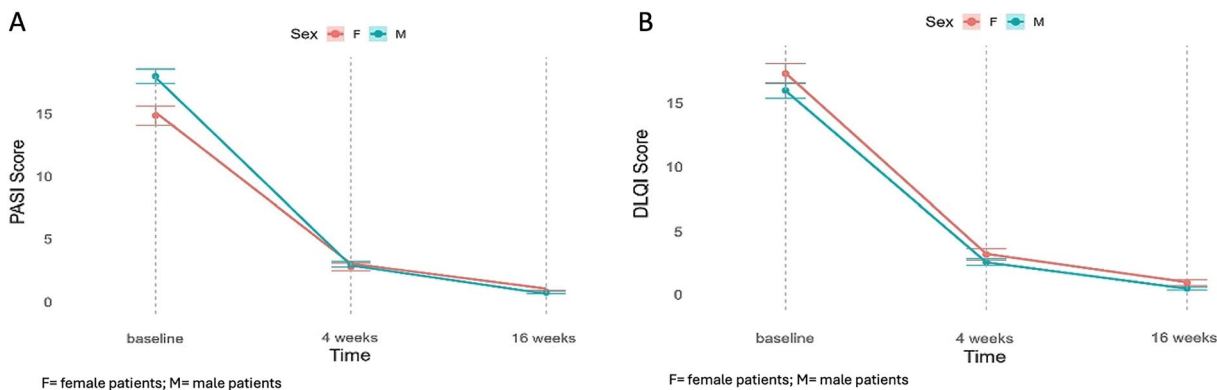


Fig. 2 PASI (Psoriasis Area and Severity Index) and DLQI (Dermatology Life Quality Index) reduction in 16 weeks treated patients with bimekizumab according to gender



Fig. 3 62-year-old male (M) patient and 60-year-old female patient (F) at baseline (a, c) and after 4 weeks of bimekizumab (b, d). The patients provided written informed consent for the publication of these images

patients. Nevertheless, by 16 weeks, both genders show substantial clinical improvement, with the difference in the rate of reduction of PASI and DLQI between genders becoming less pronounced.

No treated patients experienced serious drug-related adverse events. The following adverse events noted in the EU Summary of Product Characteristics (SmPC) were evaluated regarding frequency, drug-relatedness, severity,

Table 2 Factors influencing PASI in patients treated with BMK over the first 16 weeks

Variables	<i>b</i>	95% CI	<i>p</i> value
Time point (vs baseline)			
4 weeks	− 12.12	− 13.54; − 10.70	< 0.001
16 weeks	− 14.12	− 15.55; − 12.70	< 0.001
Sex (male vs female)	2.80	1.52; 4.08	< 0.001
BMI (kg/m ²)	0.005	− 0.003; 0.14	0.213
Arthritis (yes vs no)	− 1.53	− 2.94; − 0.13	0.035
Special area involvement (yes vs no)	0.23	− 0.51; 0.97	0.554
Metabolic syndrome (yes vs no)	0.32	− 0.44; 1.08	0.414
Previous systemic treatment (yes vs no)	− 0.72	− 1.61; 0.17	0.118
Naïve to biologic treatment (yes vs no)	1.74	1.00; 2.48	< 0.001
Time point × Sex (male vs female)			
4 weeks vs baseline	− 2.95	− 4.62; − 1.27	0.001
16 weeks vs baseline	− 3.22	− 4.90; − 1.55	< 0.001

The *b* coefficient represents the estimated change in PASI associated with each variable. A negative *b* value indicates a reduction in PASI, while a positive *b* value indicates an increase in PASI. *p* values < 0.05 are considered statistically significant
BMK bimekizumab, *BMI* body mass index

Table 3 Factors influencing DLQI in patients treated with BMK over the first 16 weeks

Variables	<i>b</i>	95% CI	<i>p</i> value
4 weeks vs baseline	− 13.65	− 14.45; − 12.85	< 0.001
16 weeks vs baseline	− 15.76	− 16.56; − 14.96	< 0.001
Sex (male vs female)	− 0.85	− 1.81; 0.10	0.063
BMI, kg/cm ²	− 0.04	− 0.14; 0.05	0.38
Arthritis (yes vs no)	− 1.14	− 2.72; 0.45	0.165
Special area (yes vs no)	− 0.86	− 1.7; 0.002	0.047
Metabolic syndrome (yes vs no)	1.19	0.34; 2.05	0.007
Systemic treatment (yes vs no)	0.37	− 0.64; 1.37	0.482
Naïve biologic treatment (yes vs no)	0.54	− 0.3; 1.38	0.212

The *b* coefficient indicates the change in DLQI associated with each factor, and the *p* value represents statistical significance. A *p* value < 0.05 indicates a statistically significant factor
BMK bimekizumab, *BMI* body mass index

seriousness, duration, and timing of onset: oral/oropharyngeal candidiasis, herpes simplex infection, folliculitis, neutropenia, fatigue, headache, diarrhea, nausea, flatulence, abdominal pain, upper abdominal pain, injection site reaction, eczema. Of 318 patients, 64 (20%) experienced one or more adverse events. All patients (100%) continued taking BMK.

Among the adverse events evaluated, none was reported as serious and none resulted in discontinuing treatment; most were mild or moderate, reported only once, not considered BMK-related, and did not lead to drug discontinuation. Furthermore, no differences in the type, severity, and speed of onset of adverse events were observed on the basis of gender.

DISCUSSION

Our study provides evidence that gender can influence the severity of psoriasis, with male patients exhibiting more severe disease compared to female patients. This finding aligns with several previous studies reporting that male patients generally experience more severe psoriasis, as assessed by PASI [6–9]. However, existing data from the literature show conflicting findings regarding gender differences in therapeutic response to biologics, with some studies showing weak evidence in favor of female patients for IL-17 and IL-23 inhibitors [10, 11].

Given these discrepancies, it is reasonable to hypothesize that male patients may face challenges in achieving a clear or almost clear disease status with certain biologics compared to female patients. Despite this, most patients in our cohort were able to achieve clear or almost clear status after just 4 weeks of therapy, regardless of gender.

In our study male patients exhibited higher disease severity at baseline and a faster decrease in PASI score from baseline to 4 weeks than female patients. Moreover, our data shows that both male and female patients achieved complete or nearly complete disease remission within 4 weeks of BMK treatment, and both groups maintained this response through 16 weeks. The initial faster reduction in PASI scores among male patients suggests that they

may experience a more rapid early response to BMK. The higher baseline severity of male patients could represent a disadvantage, but also the ideal condition to highlight the efficacy of a drug that acts profoundly on the molecular mechanisms supporting psoriasis and is able to eliminate the clinical disadvantage related to gender. Furthermore, the difference in early response could reflect gender-related differences in immune pathways or inflammatory mediators, which should be further investigated.

In the existing literature, there are only a few studies specifically addressing gender differences in response to biologic treatments in psoriasis. Colombo et al. analyzed a cohort of patients with psoriasis undergoing biologic therapies, including secukinumab, ustekinumab, adalimumab, ixekizumab, etanercept, certolizumab, and golimumab, and found that the response to biologic treatments was generally high by week 16, with no gender differences observed. Moreover, the study showed that there were no clinically significant differences in total PASI 75/90/100 and BSA response rates at any time point, and the sustained responder rates were similar between genders. Interestingly, male patients exhibited a numerically slightly higher proportion of responders for both PASI and BSA, suggesting that, at least for some biologics, male patients may demonstrate a marginally better response [13].

Contrastingly, a study by Van Voorhees et al. [14] demonstrated that female sex was significantly associated with a decreased likelihood of achieving a response to anti-tumor necrosis factor alpha (TNF α) therapy compared to male sex. These findings were supported by studies from De Simone et al. [15] and Hojgaard et al. [16], who also observed a gender-related difference in therapeutic response to anti-TNF α treatments. These contrasting results highlight the complexity of the relationship between gender and treatment outcomes, underscoring the need for further research to understand the factors that drive these differences, including the specific biologic agent used, disease severity, and other patient characteristics. The impact of gender on therapeutic response to drugs against molecular targets may be dependent from genetic background of patients, particularly single nucleotide

polymorphisms (SNPs) may affect clinical features of multifactorial diseases like psoriasis, as already demonstrated from studies on other diseases systemic multifactorial diseases than psoriasis [17, 18]. In this regards, IL-20 gene polymorphisms should have a role in determining susceptibility to plaque-type psoriasis both in male and female patients; the possible role of the studied SNPs in the regulation of the expression of IL-20 is unknown yet and needs further studies.

Moreover, difference in treatment response could be related also to sex differentiation in epigenetic mechanisms of gene upregulation, thus future research directions will move towards sex-related gene expression profile of intracellular signaling pathways underlying psoriasis, and the complex relationship between expressing disease-specific genes and genetic networks.

These networks could be useful to clarify the complex connections between gender, genetics, molecular patterns, and clinical therapeutic outcomes in patients with psoriasis [19].

It is interesting to note gender disparity in the available BMK data, with significantly more data from male (229) compared to female patients (89). While the prevalence of psoriasis is similar between the sexes, male patients often present with more severe disease, which may make biologics a more apparent treatment option for them. In contrast, female patients, despite experiencing significant disease burden in terms of quality of life, typically exhibit milder clinical manifestations, which may result in a lower perceived need for biologic treatment [2, 6–9]. Additionally, precautions for use of biologics during pregnancy or in women planning to conceive may result in women receiving these treatments less frequently than men, as physicians may opt for alternative therapies to avoid potential risks. This, in turn, can further reduce the representation of female patients in real-life clinical studies, as their treatment options become more limited.

This gender-based disparity in disease severity and treatment decisions is not unique to psoriasis but can also be observed in other chronic skin conditions, such as

atopic dermatitis. A study by Marani et al. [20] found that, like psoriasis, male patients with AD typically experience more severe disease and require more intensive treatments, while female patients often have milder disease and fewer treatment needs. These patterns highlight the significant role gender plays in determining the course of chronic skin conditions and their management.

Our results confirm efficacy and safety of BMK in a real-life setting. To our knowledge, this is the first study to evaluate gender differences in response to BMK. Our results suggest that both male and female patients benefit equally from BMK treatment in terms of efficacy and safety. The therapeutic benefit of BMK may be due to the rapid dual inhibition of IL-17A and IL-17F, which may lead to a consistent and robust clinical response across genders, independent of baseline disease severity. This results in a “gender severity-invariant effect” of BMK, suggesting that the treatment is equally effective in both sexes despite initial differences in disease severity.

However, as with all studies, there are some limitations that must be considered. The retrospective nature of our study and the relatively small sample size, particularly for female patients, may introduce potential biases related to unequal sample size for the male vs female participants that need to be addressed in future research. Additionally, while our study focused on short-term responses to BMK, long-term studies are necessary to assess whether the observed therapeutic benefit persists over a more extended treatment period in both sexes. Future research should also investigate other factors, such as genetic differences, hormonal influences, and comorbidities, that could potentially modulate the response to biologic therapies like BMK.

CONCLUSIONS

Our study provides valuable evidence that BMK offers a reliable and consistent therapeutic option for patients with psoriasis, independent of gender or disease severity. Further long-term

studies are needed to determine whether these findings hold over a more extended treatment period, and to explore the potential mechanisms underlying the observed gender-neutral effect of BMK. These insights could ultimately lead to more personalized and effective treatment strategies for patients with psoriasis.

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Conflict of Interest. Maria Esposito: Has served as a speaker/consultant for Abbvie, Amgen, Almirall, Eli Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Sanofi, uCB. Maria Concetta Fagnoli: Has served as a consultant/advisor, received speaker honoraria and/or grants, and/or participated as an investigator for Amgen, Almirall, Abbvie, Boehringer Ingelheim, BMS, Galderma, Kyowa Kyrin, Incyte, Leo Pharma, Pierre Fabre, uCB, Lilly, Pfizer, Janssen, MSD, Novartis, Sanofi, Regeneron, Sun Pharma, Takeda. Matteo Megna: Has acted as a speaker or consultant for Abbvie, Amgen, Almirall, Eli Lilly, Novartis, Janssen, uCB, Leo Pharma. Anna Balato: Has acted as a speaker and/or consultant for Abbvie, Almirall, Amgen, Boehringer Ingelheim, Bristol-Meyer-Squibb,

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Ethical Approval. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. The ethics committee of UNIVPM approved the study protocol and all enrolled participants provided written informed consent. The patients in this manuscript have given written informed consent to publication of their case details. The study was approved by local ethical committees of each center (see supplementary material).

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