ORIGINAL ARTICLE

Female patients are less satisfied with biological treatment for psoriasis and experience more side-effects than male patients: results from the prospective BioCAPTURE registry

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Abstract

Background Female sex has been reported as a predictor for treatment discontinuation with biological therapies for psoriasis, although reasons remain unclear. It can be hypothesized that lower satisfaction with biological treatment in women might add to the lower drug survival rates.

Objectives To identify possible differences in satisfaction with biological treatment between female and male patients using the Treatment Satisfaction Questionnaire for Medication (TSQM).

Methods Data of psoriasis patients treated with biologics were obtained from the prospective, multicentre, daily-practice BioCAPTURE registry. Longitudinal TSQM data were analysed by linear mixed models. Relevant patient characteristics were incorporated as possible confounding factors. *Post hoc* analysis of adverse events was performed in order to investigate differences between sexes.

Results We included 315 patients with 396 corresponding treatment episodes (137 adalimumab, 90 etanercept, 137 ustekinumab, 24 secukinumab and 8 infliximab). Almost forty per cent of the patients were female. Women had significantly lower baseline PASI scores ($P = 0.01$). Longitudinal analyses demonstrated lower TSQM scores for 'side-effects' ($P = 0.05$) and 'global satisfaction' ($P = 0.01$) in female patients compared with male patients over 1 year of treatment. Women reported more relevant adverse events in the context of biologic treatment compared to men (rate ratio 1.79; $P < 0.001$), with more fungal (rate ratio 2.20; $P = 0.001$) and herpes simplex infections (rate ratio 3.25; $P = 0.005$).

Conclusions This study provides a prospective, longitudinal analysis of treatment satisfaction with biologics in female and male patients with psoriasis. Women were slightly less satisfied with treatment regarding side-effects and global satisfaction. Differences in treatment satisfaction and side-effects might add to the fact that women discontinue biological treatments more often.

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Conflict of interest

LS van der Schoot has no conflict of interest. JMPA van den Reek carries out clinical trials for AbbVie, Celgene and Janssen and has received speaking fees from AbbVie and Janssen and reimbursement for attending a symposium from Celgene and AbbVie. All funding is not personal but goes to the independent research fund of the department of dermatology of Radboud university medical centre Nijmegen, the Netherlands. ME Otero has acted as consultant for Eli Lilly. JM Mommers has received consultant fees and speaker fees of Janssen,

Celgene and Novartis. WP Arnold carried out clinical trials for LEO Pharma, received speaking fees from AbbVie and reimbursement for attending symposia of Janssen, Pfizer, AbbVie and UCB Pharma. EMGJ de Jong has received research grants for the independent research fund of the department of dermatology of the Radboud university medical centre, Nijmegen, the Netherlands from AbbVie, Pfizer and Janssen; has acted as consultant and/or paid speaker for and/or participated in research sponsored by companies that manufacture drugs used for the treatment of psoriasis including AbbVie, Janssen, MSD, Pfizer, Novartis, Lily and Celgene; all funding is not personal but goes to the independent research fund of the department of dermatology of Radboud university medical centre, Nijmegen, the Netherlands. Other authors: None declared.

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Introduction

Biological agents have enlarged the treatment options for patients with psoriasis, and still new biologics are developed.[1,2] Many daily-practice registries are nowadays available in order to evaluate and optimize treatment with biologics.[3–7] These studies have assessed drug survival of individual biologics, or they searched for clinical characteristics that predict the discontinuation with biological treatment. Data from several studies suggest that female sex is a predictor for treatment discontinuation with biologics.[4–10] Although Zweegers *et al.*[8] reported female sex as a predictor for treatment discontinuation due to side-effects, other reasons remain unclear. We hypothesized that female patients have lower drug survival rates compared with male patients as a result of lower satisfaction with biological treatment.

Treatment satisfaction is important in patients with psoriasis, as it corresponds with adherence, patients' preferences and health-related quality of life.[11,12] Therefore, 'satisfaction with medication' is an important patient-reported outcomes (PROs) in the field of psoriasis used in the evaluation of treatments.[13] For this purpose, the Treatment Satisfaction Questionnaire for Medication (TSQM) can provide insight into different domains of treatment satisfaction: effectiveness, convenience, global satisfaction and side-effects.[14] In general, treatment satisfaction with biologics is high,[3,15–19] although we previously demonstrated that there still remains room for improvement in treatment satisfaction.[3]

In recent years, several publications have provided information on gender differences in health care.[20,21] It has been observed that sex differences exist in the presentation of symptoms, communication and treatment outcomes.[21,22] Although there is no difference in the male-to-female prevalence ratio for patients with psoriasis,[23] there is some evidence for gender differences in psoriasis with regard to response to biological treatment.[24,25]

In order to identify possible differences in satisfaction with biological treatment between female and male patients using the TSQM, this study provides a prospective, longitudinal analysis of treatment satisfaction in female and male patients with psoriasis treated with biologics in daily practice care. This approach may further elucidate reasons for worse drug survival with biologics in women compared to men with psoriasis.

Materials and method

The BioCAPTURE database

Data were extracted from the prospective, multicentre, long-term Continuous Assessment of Psoriasis Treatment Use Registry with Biologics (BioCAPTURE registry). Since 2005, daily practice data from patients with psoriasis treated with biologics have been imported into this registry. The registry contains data from two academic and 14 non-academic centres in the Netherlands. Currently used biologics in the BioCAPTURE registry are adalimumab, etanercept, ustekinumab, infliximab, secukinumab, ixekizumab, guselkumab, brodalumab and the small molecule apremilast. BioCAPTURE was approved by our medical ethics committee. Although not mandatory for this non-interventional study according to the Dutch Law, informed consent was obtained from every patient in this registry. Patients included in the registry received treatment according to the Dutch guidelines.[26]

Treatment satisfaction questionnaire for medication (TSQM)

From 2010, all patients included in the BioCAPTURE registry starting a biologic for the first time or switching to another biologic were asked to fill out a TSQM (version II). Patients received questionnaires at baseline and at every 3 months, or until the moment of discontinuation. From 12 months, patients were asked to fill out questionnaires every year.

The TSQM (version II) is a generic, multilingual validated questionnaire developed for different patients and medications, and is therefore applicable to our patient group. The TSQM covers four domains: effectiveness, convenience, global satisfaction and side-effects. The score for every domain ranges from 0 (extremely dissatisfied) to 100 (extremely satisfied).[14] Baseline measures provide information about the last treatment used before the initiation of the biologic, as the questionnaire refers to the timeframe 2–3 weeks prior to completion of the questionnaire.

Data collection and extraction

Scores retrieved from TSQM questionnaires were entered into the BioCAPTURE database. Patient characteristics and TSQM scores were extracted from the BioCAPTURE database for all patients from 2010 until August 2018. We included TSQM scores over 1 year of treatment or until the moment of discontinuation whichever came first. Baseline characteristics extracted from the database were sex, age at start with biological therapy, type of biologic, duration of psoriasis until start with biological therapy, body mass index (BMI), baseline PASI score, experience with prior biologics, presence of psoriatic arthritis and hospital type (academic or non-academic).

All treatment episodes with biologics in the BioCAPTURE registry with completed longitudinal TSQM questionnaires were included in this study: adalimumab, etanercept, ustekinumab, infliximab and secukinumab. One treatment episode accounted for the time the patient was actively treated with a biologic; interruptions with a maximum of 90 days were accepted within a treatment episode. When patients had received different biologics over time, all treatment episodes with completed TSQM questionnaires were included. TSQM questionnaires of treatment episodes with brodalumab, guselkumab and ixekizumab were not available yet. Treatment episodes with the small molecule apremilast and treatment episodes without completed TSQM questionnaires at all time frames were excluded from analyses.

Statistical analysis

Cross-sectional Data were extracted from the BioCAPTURE database and imported into SPSS version 25.0 (IBM, Armonk, NY, USA) for further analysis. A P-value <0.05 was considered significant in all analyses.

Descriptive statistics [means $\pm$ SD or medians (range)] were used to summarize continuous patient and treatment characteristics of the first available treatment episode. For categorical variables, numbers and percentages were used. Baseline continuous variables were compared between male and female patients using an independent t-test in case of a parametric distribution, or a Mann–Whitney U-test in case of a non-parametric distribution. Differences in categorical variables between male and female patients were analysed by Pearson's chi-square tests for independence.

Longitudinal Treatment Satisfaction Questionnaire for Medication scores per domain ('effectiveness', 'side-effects', 'convenience' and 'global satisfaction') over time were studied using linear mixed models (LMMs). LMMs were chosen in order to account for the unbalanced data with a different number of treatment episodes per patient. LMMs are able to accommodate all available data with flexible assumptions regarding missing data.[27]

The TSQM subdomain scores were defined as dependent variables, and time (in months) from baseline visit, sex and TSQM subdomain baseline score were key independent variables. Possible confounding factors based on clinical relevance were incorporated in the models: age, duration of psoriasis, baseline PASI score, BMI, presence of psoriatic arthritis, type of biologic and experience with prior biologics.

Confounders that altered the unadjusted exposure–outcome effect by $\geq$10% or confounders that contributed statistically significant were kept in the model. Consequently, every TSQM subdomain model contains different confounders. Variance components were used as covariance type (default setting of SPSS). Statistics were based on all cases with valid data for all variables in the model. Corresponding estimated marginal means (EMMs) over time and for each moment of time from baseline visit were calculated for male and female patients.

Post hoc analysis of adverse events

Post hoc analysis of adverse events was performed in order to further explain differences in satisfaction with side-effects between female and male patients. Adverse events were defined as any undesirable medical event that occurred during biological treatment. In general, physicians inquired actively for adverse events at every BioCAPTURE visit. In case of serious adverse events (SAEs), additional information was requested from the treating physicians in most cases. We analysed SAEs and defined clinical relevant adverse events of special interest (AEoSI) in the context of biologic use, see Table 2. Other mild adverse events were excluded. AEoSI, which were also covered by criteria for SAEs, were included in both groups. Incidence rates were calculated, based on the number of events per 100 actively treated patient-years. The incidence rates were compared between men and women using Mid-P exact tests (open source calculator OpenEpi, V.3).[28] Sensitivity analyses were performed in order to correct for gender-related adverse events, such as gynaecological events in female patients.

Results

Patient and treatment characteristics

In total, 315 patients were included in this study, with a total of 396 treatment episodes. Corresponding total patient-years 'on drug' were 417 years for female patients, and 677 years for male patients. Seventy-eight patients without completed TSQM

questionnaires at all timeframes were excluded. Baseline patient characteristics of the first treatment episode and number of used agents in all treatment episodes are presented in Table 1. More than half of the patients were male (59.7%, $n = 188$). In both groups, patients had median BMIs in the range of overweight (median BMI 28.09 and 28.07, for male and female patients, respectively). The median baseline PASI score was significantly higher in male patients (11.4 vs. 10.1 in female patients; $P = 0.01$).

Female patients report lower 'side-effects' and 'global satisfaction' scores

Longitudinal analysis for the 'effectiveness' domain showed no difference in 'effectiveness' scores between male and female patients over time [male, EMM 68.40 (95% CI: 62.28–74.50); female, EMM 62.31 (95% CI: 56.22–68.40); $P = 0.06$]. Results were corrected for possible confounders at baseline, including presence of psoriatic arthritis and type of biological agent.

For the 'side-effects' domain, the LMM demonstrated an overall lower score over time in female patients compared with male patients [female, EMM 87.99 (95% CI: 84.55–91.44); male, EMM 92.86 (95% CI: 89.26–96.45); $P = 0.05$]. Results were corrected for possible confounders at baseline, including presence of psoriatic arthritis, age, duration of psoriasis and baseline PASI score.

The LMM of the TSQM 'convenience' domain demonstrated no differences over time between male and female patients [male, EMM 79.20 (95% CI: 75.00–83.41); female, EMM 78.65 (95% CI: 74.52–82.78); $P = 0.82$]. Results were corrected for type of biologic, presence of psoriatic arthritis,

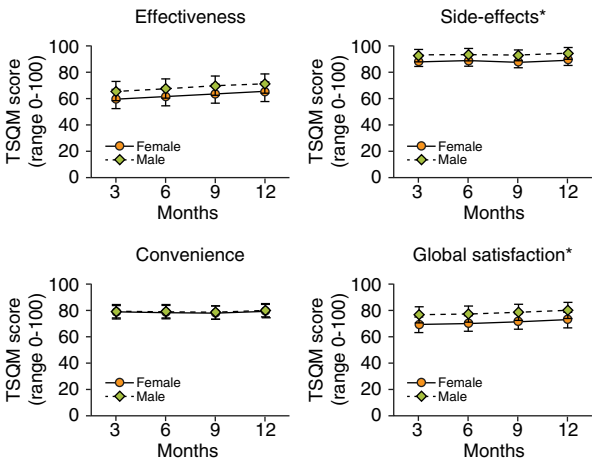

Figure 1 Treatment Satisfaction Questionnaire for Medication (TSQM) measures for female and male patients over 1 year of treatment with biologics. Each figure shows estimated marginal means (EMMs) for the specific TSQM domain with 95% confidence intervals (whiskers) as results of the linear mixed models. Asterisk represents a significant difference ($P < 0.05$) between male and female patients for the specific TSQM domain over time.

Table 1 Patient and treatment characteristics of the first treatment episode of male and female patients ($n = 315$)

	Total ($n = 315$)	Men ($n = 188$, 59.7%)	Women ($n = 127$, 40.3%)	*P*-value†
Age (years), mean ± SD	48.85 ± 13.10	48.71 ± 12.58	49.06 ± 13.88	0.82‡
Duration of psoriasis until start of biologic (years), median (IQR)	19.49 (14.93)††	19.49 (13.67)‡‡	19.80 (19.07)§§	0.63§
BMI (kg/m^2), median (IQR)	28.07 (7.48)¶¶	28.09 (5.79)†††	28.07 (10.07)‡‡‡	0.61§
Baseline PASI score, median (IQR)	11.20 (8.5)§§§	11.4 (8.7)¶¶¶	10.1 (9.0)††††	0.01§
Psoriatic arthritis (yes)	76 (24.1)‡‡‡‡	36 (19.1)§§§§	40 (31.5)¶¶¶¶	0.07¶
Treatment†††††	396 (100)	229 (100)	167 (100)	–
Adalimumab	137 (34.6)	76 (33.2)	61 (36.5)	–
Etanercept	90 (22.7)	54 (23.6)	36 (21.6)	–
Infliximab	8 (2.0)	4 (1.7)	4 (2.4)	–
Secukinumab	24 (6.1)	13 (5.7)	11 (6.6)	–
Ustekinumab	137 (34.6)	82 (35.8)	55 (32.9)	0.91¶
Hospital type				
Academic	213 (67.6)	123 (65.4)	90 (70.9)	–
Non-academic	102 (32.4)	65 (34.6)	37 (29.1)	0.33¶
Experience with prior biologics				
Experienced (non-naïve)	140 (44.4)	84 (44.7)	56 (44.1)	–
Inexperienced (naïve)	175 (55.6)	104 (55.3)	71 (55.9)	1.00¶

†Based on the difference between male and female patients. ‡Independent t-test, §Mann–Whitney U-test, ¶Pearson's chi-square test. Missing data: ††12, ‡‡9, §§3, ¶¶37, †††27, ‡‡‡10, §§§53, ¶¶¶34, ††††19, ‡‡‡‡65, §§§§48, ¶¶¶¶17. †††††Total number of treatment episodes for all used biologics.
Data are *n* (%) unless otherwise indicated.
BMI, body mass index; IQR, interquartile range; PASI, Psoriasis Area and Severity Index.

age, duration of psoriasis, BMI, prior experience with biologics and baseline PASI score.

Female patients had an overall lower 'global satisfaction' score over time compared with male patients [female, EMM 71.57 (95% CI: 66.25–76.89); male, EMM 78.69 (95% CI: 73.26–84.13); $P = 0.01$]. Results for the 'global satisfaction' model were corrected for type of biologic, presence of psoriatic arthritis and BMI.

Estimated marginal means calculated by the LMMs for the different timeframes for male and female patients are presented in Fig. 1. Tables S1–S4 provide detailed information about the models used.

Adverse events

Serious adverse events and AEoSI were incorporated in these analyses. Total numbers and corresponding incidence rates per 100 patient-years (PY) of SAEs and AEoSI are presented in Table 2. The total number of SAEs in women was 41, compared to 48 SAEs in men. No significant difference was found between men and women (rate ratio 1.30; $P = 0.13$). Regarding AEoSI,

Table 2 Incidence rates per 100 patient-years of serious adverse events (SAEs) and adverse events of special interest (AEoSI)

	Female		Male		Total		Rate ratio†	*P*-value‡
	Number of AEs	Incidence per 100 PY	Number of AEs	Incidence per 100 PY	Number of AEs	Incidence per 100 PY		
SAEs (total)	41	9.8 (7.2–13.2)	48	7.1 (4.3–9.3)	89	8.1 (6.6–9.9)	1.39	0.13
Life-threatening events	9	2.2 (1.1–3.9)	13	1.9 (1.1–3.2)	22	2.0 (1.3–3.0)	1.13	0.78
Death	2	0.5 (0.1–1.6)	1	1.5 (0.1–7.3)	3	0.3 (0.7–7.5)	0.32	0.38
(Prolonged) hospitalization	24	5.8 (3.8–8.4)	29	4.3 (2.9–6.1)	53	4.8 (3.7–6.3)	1.35	0.29
Persistent or significant disability or incapacity	6	1.4 (0.6–3.0)	5	0.7 (0.3–1.6)	11	1.0 (0.5–1.7)	1.95	0.28
Congenital anomaly or birth defects	0	–	0	–	0	–	–	–
AEoSI (total)	120	28.8 (24.0–34.3)	109	16.1 (13.3–19.3)	229	20.9 (18.3–23.7)	1.79	<0.001
Malignancies§	1	0.2 (0.01–1.2)	4	0.7 (0.2–1.4)	5	0.5 (0.2–1.0)	0.41	0.46
Melanoma	1	0.2 (0.01–1.2)	4	0.7 (0.2–1.4)	5	0.5 (0.2–1.0)	0.41	0.46
NMSC	9	2.2 (1.1–4.0)	14	2.1 (1.2–3.4)	23	2.1 (1.4–3.1)	1.04	0.91
Haematological cancers	1	0.2 (0.01–1.2)	0	–	1	0.1 (0.01–0.5)	–	–
MACE	7	1.7 (0.7–3.3)	6	0.9 (0.4–1.8)	13	1.2 (0.7–2.0)	1.89	0.26
Haematological events	1	0.2 (0.01–1.2)	0	–	1	0.1 (0.01–0.5)	–	–
Neurological events	1	0.2 (0.01–1.2)	2	0.3 (0.1–1.0)	3	0.3 (0.1–0.7)	0.80	0.91
Autoimmune diseases	4	1.0 (0.3–0.2)	1	0.2 (0.01–0.7)	5	0.5 (0.2–1.0)	6.50	0.08
Severe infections leading to clinical admission	11	2.6 (1.4–4.6)	12	1.8 (1.0–3.0)	23	2.1 (1.4–3.1)	1.49	0.35
TBC, HIV, hepatitis	3	0.7 (1.8–2.0)	0	–	3	0.3 (0.1–0.7)	–	–
Herpes infections								
Total	17	4.1 (2.5–6.4)	15	2.2 (1.3–3.6)	32	2.9 (2.0–4.1)	1.84	0.09
Herpes simplex	16	2.8 (2.3–6.1)	8	1.2 (0.6–2.2)	24	2.2 (1.4–3.2)	3.25	0.005
Herpes zoster	1	0.2 (0.01–1.2)	7	1.0 (0.5–1.1)	8	0.7 (0.3–1.4)	0.23	0.15
Fungal infections	38	9.1 (6.5–12.4)	28	4.1 (2.8–5.9)	66	6.0 (4.7–7.6)	2.20	0.001
Skin	22	5.3 (3.4–7.9)	26	3.8 (2.6–5.6)	48	4.4 (3.3–5.8)	1.37	0.28
Mucosa	16	3.8 (2.3–6.1)	2	0.3 (0.1–1.0)	18	1.6 (1.0–2.5)	12.99	<0.001
Adverse drug reactions and injection site reactions	17	4.1 (2.5–6.4)	16	2.4 (1.4–3.8)	33	3.0 (2.1–4.2)	1.73	0.12
Exacerbation of psoriasis	1	0.2 (0.01–1.2)	1	0.2 (0.01–0.7)	2	0.2 (0.03–0.6)	1.62	0.76
Liver fibrosis or steatosis	3	0.7 (1.8–2.0)	2	0.3 (0.1–1.0)	5	0.5 (0.2–1.0)	2.40	0.36
Depression	3	0.7 (1.8–2.0)	2	0.3 (0.1–1.0)	5	0.5 (0.2–1.0)	2.40	0.36
Diabetes mellitus	2	0.5 (0.1–1.6)	2	0.3 (0.1–1.0)	4	0.4 (0.1–0.9)	1.60	0.65

†Rate ratio based on female vs. male incidence rates per 100 patient-years.
‡Mid-P exact test.
§Excluding melanoma, NMSC, haematological cancers.
Number of adverse events are cumulative. Incidence rates per 100 patient-years are *n* (95% confidence interval).
AE, adverse events; HIV, human immunodeficiency virus; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PY, patient-years; TBC, tuberculosis.

the total number was significantly higher in women, with 120 AEoSI in women vs. 109 in men (rate ratio 1.79; $P < 0.001$). Regarding subcategories, there were significantly more fungal infections reported among female patients ($n = 38$ vs. $n = 28$; rate ratio 2.20; $P = 0.001$). Female patients also reported more mucosal fungal infections compared with male patients (rate ratio 12.99; $P < 0.001$) and more herpes simplex infections compared with male patients (rate ratio 3.25; $P = 0.005$). Adjustment for gender-related AEoSI revealed no differences in significance (rate ratio 1.68; $P = 0.01$; data not presented).

After stratifying per type of biologic, incidence rates for SAEs did not differ between male and female patients for all biologics. With regard to AEoSI, female patients had higher incidence rates compared with male patients for etanercept (rate ratio 2.29; $P = 0.002$) and infliximab (rate ratio 9.89; $P = 0.001$). No differences in pattern of adverse events were found between all biologics for female and male patients.

Discussion

This prospective, multicentre, longitudinal study showed that female patients reported significantly lower treatment satisfaction, measured by TSQM, regarding the domains 'side-effects' and 'global satisfaction' compared with male patients. In general, treatment satisfaction with biologics was high in both groups. *Post hoc* analyses on side-effects revealed that female patients had more fungal infections and herpes simplex infections. The number of reported SAEs did not differ between men and women. Unique in our study is the confounder corrected, longitudinal analysis of treatment satisfaction in male and female patients treated with biologics for psoriasis in daily practice care. As such, our study exceeds previous cross-sectional and longitudinal studies on treatment satisfaction with shorter follow-up duration.[15]

The purpose of this study was to find possible explanations for the lower drug survival with biologics in female patients, which has been reported before by several large studies.[4–10,29] However, reasons for the lower drug survival in women remain scarce. We assessed treatment satisfaction because this is an important PRO related to adherence and patients' preferences.[11,12,30] Therefore, lower treatment satisfaction in women might partly explain the lower drug survival in women.

In our cohort, female patients scored significantly lower on the 'global satisfaction' domain and were also less satisfied regarding 'side-effects' than men, although differences were small. Our *post hoc* analyses showed more AEoSI in female patients, with significantly more fungal infections and more herpes simplex infections in females. Adjustment for gender-related adverse events revealed no differences in significance. After sensitivity analyses with correction for recurrent episodes of infections, a trend of more mucosal fungal infections was seen in women (data not presented). These differences could explain the difference in satisfaction rates and might partly explain the lower drug survival rates in women. Despite possible reporting bias due to patient-reported adverse events, we can assume that the burden of patient-reported adverse events is higher than the burden of unreported adverse events. In general medicine, women tend to have more adverse drug reactions.[20,31] Therefore, we suppose that differences regarding reported adverse events between men and women with psoriasis need attention. This could be conductive to the development of more personalized medicine.[32]

Besides differences in side-effects between sexes, other differences in disease perception have been described and could explain the lower satisfaction among female patients. Lesuis *et al.*[33] demonstrated a higher symptomatic disease burden compared to male patients. Another study reported that women with psoriasis perceived a greater impact of their psoriasis on mental health and quality of life.[34] Whereas these results indicate worse subjective disease perception in female patients, it has been documented that men have more severe disease.[24,25] This is also found in our study: baseline analyses (start of medication) showed that almost sixty per cent of the patients were male, and men had higher baseline PASI scores compared with women.

Our study is the first to provide a longitudinal analysis of treatment satisfaction with adalimumab, etanercept, infliximab, secukinumab and ustekinumab over 1 year of treatment, in order to investigate differences between male and female patients. Furthermore, we performed correction for possible confounders, and we investigated differences in adverse events between male and female patients. As such, our findings go beyond previously reported cross-sectional findings and longitudinal studies with shorter follow-up duration.[15] For example, a previous BioCAPTURE study assessed treatment satisfaction with all biologics as one group in 106 patients for a period of 6 months.[3] The present study contains data until 2018, from 315 male and female patients with 396 corresponding treatment episodes, with newer biologics for a period of 12 months. The latter is important, as satisfaction scores could change over time and patients are mostly on biologics for many years. Moreover, our gender-focused approach could contribute to more personalized medicine.

A limitation of this study is the possibility of responder bias as a result of questionnaire research and regarding side-effects. Furthermore, we had to deal with missing data due to non-responders to questionnaires and incomplete follow-up. We used LMMs, which are able to accommodate all available data with flexible assumptions regarding missing data.[27] Therefore, imputation of missing data was not useful, as estimated outcomes from our models would be similar. Still bias can occur as a result of incomplete prediction by the model due to missing data. When we analysed TSQM scores from the first vs. subsequent treatment episodes separately, we found no large differences in TSQM scores (data not presented). Furthermore, the LMMs accounted for the fact that some patients had more than one

treatment episode. Correction for possible influence of the different types of biologics used was performed in the mixed models, although some of the groups were small.

In conclusion, this prospective, multicentre, longitudinal study shows that female patients are less satisfied with biological treatment for psoriasis over 1 year of treatment regarding TSQM 'side-effects' and 'global satisfaction' domains. Female patients reported more AEoSI, with more fungal infections and herpes simplex infections. From a clinical perspective, this study shows that treatment with biologics for psoriasis is not the same for men and women. Our results might give an explanation for the earlier discontinuation with biological treatment of female patients. Further clarifying the background of gender differences in psoriasis patients treated with biologics is valuable to increase awareness and provide more personalized care according to the patients' needs. This might improve satisfaction and will consequently lead to better adherence, improved health outcomes, and reduced costs of treatment with biologics.[35]

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Linear Mixed Model used to estimate TSQM subdomain 'Effectiveness' scores during 1 year follow up in male (N = 188) and female (N = 127) psoriasis patients treated with biologics, with a total of 396 treatment episodes.

Table S2. Linear Mixed Model used to estimate TSQM subdomain 'Side-Effects' scores during 1 year follow up in male (N = 188) and female (N = 127) psoriasis patients treated with biologics, with a total of 396 treatment episodes.

Table S3. Linear Mixed Model used to estimate TSQM subdomain 'Convenience' scores during 1 year follow up male (N = 188) and female (N = 127) psoriasis patients treated with biologics, with a total of 396 treatment episodes.

Table S4. Linear Mixed Model used to estimate TSQM subdomain 'Global Satisfaction' scores during 1 year follow up in male (N = 188) and female (N = 127) psoriasis patients treated with biologics, with a total of 396 treatment episodes.