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ORIGINAL RESEARCH

Real-World Data on Brodalumab Treatment in Patients with Moderate-to-Severe Plaque Psoriasis: An Observational Study from the Czech Republic BIOREP Registry

Martina Kojanova · Barbora Turkova · Spyridon Gkalpakiotis · Petra Cetkovska · Jorga Fialova · Tomas Dolezal · Alena Machovcova · Eydna Didriksen Apol · the BIOREP Study Group

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ABSTRACT

Introduction: The aim of this observational, multicenter study was to assess the real-world use of brodalumab for the treatment of moderate-to-severe plaque psoriasis in patients in the Czech Republic, using data from the BIOREP registry.

Methods: The study included 273 patients aged ≥ 18 years with moderate-to-severe psoriasis who received brodalumab. Endpoints were drug survival (time from treatment initiation to discontinuation), effectiveness [Psoriasis Area and Severity Index (PASI)], and health-related quality-of-life [Dermatology Life Quality Index (DLQI)].

Results: Predicted drug survival probability was 92.4% [95% confidence interval (CI): 89.1, 95.7%] at 6 months and 84.2% (95% CI 79.5, 89.1%) at 12 months; this was maintained at 24 months [80.4% (95% CI 74.5, 86.8%)]. Younger age, higher body mass index, and no previous biologic treatment were significantly associated with longer drug survival. Absolute PASI ≤ 3 after 3 months was achieved by 89.8% of patients; 92.4%, 77.8%, and 59.1% reached PASI 75, PASI 90, and PASI 100, respectively. After 12 months, 96.5% of 141 patients had an absolute PASI ≤ 3. The proportion of patients achieving DLQI 0/1 was 87.3% at 12 months.

Conclusion: This study demonstrated high and sustained drug survival with high rates of skin clearance and improved quality of life in patients with relatively severe disease treated with brodalumab. Improvements were observed as early as 3 months post-treatment initiation and were sustained for up to 24 months in a real-life setting.

M. Kojanova (✉) · J. Fialova
Department of Dermatovenereology, First Faculty of Medicine and General University Hospital, Charles University, Prague, Czech Republic
e-mail: martina.kojanova@vfn.cz

B. Turkova · T. Dolezal
Value Outcomes, Prague, Czech Republic

S. Gkalpakiotis
Department of Dermatovenereology, Third Faculty of Medicine, Charles University and Kralovske Vinohrady University Hospital, Charles University, Prague, Czech Republic

P. Cetkovska
Department of Dermatovenereology, Faculty of Medicine in Pilsen, Charles University, Prague, Czech Republic

A. Machovcova
Department of Dermatovenereology, University Hospital Motol, Prague, Czech Republic

E. D. Apol
LEO Pharma A/S, Ballerup, Denmark

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Key Summary Points

In several Phase III trials, brodalumab was more effective than placebo and ustekinumab in reducing the area and severity of moderate-to-severe plaque psoriasis. It also demonstrated efficacy in difficult-to-treat nail and scalp psoriasis.

Several recent network meta-analyses comparing biological agents suggest that brodalumab may be like ixekizumab and superior to several anti-tumor necrosis factor biologics in Psoriasis Area and Severity Index (PASI) 50,75, 90, and 100 responses.

Given patient selection bias in clinical trials, it is necessary to confirm that these data can be extrapolated to routine clinical practice in the Czech Republic in a real-world setting, with a broad range of patients; patient-reported outcomes give substantial insights into treatment with modern biologics outside of a clinical trial setting.

Using real-world data from the BIOREP registry, we have shown that brodalumab treatment has led to sustained drug survival, high rates of skin clearance, and improved quality of life as early as 3 months from treatment initiation in a broad range of patients.

These data confirm differences in responses between real-life and clinical trials, in particular higher response rates (PASI 100) in real-world settings in short-term observation, and the proportion of patients achieving better PASI scores in a long-term evaluation, confirming brodalumab as an effective treatment in a broad range of patients with moderate-to-severe psoriasis.

INTRODUCTION

Psoriasis is a common chronic inflammatory disease with a substantial negative impact on health-related quality of life, affecting physical and psychological well-being and interfering with daily activities [1–3]. The advent of biological treatments for moderate-to-severe plaque psoriasis resulted in significantly improved outcomes, and complete skin clearance is now an attainable goal for many patients [2, 4]. The first biological therapies for plaque psoriasis were the tumor necrosis factor-α inhibitors, infliximab, adalimumab, and etanercept, followed by the interleukin (IL)-12/23 inhibitor, ustekinumab [5]. More recently approved biological therapies include the IL-23 inhibitors, guselkumab, tildrakizumab, and risankizumab [4], the IL-17 inhibitors, secukinumab and ixekizumab, which bind only to the IL-17A ligand, and brodalumab, which targets the IL-17-receptor subunit A (IL-17RA) [3, 6].

The fully human anti-IL-17RA brodalumab is approved for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy [7]. The efficacy and safety of brodalumab in patients with moderate-to-severe psoriasis has been established in three large, phase 3 trials in which brodalumab was compared with placebo and ustekinumab (AMAGINE-1, AMAGINE-2, and AMAGINE-3) [8–10], as well as in a phase 4 trial versus oral administrations of fumaric acid esters [11].

Patients included in clinical studies may not be fully representative of those seen in clinical practice, due to trial eligibility criteria which exclude many patients [12]. Real-world evidence provides valuable insights into the effectiveness and safety of treatments in everyday clinical practice in a broad range of patients, including groups typically excluded from clinical trials [13]. To date, real-world evidence on the use of brodalumab is limited [14–17]. The aim of this observational, multicenter study was to assess

drug survival, skin clearance, and health-related quality of life with the real-world use of brodalumab for moderate-to-severe plaque psoriasis in adult patients in the Czech Republic, using data from the BIOREP registry.

METHODS

Study Design and Patient Population

BIOREP is a nationwide registry, established in May 2005 (updated in 2011 and 2018) and supervised by the Czech Dermatovenereology Society, with the primary purpose of monitoring the safety of biologics in patients with psoriasis in the Czech Republic. The BIOREP database records drug safety and effectiveness, demographic data, Psoriasis Area and Severity Index (PASI) scores, Dermatology Life Quality Index (DLQI) scores, and comorbidities.

In the Czech Republic, biological therapy is administered at 31 specialized centers, 29 of which are included in the BIOREP registry. Biological therapy is initiated in patients with moderate-to-severe psoriasis at these centers when two of four conventional systemic treatments (acitretin, methotrexate, cyclosporine, and narrowband UVB phototherapy) cannot be used, due to intolerance, lack of efficacy, or the presence of contra-indications. Eligible patients in this analysis were adults aged ≥ 18 years who initiated brodalumab therapy at enrollment in BIOREP before February 2021 and had at least one follow-up visit at 3, 6, 12, 18, and/or 24 months. The decision to use brodalumab was at the discretion of the treating dermatologist. The study was conducted in accordance with the Helsinki Declaration of 1964 and all subsequent amendments, and all patients provided written informed consent for their data to be included in the BIOREP registry. Patient-level data used for this analysis were de-identified, and Institutional Review Board approval was not required for this study. Permission to access/use data from the BIOREP registry was obtained.

Patient Baseline Characteristics

Baseline data were collected for the following patient characteristics: age, sex, body mass index (BMI), PASI, and DLQI, previous treatment regimen and line of therapy, reason for switching to brodalumab, and number and type of comorbidities. Data for all variables were summarized descriptively.

Study Endpoints and Analysis

Study endpoints were drug survival, effectiveness (PASI), and health-related quality of life (DLQI). Drug survival was defined as time from initiation to failure of brodalumab (brodalumab treatment discontinuation, defined as termination, re-induction, or switching to a different biological therapy) in the full analysis set. Patients were censored if they were lost to follow-up or if data were not available for follow-up visits. Reasons for discontinuing brodalumab treatment were recorded. A sensitivity analysis of the primary endpoint of drug survival was also performed, which assessed time from initiation to failure of brodalumab or brodalumab dose adjustment or add-on of psoriasis therapy in the full analysis set.

Drug survival was also analyzed by previous biologic therapy (naïve, i.e., never previously treated with biologic, or experienced, i.e., had received biologic treatment prior to initiating brodalumab), age group (18–35, 36–50, 51–65, or > 65 years), sex, smoking status (current smoker, ex-smoker, or never-smoker), presence of psoriatic arthritis at baseline (yes or no), and BMI category [< 18.5 (underweight), 18.5–24.9 (normal), 25.0–29.9 (overweight), or ≥ 30.0 kg/m^2 (obese)]. Drug survival analysis was conducted by Kaplan–Meier estimation for all patients and by subgroups.

A Cox proportional hazards model was developed to investigate the association between time to discontinuation of brodalumab and potential predictor variables at the time of brodalumab initiation [i.e., age, BMI, previously naïve to biological therapy (yes or no), and presence of psoriatic arthritis at baseline (yes or no)].

Effectiveness and quality-of-life endpoints included the proportions of patients achieving an absolute PASI score of ≤ 3, PASI 75, PASI 90, and PASI 100, and DLQI 0/1 at 3 months [patients with ≥ 3 months of follow-up (short-term analysis set)] and 12 months [patients with ≥ 12 months of follow-up (long-term analysis set)]; mean changes in PASI and DLQI at 3 months (short-term analysis set); and time to response as absolute PASI ≤ 3, PASI 75, and PASI 90 (long-term analysis set). Windowing analyses were conducted for absolute PASI, PASI and DLQI for baseline (week 0), 3 months (weeks 10–18), 6 months (weeks 18–39), 12 months (weeks 39–65), 18 months (weeks 65–91), and 24 months (weeks 91–117) after treatment initiation. All analyses were conducted as observed. In cases of multiple values within a time window, the value recorded closest to the defined timepoint (i.e., 3, 6, 12, 18, or 24 months) was selected.

Ethics

The study was conducted in accordance with good pharmacoepidemiology practices by research groups belonging to the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP), in accordance with the ENCePP Code of Conduct and, if possible, under the ENCePP Study Seal. Patient-level data used for this analysis were de-identified, and Institutional Review Board approval was not required for this study. Permission to access/use data from BIOREP registry was obtained.

RESULTS

Baseline Characteristics

Demographics and baseline characteristics of the study population, overall and stratified by prior exposure to biological therapy for psoriasis, is shown in Table 1. The study included 273 patients with moderate-to-severe psoriasis who had received brodalumab. Patients were predominantly males (66.3%). Mean age at psoriasis diagnosis was 25.5 ± 13.6 years, and mean time from diagnosis to initiation of brodalumab therapy was 21.5 ± 12.8 years. Mean BMI was 29.8 ± 6.2 kg/m^2 and 44.9% of patients had obesity, with a BMI of ≥ 30 kg/m^2. Almost half of patients had a family history of psoriasis (48.4%). At baseline, mean PASI score was 17.2 ± 7.1, mean DLQI was 14.4 ± 6.7, and mean body surface area (BSA) was 24.7 ± 16.5.

Baseline comorbidities were reported in 68.5% of patients, 37.7% of whom had more than one comorbidity. The most frequently reported comorbidities were hypertension (35.2%), dyslipidemia (25.6%), psoriatic arthritis (16.5%), and diabetes (11.7%).

Over half of all patients were biologic naïve (n = 156) before initiating brodalumab therapy. Of the biologic-experienced patients (n = 117), most initiated brodalumab as second-line therapy (46.2%, n = 54); 28.2% (n = 33), 14.5% (n = 17), and 11.1% (n = 13) initiated brodalumab as third line, fourth line, or after more than four lines of therapy, respectively. Antitumor necrosis factor-α was the most common previous biological therapy (54.7%; adalimumab 34.2%, etanercept 16.2%, certolizumab pegol 3.4%, infliximab 0.9%), followed by anti-IL-17As (28.2%; secukinumab 17.1%, ixekizumab 11.1%), anti-IL-23/12 (ustekinumab 15.4%), and anti-IL-23s (1.7%; guselkumab 0.9%, risankizumab 0.9%).

Drug Survival

At the time of analysis, 41 patients (15.0%) had stopped brodalumab treatment (Table 1). Six patients (2.2%) discontinued due to adverse events (five of these patients switched to another biologic; one patient with latent tuberculosis continued brodalumab treatment after 3 months). Other reasons for discontinuation were loss of effectiveness (31 patients; 11.3%); pregnancy (one patient; 0.4%), patient non-cooperation (one patient; 0.4%), and other (two patients, 0.7%).

Predicted drug survival probability was 92.4% [95% confidence interval (CI) 89.1, 95.7%] at 6 months and 84.2% (95% CI 79.5, 89.1%) at 12 months; this was maintained at 24 months [0.4% (95% CI 74.5, 86.8%)]

Table 1 Patient demographics and clinical characteristics at baseline, overall and stratified by prior exposure to biological therapy (full analysis set)

Parameter	Biologic naïve (*n* = 156)	Biologic experienced (*n* = 117)[a]	Total (*N* = 273)[a]
Sex			
Male	106 (67.9)	75 (64.1)	181 (66.3)
Female	50 (32.1)	42 (35.9)	92 (33.7)
Age			
At diagnosis	24.6 ± 13.2	26.7 ± 14.1	25.5 ± 13.6
At brodalumab initiation	43.7 ± 12.4	51.2 ± 13.6	47.0 ± 13.5
Duration of time from diagnosis to brodalumab initiation	19.2 ± 11.7	24.7 ± 13.7	21.5 ± 12.8
Family history of psoriasis			
Yes	76 (48.7)	56 (47.9)	132 (48.4)
No	80 (51.3)	61 (52.1)	141 (51.6)
Weight, kg	92.7 ± 22.0	92.4 ± 18.9	92.6 ± 20.7
Body mass index, kg/m^2			
Mean (SD)	29.6 ± 6.7	30.1 ± 5.5	29.8 ± 6.2
Underweight (< 18.5)	1 (0.6)	0 (0.0)	1 (0.4)
Normal (18.5 to < 25.0)	39 (25.0)	22 (18.6)	61 (22.3)
Overweight (25.0 to < 30.0)	53 (34.0)	36 (30.5)	89 (32.5)
Obese (≥ 30.0)	63 (40.4)	60 (50.8)	123 (44.9)
Type of psoriasis			
Plaque	156 (100.0)	117 (100.0)	273 (100.0)
Inverse	14 (9.0)	5 (4.3)	19 (7.0)
Nail	52 (33.3)	12 (10.3)	64 (23.4)
Presence of psoriatic arthritis			
Yes	23 (14.7)	22 (18.8)	45 (16.5)
No	129 (82.7)	95 (81.2)	224 (82.1)
Missing	4 (2.6)	0 (0.0)	4 (1.5)
Type of psoriatic arthritis			
Asymmetric oligoarticular arthritis	4 (17.4)	4 (18.2)	8 (17.8)
Distal interphalangeal arthropathy	4 (17.4)	1 (4.5)	5 (11.1)
Unspecified	9 (39.1)	11 (50.0)	20 (44.4)
Spondylitis	2 (8.7)	2 (9.1)	4 (8.9)

Table 1 continued

Parameter	Biologic naïve ($n = 156$)	Biologic experienced ($n = 117$)[a]	Total ($N = 273$)[a]
Symmetrical polyarthritis	4 (17.4)	3 (13.6)	7 (15.6)
Missing	0 (0.0)	1 (4.5)	1 (2.2)
Presence of latent tuberculosis	4 (2.6)	0 (0)	4 (1.5)
Clinical parameters			
PASI	18.3 ± 6.6	15.8 ± 7.5	17.2 ± 7.1
DLQI	15.7 ± 6.7	12.6 ± 6.1	14.4 ± 6.7
BSA	28.8 ± 18.0	19.1 ± 12.3	24.7 ± 16.5
Presence of comorbidities[b]			
Yes	96 (61.5)	91 (77.8)	187 (68.5)
No	56 (35.9)	25 (21.4)	81 (29.7)
Missing	4 (2.6)	1 (0.9)	5 (1.8)
Comorbidity categories[b]			
Cardiovascular diseases	47 (30.1)	52 (44.4)	99 (36.3)
Pulmonary diseases	10 (6.4)	6 (5.1)	16 (5.9)
Metabolic/endocrine disorders	53 (34.0)	54 (46.2)	107 (39.2)
Gastrointestinal and hepatic disease	25 (16.0)	6 (5.1)	31 (11.4)
Urological/renal diseases	7 (4.5)	3 (2.6)	10 (3.7)
Musculoskeletal disorders	6 (3.8)	0 (0.0)	6 (2.2)
Malignancy	4 (2.6)	5 (4.3)	9 (3.3)
Chronic infectious diseases	0 (0.0)	2 (1.7)	2 (0.7)
Ocular diseases	2 (1.3)	0 (0.0)	2 (0.7)
Neurological diseases	5 (3.2)	2 (1.7)	7 (2.6)
Psychiatric disorders	7 (4.5)	7 (6.0)	14 (5.1)
Dermatological diseases	4 (2.6)	3 (2.6)	7 (2.6)
Hematologic diseases	4 (2.6)	3 (2.6)	7 (2.6)
Other	9 (5.8)	46 (39.3)	55 (20.1)
Number of comorbidities[b]			
Mean (SD)	1.2 ± 1.4	1.6 ± 1.3	1.4 ± 1.4
0	61 (39.1)	26 (22.2)	87 (31.9)
1	48 (30.8)	35 (29.9)	83 (30.4)
2	23 (14.7)	27 (23.1)	50 (18.3)

Table 1 continued

Parameter	Biologic naïve (*n* = 156)	Biologic experienced (*n* = 117)[a]	Total (*N* = 273)[a]
3	16 (10.3)	21 (17.9)	37 (13.6)
4	2 (1.3)	5 (4.3)	7 (2.6)
5	3 (1.9)	2 (1.7)	5 (1.8)
6	3 (1.9)	0 (0.0)	3 (1.1)
7	0 (0.0)	1 (0.9)	1 (0.4)
Selected comorbidities[b]			
Psoriatic arthritis	23 (14.7)	22 (18.8)	45 (16.5)
Latent tuberculosis	4 (2.6)	0 (0.0)	4 (1.5)
Hypertension	45 (28.8)	51 (43.6)	96 (35.2)
Dyslipidemia	34 (21.8)	36 (30.8)	70 (25.6)
Diabetes mellitus	16 (10.3)	16 (13.7)	32 (11.7)
Hepatopathy	13 (8.3)	2 (1.7)	15 (5.5)
Depression	6 (3.8)	7 (6.0)	13 (4.8)
Hypothyroidism	10 (6.4)	2 (1.7)	12 (4.4)
Hyperthyroidism	1 (0.6)	0 (0.0)	1 (0.4)
Coronary artery disease	2 (1.3)	5 (4.3)	7 (2.6)
Malignancy	4 (2.6)	5 (4.3)	9 (3.3)
Ulcerative colitis	0 (0.0)	0 (0.0)	0 (0.0)
Crohn's disease	0 (0.0)	0 (0.0)	0 (0.0)
Smoking status[b]			
Smoker	57 (36.5)	38 (32.5)	95 (34.8)
Non-smoker	99 (65.3)	79 (67.5)	178 (65.2)
Previous smoker	35 (22.4)	29 (24.8)	64 (23.4)
Never smoker	64 (41.0)	50 (42.7)	114 (41.8)
Alcohol use[b]			
Yes	109 (69.9)	81 (69.2)	190 (69.6)
No	46 (29.5)	35 (29.9)	81 (29.7)
Missing	1 (0.6)	1 (0.9)	2 (0.7)
Prior use of systemic therapy[c]			
Phototherapy	124 (79.5)	101 (86.3)	225 (82.4)
Methotrexate	129 (82.7)	90 (76.9)	219 (80.2)

Table 1 continued

Parameter	Biologic naïve (*n* = 156)	Biologic experienced (*n* = 117)[a]	Total (*N* = 273)[a]
Cyclosporine	43 (27.6)	62 (53.0)	105 (38.5)
Retinoid	98 (62.8)	87 (74.4)	185 (67.8)
Other	7 (4.5)	5 (4.3)	12 (4.4)
Use of prior biological therapy			
Naïve	156 (100.0)	0 (0.0)	156 (57.1)
Experienced	0 (0.0)	117 (100.0)	117 (42.9)
Adalimumab	–	40 (34.2)	40 (14.7)
Certolizumab pegol	–	4 (3.4)	4 (1.5)
Etanercept	–	19 (16.2)	19 (7.0)
Guselkumab	–	1 (0.9)	1 (0.4)
Infliximab	–	1 (0.9)	1 (0.4)
Ixekizumab	–	13 (11.1)	13 (4.8)
Risankizumab	–	1 (0.9)	1 (0.4)
Secukinumab	–	20 (17.1)	20 (7.3)
Ustekinumab	–	18 (15.4)	18 (6.6)
Lines of brodalumab therapy			
1	156 (100.0)	0 (0.0)	156 (57.1)
2	0 (0.0)	54 (46.2)	54 (19.8)
3	0 (0.0)	33 (28.2)	33 (12.1)
4	0 (0.0)	17 (14.5)	17 (6.2)
5	0 (0.0)	9 (7.7)	9 (3.3)
6	0 (0.0)	2 (1.7)	2 (0.7)
7	0 (0.0)	2 (1.7)	2 (0.7)
Reason for change to brodalumab			
Adverse events	–	7 (6.0)	7 (2.6)
Loss of effectiveness	–	107 (91.5)	107 (39.2)
Other	–	2 (1.7)	2 (0.7)
Missing	–	1 (0.9)	1 (0.4)
Reason for brodalumab discontinuation			
Any reason	13 (8.3)	28 (23.7)	41 (15.0)
Adverse events	1 (0.6)	5 (4.2)	6 (2.2)[d]

Table 1 continued

Parameter	Biologic naïve (n = 156)	Biologic experienced (n = 117)[a]	Total (N = 273)[a]
Loss of effectiveness	10 (6.4)	21 (17.8)	31 (11.3)
Other	0 (0.0)	2 (1.7)	2 (0.7)
Patient non-cooperation	1 (0.6)	0 (0.0)	1 (0.4)
Pregnancy	1 (0.6)	0 (0.0)	1 (0.4)

Data are n (%) or mean ± SD

BSA body surface area, *DLQI* Dermatology Life Quality Index, *PASI* Psoriasis Area and Severity Index, *SD* standard deviation

[a]One patient in the experienced group had two brodalumab treatments, and both are included (n = 117 with 118 brodalumab treatments, N = 273 with 274 brodalumab treatments)

[b]From last patient visit (not baseline)

[c]Before first biological therapy (not brodalumab for the experienced group)

[d]One each of latent tuberculosis, paradoxical worsening of psoriasis (palmoplantar and scalp psoriasis with alopecia), depression with suicidal ideation in alcohol abuser, vulvovaginal candida albicans infection, arthralgia, and leukopenia

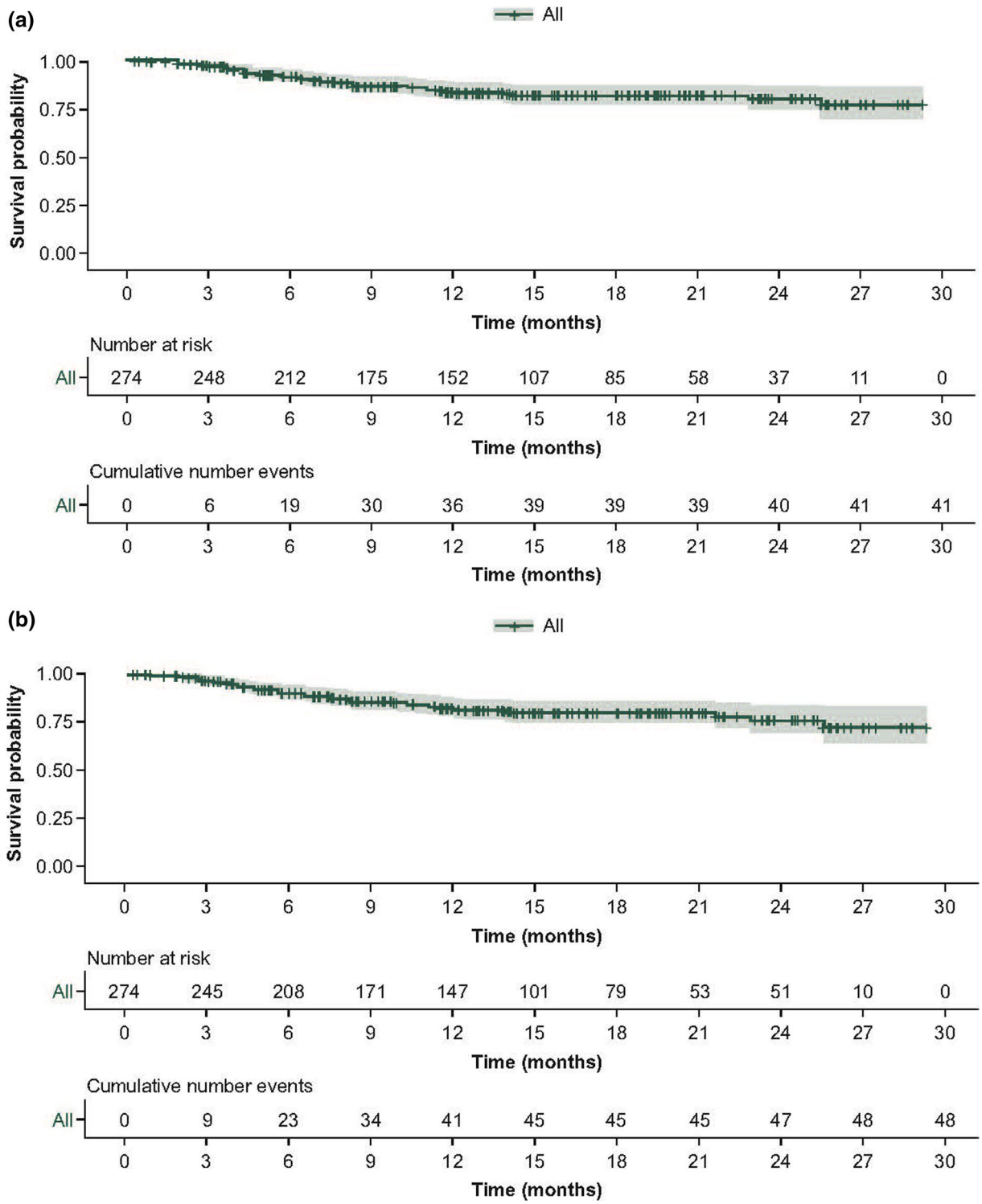
(Fig. 1). For the sensitivity analysis (time from initiation to failure of brodalumab, brodalumab dose adjustment during the study period or add-on of psoriasis therapy after initiation of brodalumab), no dose adjustments were made and seven patients had add-on systemic therapy (methotrexate, n = 5; prednisone, n = 2); predicted drug survival probability was 90.7% (95% CI 87.2, 94.4%) at 6 months and 82.0% (95% CI 77.1, 87.2%) at 12 months.

Kaplan–Meier analysis estimated that biologic-naïve patients had a 67.4% lower risk of discontinuation compared to biologic-experienced patients; 12-month drug survival of biologic-naïve patients was 91.2% (95% CI 86.3, 96.4%) compared to 76.7% (95% CI 69.0, 85.2%) for biologic-experienced patients (Fig. 2A). Estimated drug survival at 12 months appeared to be better in patients aged > 65 years, compared with younger age groups (Fig. 2B); however, patient numbers were low in this oldest age group (aged > 65 years), with only 18 patients at 12-month follow-up. When stratifying by BMI category, estimated drug survival at 12 months appeared to be better in patients who were overweight, and worse in those who were obese, compared with patients of normal weight (Fig. 2C). No statistically significant differences were observed in estimated drug survival at 12 months between female and male patients [81.1% (95% CI 72.6, 90.7) vs. 85.6% (95% CI 80.2, 91.4); p = 0.53], patients with or without psoriatic arthritis [79.5% (95% CI 67.7, 93.4%) vs. 85.1% (95% CI 80.1, 90.4%); p = 0.73], and patients who were current, ex- or non-smokers [81.0% (95% CI 72.6, 90.3), 88.5% (95% CI 80.1, 97.7), and 84.3% (95% CI 77.2, 92.0); p = 0.76] (Fig. 2D–F).

In a Cox proportional hazards regression model, lower age [hazard ratio (HR) 0.968, (95% CI 0.944, 0.992), p = 0.009], higher BMI [HR 1.081, (95% CI 1.037, 1.126), p < 0.001], and being biologic naïve [HR 0.326, (95% CI 0.165, 0.644), p < 0.001] were significantly associated with time to discontinuation and seemed to be predictors of better drug survival. The risk of discontinuation of brodalumab treatment was 3.2 times lower for every 1-year age increase since initiation of brodalumab treatment and 1.1 times higher for every increase in BMI of one unit (kg/m^2).

Effectiveness

Of the 273 patients who initiated brodalumab therapy, 224 (82.1%) had a 3-month follow-up



visit in the registry (short-term analysis set) and 141 had a 12-month follow-up (long-term analysis set). In the short-term analysis set, an absolute PASI ≤ 3 after 3 months was achieved by 89.8% of patients. Numerically more biologic-naïve than biologic-experienced patients

◂**Fig. 1** Drug survival probability over time for patients initiated on brodalumab treatment in the full analysis set: **A** time from initiation to failure of brodalumab (brodalumab treatment discontinuation); **B** time from initiation to failure or dose-adjustment or add-on of psoriasis therapy (sensitivity analysis; no dose adjustments were made). All patients with brodalumab therapy in registry BIOREP were analyzed. One patient had two brodalumab treatments, both of which are included. Add-on therapy included the systemic therapies methotrexate, cyclosporin, retinoids, and other therapies, added after the start of brodalumab therapy. Add-on therapies were reported on seven occasions (methotrexate, $n = 5$; prednisone, $n = 2$)

achieved absolute PASI ≤ 3 (95.9% vs. 82.7%, respectively) (Fig. 3; Table 2). Mean PASI at baseline was 17.0 and decreased to 1.1 (mean change: – 16.0) after 3 months. A total of 92.4% of patients reached PASI 75, 77.8% reached PASI 90, and 59.1% reached PASI 100 after 3 months (Fig. 3; Table 2).

After 12 months, 96.5% of 141 patients with 12 months' follow-up had an absolute PASI ≤ 3, with a similar proportion of responders in patients who were biologic naïve (97.4%) and biologic experienced (95.5%) (Fig. 3; Table 2). A total of 95.1%, 87.3%, and 69.7% of patients achieved PASI 75, PASI 90, and PASI 100, respectively (Fig. 3; Table 2).

A decrease in DLQI was observed at 3 months from 14.2 to 1.3 (– 12.9), and 73.8% of patients achieved DLQI 0/1 (Fig. 3; Table 2). The proportion of patients achieving DLQI 0/1 increased to 87.3% at month 12 (Fig. 3; Table 2). These high proportions for PASI and DLQI remained through to 18 and 24 months.

DISCUSSION

Real-world evidence can provide valuable insights into treatment effectiveness in more diverse clinical settings and in a broader range of patients than provided by clinical trials, which often have strict eligibility criteria [18, 19], with many patients, including the elderly and those with comorbidities, typically excluded [20]. This can result in selection bias and uncertainty about external validity when applied to the real-world setting. Patients in the real-world setting may also be more likely to have failed previous biological therapy, especially when newer agents are being investigated [20]. Previous analyses of the BIOREP registry showed that half the patients had cardiovascular risk factors, approximately 70% patients were either overweight or obese, and over a third (41.0%) reported a history of psoriatic arthritis [21], while 62% of patients initiating risankizumab had failed previous biological therapy [20]. Similarly, this study showed that close to 7 in 10 patients initiated on brodalumab therapy had comorbidities, most frequently those associated with metabolic syndrome, in particular hypertension, dyslipidemia, and type 2 diabetes, while 43% were biologic experienced.

Drug survival is often used as a surrogate measure to evaluate the effectiveness, safety, and real-world utility of biologics in psoriasis [22]. Biological drug survival reflects long-term treatment success and is an important measure in guiding clinical decision-making [22]. This analysis of real-world data demonstrated high and sustained drug survival for patients with moderate-to-severe plaque psoriasis treated with brodalumab for up to 24 months in a real-life setting. Moreover, data were analyzed at a 24-month cut-off, and it should be noted that drug survival may continue beyond this point.

The predicted drug survival probability was 84.2% and 80.4% at 12 and 24 months, respectively, with these results largely consistent with those from other real-world studies of biologics, although direct comparisons are not possible due to differences in their designs, patient populations, and definitions of drug survival. Previous analysis of BIOREP data estimated a 76% survival rate for adalimumab at month 20, falling to 58.1% in the 80th month of treatment [23], while analysis of five PSONET registries including BIOREP reported survival rates after 1 year of 43–92% with etanercept, 28–83% with adalimumab, 65–87% with infliximab, and 53–77% with ustekinumab, all when combined with methotrexate [24]. In a meta-analysis of 29 cohort studies in psoriasis, estimated pooled drug survival rates at 2 years were 53.2% for adalimumab, 48.9% for infliximab, and 47.6% for etanercept [22], while a retrospective,

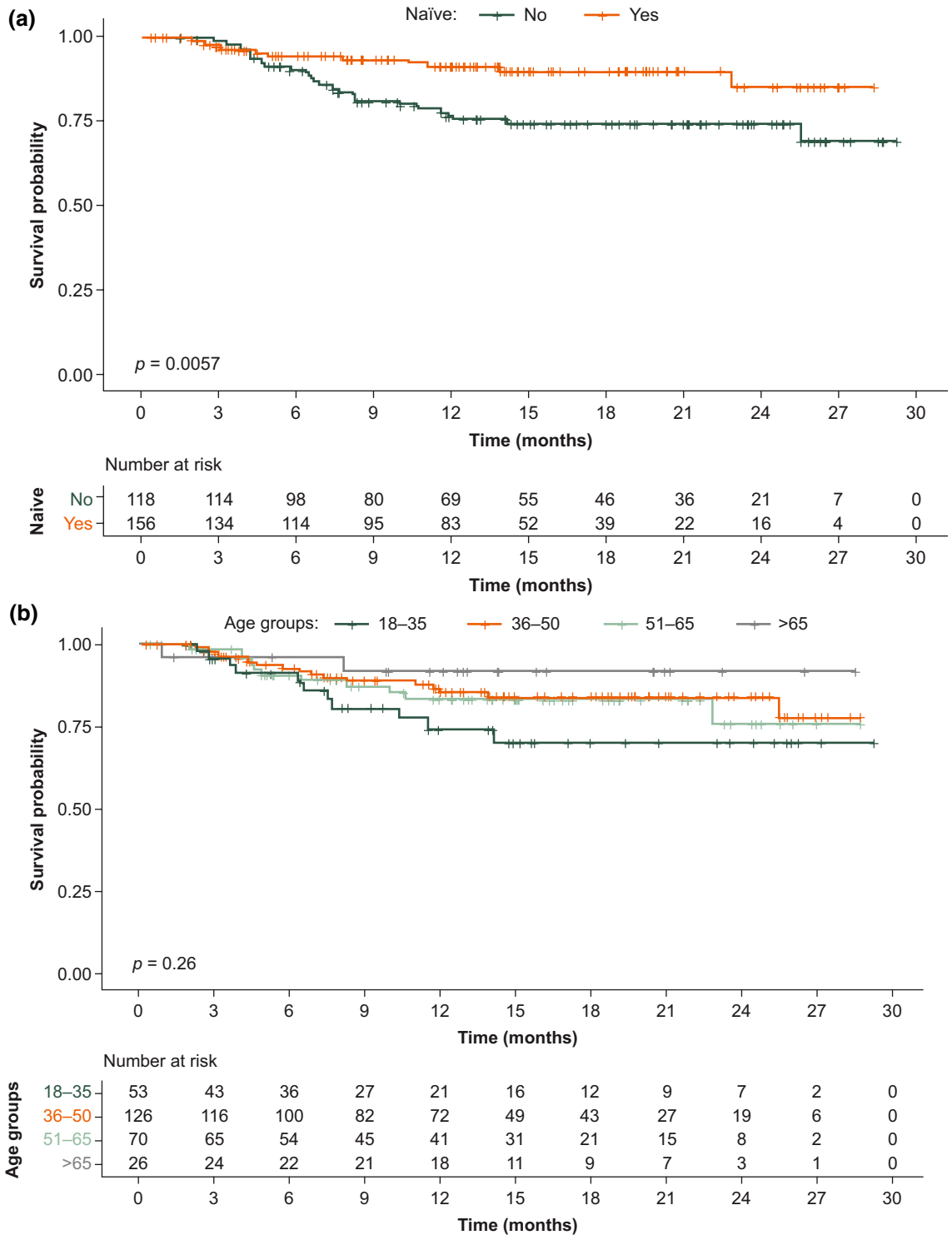


Fig. 2 Drug survival probability over time for patients initiated on brodalumab treatment in the full analysis set, stratified by **A** prior biological therapy exposure, **B** age group, **C** BMI category, **D** sex, **E** presence of PsA at baseline, or **F** smoking. *BMI* body mass index, *PsA* psoriatic arthritis

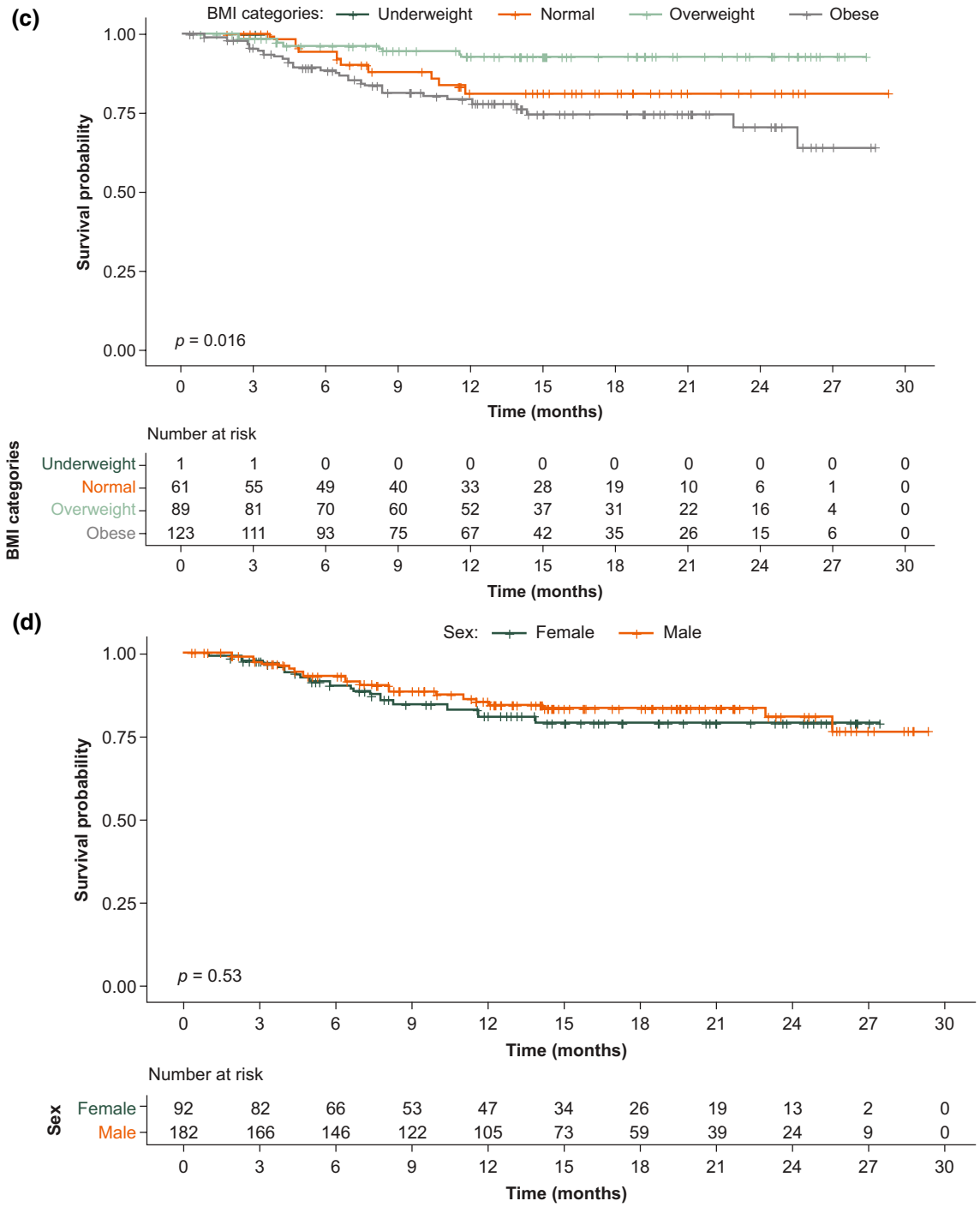
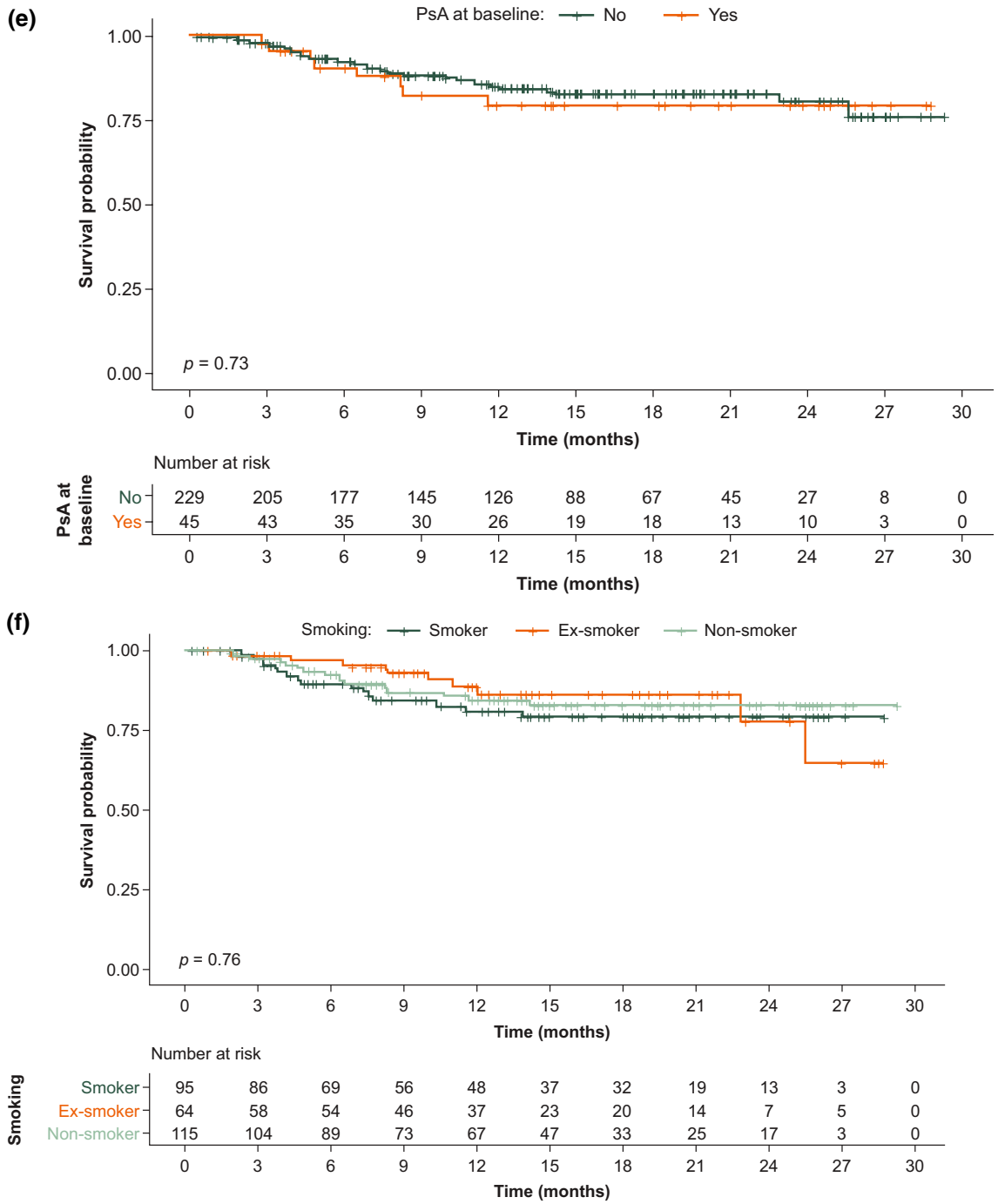


Fig. 2 continued

multicenter cohort study of 3145 patients from 16 centers across Europe and North America reported cumulative probabilities of drug survival at 18 months of 96.4% for risankizumab, 91.1% for guselkumab, 86.3% for brodalumab, 86.1% for ustekinumab, 82.0% for ixekizumab, and 79.9% for secukinumab [25].



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Previous reports have indicated negative predictors of drug survival as female gender, obesity, and previous failed biological therapies [23, 26–29]. Consistent with this, in our analysis, biologic-naïve patients had a 76.5% lower risk of discontinuation after 12 months compared to biologic-experienced patients. However, no difference in drug survival rates were observed between males and females, while, rather surprisingly, patients who were

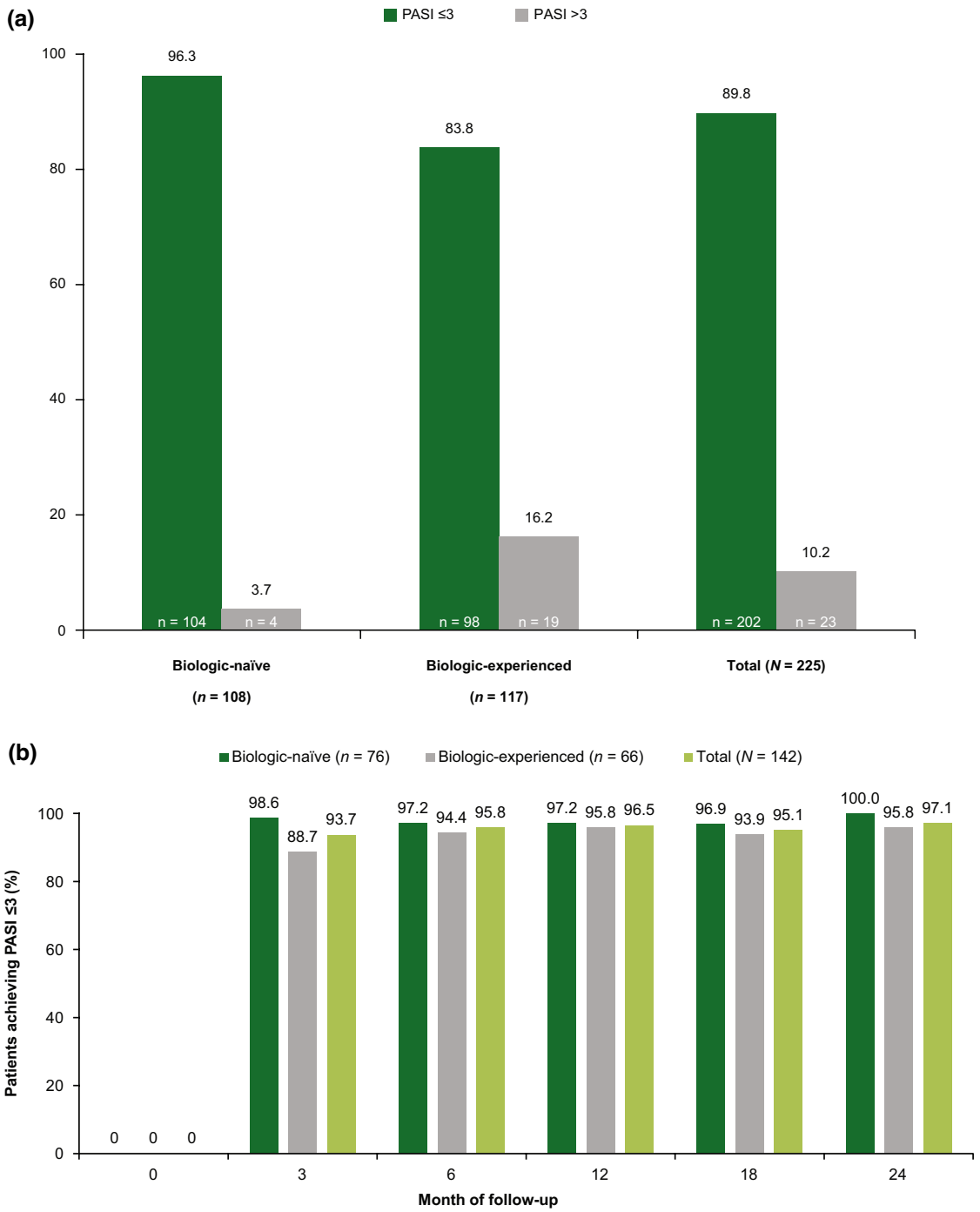
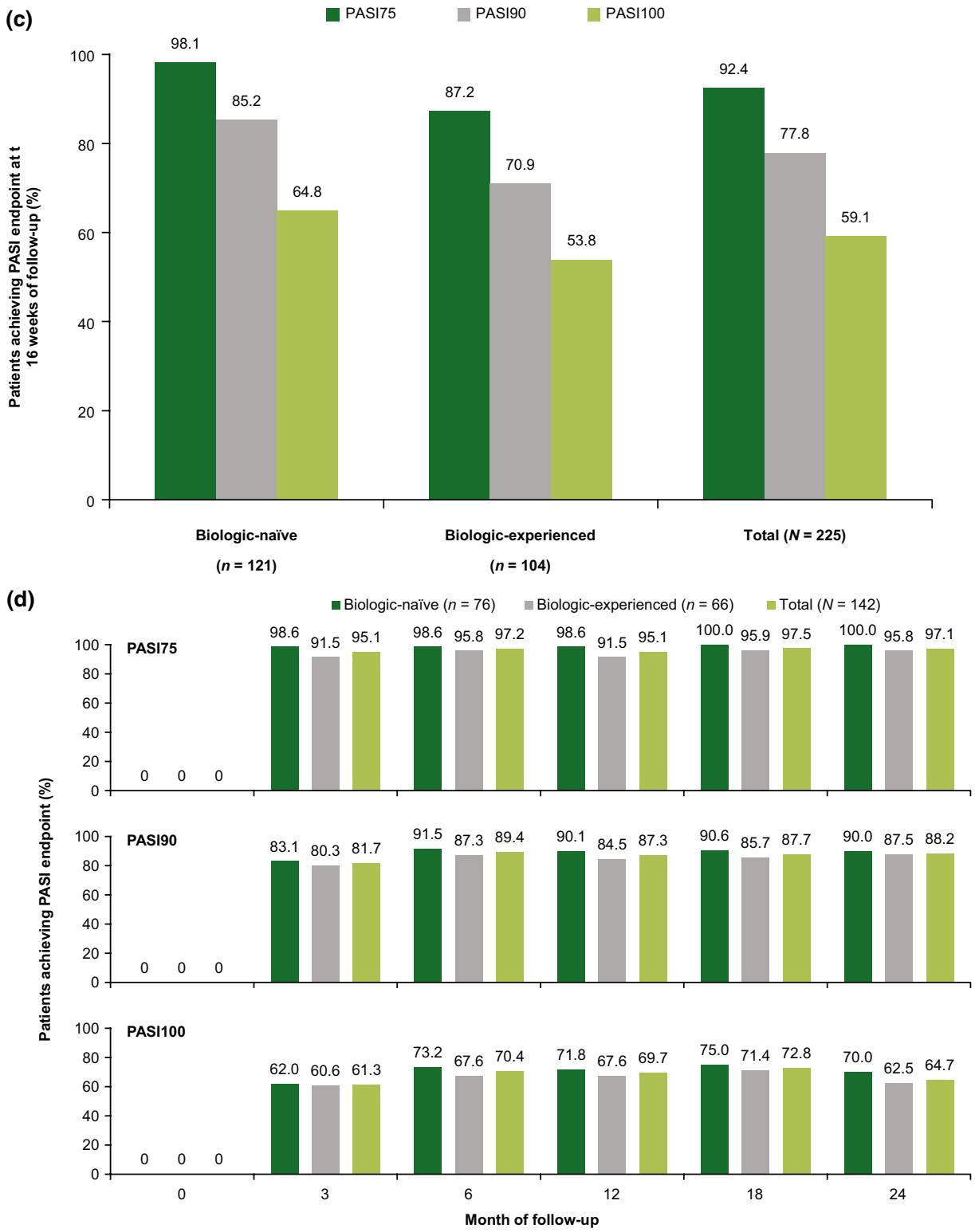


Fig. 3 Proportions of patients achieving an absolute PASI score of ≤ 3, PASI 75, PASI 90, and PASI 100, and DLQI 0/1 at 3 months (short-term analysis set) and over 24 months (long-term analysis set). Data analyzed as observed. *DLQI* Dermatology Life Quality Index, *PASI* Psoriasis Area and Severity Index, *PASI 75/90/100*: 75/90/100% reduction in PASI score. **A** Absolute PASI (short-term analysis set), **B** absolute PASI (long-term analysis set), **C** PASI 75, PASI 90, and PASI 100 (short-term analysis set), **D** PASI 75, PASI 90, and PASI 100 (long-term analysis set), **E** DLQI (short-term analysis set), **F** DLQI (long-term analysis set)



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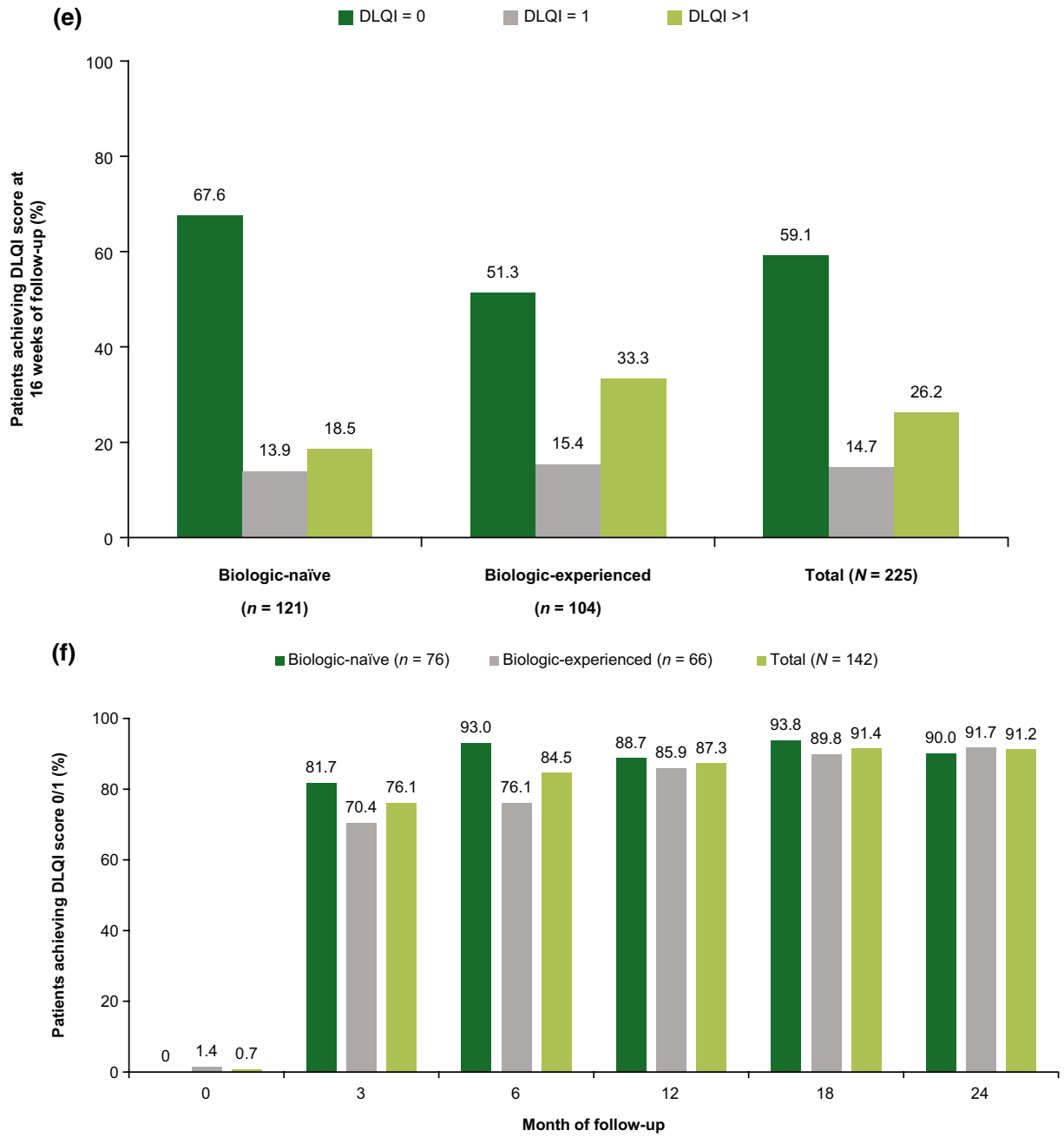

Fig. 3 continued

overweight had better drug survival than normal weight patients, although drug survival was lower in patients with obesity. This may be due to the relatively small patient numbers in each of the different body weight groups, so these data should be interpreted with caution. Drug survival also appeared to be higher in patients aged over 65 years treated with brodalumab, although, again, the number of patients included in the analysis was small ($n = 26$) and this failed to reach statistical significance. However, age was found to be significantly associated with time to discontinuation ($p = 0.009$), and appeared to predict drug survival. There

Table 2 Number of brodalumab treatment episodes and change in the proportion of patients achieving PASI and DLQI response per visit

Month	PASI ≤ 3	PASI 75	PASI 90	PASI 100	DLQI 0/1
0	0% ($n = 0$)	0% ($n = 0$)	0% ($n = 0$)	0% ($n = 0$)	0.7% ($n = 1$)
3 (short-term analysis set)	89.8% ($n = 202$)	92.4% ($n = 208$)	77.8% ($n = 175$)	59.1% ($n = 133$)	73.8% ($n = 166$)
3 (long-term analyses set)	93.7% ($n = 133$)	95.1% ($n = 135$)	81.7% ($n = 116$)	61.3% ($n = 87$)	76.1% ($n = 108$)
6	95.8% ($n = 136$)	97.2% ($n = 138$)	89.4% ($n = 127$)	70.4% ($n = 100$)	84.5% ($n = 120$)
12	96.5% ($n = 137$)	95.1% ($n = 135$)	87.3% ($n = 124$)	69.7% ($n = 99$)	87.3% ($n = 124$)
18	95.1% ($n = 77$)	97.5% ($n = 79$)	87.7% ($n = 71$)	72.8% ($n = 59$)	91.4% ($n = 74$)
24	97.1% ($n = 33$)	97.1% ($n = 33$)	88.2% ($n = 30$)	64.7% ($n = 22$)	91.2% ($n = 31$)

Data analyzed as observed. All timepoints for the long-term analyses set, unless indicated otherwise. Short-term analysis set included patients with ≥ 3 months of follow-up and long-term analysis set included patients with ≥ 12 months of follow-up

DLQI Dermatology Life Quality Index, *PASI* Psoriasis Area and Severity Index

was also no statistically significant difference in drug survival between patients with and without psoriatic arthritis, although patients with psoriatic arthritis had a 1.28 times higher risk of discontinuation of treatment.

Loss of effectiveness and adverse events were the most common reasons for discontinuation of brodalumab (11% of patients), which is consistent with other studies of biologics for the treatment of psoriasis in real-world settings [30].

This real-world study also demonstrated the effectiveness of brodalumab when assessed by PASI, with improvements in PASI 75, 90, and 100 observed as early as 3 months (rates of 92.4%, 77.8%, and 59.1%, respectively), and being sustained at 1-year (95.1%, 87.3%, and 69.7%, respectively) and for up to 2 years. In two phase 3 trials of brodalumab in patients with moderate-to-severe psoriasis (AMAGINE-2 and -3), PASI 75 rates were 85% and 86% at week 12 and 80% and 80% at week 52, while PASI 100 rates were 44% and 37% at week 12 and 56% and 53% at week 52 [8]. Also, in a smaller real-world Italian study in 78 adult patients, a higher proportion achieving PASI 100 (51.3%) was observed in the short-term evaluation after 12 weeks [31]. Similarly, a real-world study of risankizumab in moderate-to-severe psoriasis recorded PASI 90 and PASI 100 rates of 63.8% and 44.7% after 16 weeks, increasing to 82.4% and 67.6%, respectively, at week 52 [20]. These data confirm differences in responses between real-life and clinical trials, in particular higher response rates (PASI 100) in short-term observation, and the proportion of patients achieving better PASI scores in a long-term evaluation. Improvements in quality of life were also reported for patients with psoriasis on brodalumab therapy with 74% of patients reporting DLQI 0/1 at week 12, increasing to 87% at 1 year. In AMAGINE-2 and -3, 60% of patients with a DLQI score > 1 at baseline treated with brodalumab achieved a DLQI score of 0/1 at 12 weeks and 55% at 1 year [2].

Strengths and Limitations of the Study

Key strengths of the study were the large patient population and representation of most specialist centers in the Czech Republic within the

BIOREP registry, ensuring high internal validity. However, the study had several weaknesses inherent in its design. Firstly, real-world data are subject to various sources of potential bias and confounding factors [18]. Secondly, effectiveness endpoints were based on observed data as collected in routine clinical practice, and may therefore be incomplete or missing; in particular, missing data for later study visits due to premature discontinuations may reduce the accuracy of long-term estimations of treatment effectiveness. However, assumptions about data being missing at random, as carried out in a clinical trial setting, may not be valid in a real-world situation, with multiple imputation and non-responder imputation leading to a larger bias than simply analyzing data as observed. Finally, the study was conducted in a single country, which could limit the generalizability of the results, particularly as prescribing patterns for psoriasis may differ between countries.

CONCLUSIONS

This multicenter, observational study demonstrated high and sustained drug survival as well as high rates of skin clearance and improvement in quality of life for patients with moderate-to-severe plaque psoriasis treated with brodalumab for up to 24 months in a real-life setting.

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Declarations

Conflict of Interest. Martina Kojanova, Spyridon Gkalpakiotis, Petra Cetkovska, Jorga Fialova, Alena Machovcova, and Tomas Dolezal have served as consultants, speakers, or investigators for AbbVie, Amgen, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, and UCB. Barbora Turkova declares that she has nothing to disclose. Eydna Didriksen Apol is an employee of Leo Pharma A/S.

Ethical Approval. The study was conducted in accordance with good pharmacoepidemiology practices by research groups belonging to the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP), in accordance with the ENCePP Code of Conduct and, if possible, under the ENCePP Study Seal. Patient-level data used for this analysis were de-identified, and Institutional Review Board approval was not required for this study. Permission to access/use data from BIOREP registry was obtained.

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