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Treatment preferences for biologicals in psoriasis: experienced patients appreciate sustainability

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Summary

Background and objectives: Treatment satisfaction can be improved by integrating patients' preferences into shared decision-making. We recently investigated patients' preferences for attributes of biologicals, and showed high preferences for safety and efficacy. The objective of the present study was to assess the impact of treatment experience on these preferences.

Patients and methods: Preferences for outcome (probability of 50 % and 90 % improvement, time until response, sustainability of success, probability of mild and severe adverse events, probability of ACR 20 response) and process attributes (treatment location, frequency, duration, and delivery method) were analyzed in 200 participants with moderate-to-severe psoriasis using conjoint analysis. The impact of current and previous therapies, disease duration, and treatment satisfaction on 'Relative Importance Scores' was determined by analysis of variance, post hoc tests, and multivariate regression.

Results: Participants presently on topical therapy ($p = 0.02$) or phototherapy ($p = 0.032$) placed more importance on treatment duration than others. Individuals who had previously been given traditional systemic agents ($p = 0.028$) or biologicals ($p = 0.044$) favored sustainability more than others. With an increasing number of systemic agents ever received ($p = 0.045$) and longer disease duration ($p = 0.018$), the latter attribute became increasingly important.

Conclusions: Patients' preferences for biologicals vary in correlation with treatment experience and disease duration, aspects to be addressed in the context of shared decision-making.

Introduction

With a prevalence of 1–3 % in Western countries, psoriasis is one of the most common chronic inflammatory diseases of the skin and joints [1]. Not only do affected patients experience both physical as well as mental hardship [2, 3], their quality of life and well-being are also considerably impacted by the treatment prescribed, in particular by its efficacy, safety, and convenience [4–6]. The introduction of biologicals represented a milestone in the treatment of moderate-to-severe psoriasis. In Germany, the tumor necrosis factor (TNF) antagonists etanercept, adalimumab, and infliximab as well as the interleukin 12/23 antagonist ustekinumab were available as second-line therapies for refractory psoriasis and psoriatic arthritis until the beginning of 2015 [7]. Highly effective and marked by a favorable risk-benefit profile [8–10], all of the aforementioned agents significantly contribute to health-related quality of life improvement [11–13].

Treatment satisfaction with biologicals is markedly higher than with other modalities [5, 11, 12, 14, 15], both due

to their efficacy as well as the convenience associated with their administration. Indeed, patient satisfaction largely depends on the process attributes of the treatments prescribed, e.g., treatment location and time required for administration [4, 14]. Conversely, a treatment process that is incompatible with an individual's preferences or personal and professional needs is likely to result in dissatisfaction and nonadherence, problems commonly encountered in psoriasis [16, 17]. Hence, greater integration of patients' preferences into shared decision-making is warranted in order to optimize treatment outcome.

Among various preference elicitation methods, conjoint analysis (CA) has gained increasing popularity in health care research, as it realistically reflects decision-making processes in clinical practice [18–21]. We previously conducted CA (discrete choice experiments) to identify preferences in patients with moderate-to-severe psoriasis with respect to treatment attributes of biologicals, and demonstrated high preferences for safety and efficacy [22]. However, we also noted that preferences vary significantly depending on age, gender, disease severity, and comorbidities [22, 23]. The objective of the present study was to investigate the impact of treatment experience and disease duration on patients' preferences for outcome and process attributes of TNF antagonists and ustekinumab. We will show that patients with longstanding disease and extensive experience with systemic therapies particularly value sustainability, an aspect to be increasingly considered during therapeutic decision-making in this severely affected subgroup.

Patients and methods

Study population

Outpatients treated at the Department of Dermatology, University Medical Center Mannheim, Germany, were recruited between March 1 and September 30, 2013. Inclusion criteria were age ≥ 18 years and moderate-to-severe psoriasis according to criteria issued by the Committee for Medicinal Products for Human Use (CHMP) [24] (for details see [19]). Patients unable to complete the survey due to difficulties with the German language or understanding CA exercises were excluded (cf. [22]). The study was conducted according to the principles of the Declaration of Helsinki and approved by the Ethics Committee of the Medical Faculty Mannheim (Ethics Approval 2009–329E-MA, October 22, 2009; Amendment, September 27, 2012).

Data collection

Following written informed consent, participants completed a computerized survey while waiting for their clinical consultation. The survey included information on age (in years), gender (male/female), disease duration (duration since onset of initial symptoms of psoriasis) (in years), currently and previously prescribed antipsoriatic therapies, as well as prior inpatient psoriasis treatment (inpatient care at a hospital, day care at a hospital, stay at a health resort, or exclusive outpatient treatment). With regard to current and previous antipsoriatic therapies, participants were asked about treatment modalities (topical treatment, phototherapy, traditional systemic therapy, or biologicals) as well as specific medications. Details on currently and previously prescribed agents were assessed by having patients choose items from lists of topical therapies, phototherapies, traditional systemic therapies, and biologicals that had been approved for the treatment of psoriasis at the time of data collection. The lists contained both generic and brand names (from various manufacturers, if available). In addition to selecting options from the lists, patients were able to state "yes, unknown which" or "yes, other", and provide detailed free-text information. Selection of more than one option was allowed. Medical records were reviewed by two of the investigators (C.K. and M.-L.S.) to identify unknown treatments and verify answers.

Furthermore, the Dermatology Life Quality Index (DLQI) [25] and the Treatment Satisfaction Questionnaire for Medication (TSQM) Version 1.4 validated in German [26] were part of the questionnaire. The TSQM score can range between 0 and 400, with 0 points indicating complete dissatisfaction and 400 points corresponding to maximum treatment satisfaction. The Psoriasis Area and Severity Index (PASI) of each participant was assessed by two of the investigators (C.K. and M.-L.S.) on the day of the survey [27]. If psoriatic arthritis was suspected, Classification for Psoriatic Arthritis (CASPAR) criteria were applied to verify the diagnosis [28].

Generation of CA exercises has previously been described in detail [22]. Briefly, all TNF antagonists approved for psoriasis in Germany when the study was conducted and ustekinumab were decomposed into outcome attributes (probability of 50 % improvement, probability of 90 % improvement, time until response, sustainability of success, probability of mild adverse events [AE], probability of severe AE, and probability of American College of Rheumatology [ACR] 20 response), process attributes (treatment location, frequency, duration, and delivery method), and attribute levels (Supplementary Table 1, online Supporting Information; cf. [22]). Attributes were divided into two groups to avoid information overload (for further information, see [22]). The attribute "treatment duration" was part of both groups to allow subsequent comparison and computation across attributes of both groups. Theoretical treatment options based on random combinations of the defined attributes were created using commercially available software (http://www.sawtoothsoftware.com). Several times during the survey,

Table 1 Socio-demographic and disease-related characteristics of the study cohort.

Category	n (%)
Gender	
Female	85 (42.5)
Male	115 (57.5)
Age	
Mean (SD)	50.8 (14.1)
Median (min–max; IQR)	51 (18–84; 17.8)
PASI	
Mean (SD)	3.4 (4.1)
Median (min–max; IQR)	2 (0–26.7; 4.4)
DLQI	
Mean (SD)	6.2 (7.1)
Median (min–max; IQR)	4 (0–30; 9)
Disease duration	
Mean (SD)	19.9 (13.1)
Median (min–max; IQR)	19.5 (1–60; 21)
TSQM score	
Mean (SD)	298.2 (68.3)
Median (min–max; IQR)	300.8 (22.9–400; 98.9)
Current treatment	
Topical therapy	153 (76.5)
Merely moisturizing skin care with urea	29 (14.5)
Phototherapy[a]	20 (10)
UVB 311	14 (7)
Topical PUVA	6 (3)
Broadband UVB/SUP	1 (0.5)
Traditional systemic therapies[b]	75 (37.5)
Acitretin	7 (3.5)
Fumaric acid esters	32 (16)
Methotrexate	32 (16)
Alitretinoin	4 (2)
Biologicals	87 (43.5)
Infliximab	14 (7)
Etanercept	8 (4)
Adalimumab	37 (18.5)
Golimumab	3 (1.5)
Ustekinumab	26 (13)
Previous treatments	
Topical therapy	194 (97)
Phototherapy[c]	160 (80)
UVB 311	85 (42.5)
Topical PUVA	77 (38.5)
Systemic PUVA	28 (14)
Broadband UVB/SUP	31 (15.5)
Excimer laser	5 (2.5)
Traditional systemic therapies[d]	149 (74.5)
Acitretin	31 (15.5)
Fumaric acid esters	86 (43)
Methotrexate	92 (46)
Cyclosporine	13 (6.5)
Leflunomide	2 (1)
Alitretinoin	7 (3.5)
Biological[e]	86 (43)
Infliximab	19 (9.5)
Etanercept	22 (11)
Adalimumab	50 (25)
Golimumab	4 (2)
Ustekinumab	25 (12.5)
Number of different systemic treatments ever used	
Mean (SD)	1.9 (1.5)
Median (min–max; IQR)	2 (0–8; 2)
Number of traditional systemic therapies	
Mean (SD)	1.2 (1)
Median (min–max; IQR)	1 (0–4; 1)
Number of biologicals	
Mean (SD)	0.7 (0.9)
Median (min–max; IQR)	0 (0–4; 1)
Inpatient care	
Hospital	106 (53)
Day hospital	32 (16)
Health resort	63 (31.5)
Exclusive outpatient care	61 (30.5)

[a]No participant was being treated with systemic PUVA or excimer laser.
[b]No respondent was on cyclosporine; only one patient was on systemic corticosteroids.
[c]Three individuals reported prior phototherapy using a UV comb. Four participants did not remember which phototherapy they had received in the past.
[d]One participant had previously been treated with systemic corticosteroids; another, with mycophenolate mofetil; and a third, with a traditional systemic drug that he did not recall.
[e]Seven participants had experience with another biologic (alefacept: n = 1, efalizumab: n = 5, unknown biologic: n = 1).
Abbr.: DLQI, Dermatology Life Quality Index; IQR, interquartile range; min, minimum; max, maximum; n, number; PASI, Psoriasis Area and Severity Index; PUVA, psoralen plus UVA; SD, standard deviation; TSQM, Treatment Satisfaction Questionnaire for Medication.

patients were asked to choose their preferred option from various treatment scenarios (presented in a pairwise manner) (for examples see [22]).

Preferences were calculated as the sum of part-worth utilities of attributes' levels, using logit regression [22]. A 'Relative Importance Score' (RIS) was computed for each attribute as the proportion of one attribute's range between the highest and lowest part-worth utility across the sum of all attributes' ranges (for further details see [22]). RIS for each attribute were calculated individually for each participant and subsequently averaged across the entire sample. Logarithmic and square root transformations led to approximately normally distributed variables.

Subgroup analyses

Subgroup analyses were performed with SPSS software based on current treatment (topical therapy, phototherapy, traditional systemic medication, or biologicals: yes or no), treatment experience (previous use of topical therapy, phototherapy, traditional systemic medication, or biologicals: yes or no), number of traditional systemic medications ever used (continuous), number of biologicals ever received (continuous), and number of all systemic treatments ever used, including both traditional medications and biologicals (continuous). Biologicals were generally administered as continuous treatment [29]. Participants treated with a combination of different modalities were included into more than one subgroup. For example, a participant currently receiving a biologic in combination with methotrexate was assigned both to the subgroup "current traditional systemic medication" and to the subgroup "current biological treatment". Skin products with urea were assigned to topical therapy because urea has keratolytic effects in addition to its moisturizing properties [30]. Further subgroup analyses were conducted based on disease duration (continuous in years) and TSQM (continuous, range: 0–400). The association of categorical variables with RIS was determined using analysis of variance (ANOVA); the association of continuous variables, using Pearson's correlation (PC) coefficients. For sensitivity analyses nonparametric tests were applied to the untransformed variables (Kruskal-Wallis test for ANOVA and Spearman's rho for correlations).

Multivariate linear regression analyses were performed to estimate the impact of the independent variables gender, age, PASI, DLQI, disease duration, TSQM, and number of systemic treatments ever used on the RIS of each attribute (dependent variable). A standardized regression coefficient β was calculated for each independent variable, indicating the amount of change in RIS when varying the respective variable while holding the others constant. Significance was always assumed at $p \leq 0.05$.

Results

Two hundred thirty-nine eligible patients were asked to participate, and 210 provided written informed consent. Ten participants had to be excluded due to difficulties with the German language (n = 9) or inability to understand the CA exercises (n = 1). Two hundred participants completed the survey (mean age: 50.8 years, 42.5 % female) (Table 1).

Virtually all participants (99 %) were on some form of antipsoriatic treatment at the time of study participation. The mean PASI was therefore relatively low (3.4; range: 0–26.7), although all participants had moderate-to-severe psoriasis according to CHMP criteria. Mean disease-related quality of life impairment was moderate (mean DLQI: 6.2, range: 0–30). A mean TSQM score of 298.2 indicated relatively high satisfaction with the currently prescribed treatment. Disease duration averaged 19.9 years; 22.5 % of participants had psoriatic arthritis according to CASPAR criteria [28].

95.5 % of participants came to our department for a follow-up visit. 4.5 % reported treatment by an office-based dermatologist; another 4.5 %, by a general practitioner. Along with treatment provided by our department, patients usually saw their primary care physicians for regular lab tests (during systemic therapy) or follow-up prescriptions.

More than three-fourths of the participants (76.5 %) were using topical therapy at the time of the survey, including moisturizing skin care products with urea. Ten percent were being treated with phototherapy; 37.5 %, with traditional systemic medications; and 43.5 %, with biologicals (for details, see Table 1). Routinely, infliximab was prescribed in combination with methotrexate in order to prevent the formation of anti-infliximab antibodies and to increase its drug survival [31]. Other biologicals were occasionally combined with methotrexate in patients with refractory disease or with severe psoriatic arthritis (for a survey of biological/methotrexate combinations prescribed in the study cohort see Supplementary Table 2). With respect to previous therapies, 97 % of the participants had previously received topical therapy, 80 % phototherapy, 76.5 % traditional systemic medications, and 46 % biologicals (Table 1). The mean number of systemic treatments ever used was 1.9 (range: 0–8) (Table 1). Fifty-three percent of all respondents had received in-hospital treatment for their psoriasis; 16 %, at a day hospital, 31.5 %, at a health resort.

Impact of treatment experience on preferences for biologicals

Preferences averaged across the entire study population have previously been reported [22]. Briefly, the probability of severe AE (RIS = 17.3) and the probability of 90 % improvement (RIS = 14.0) were regarded as most important.

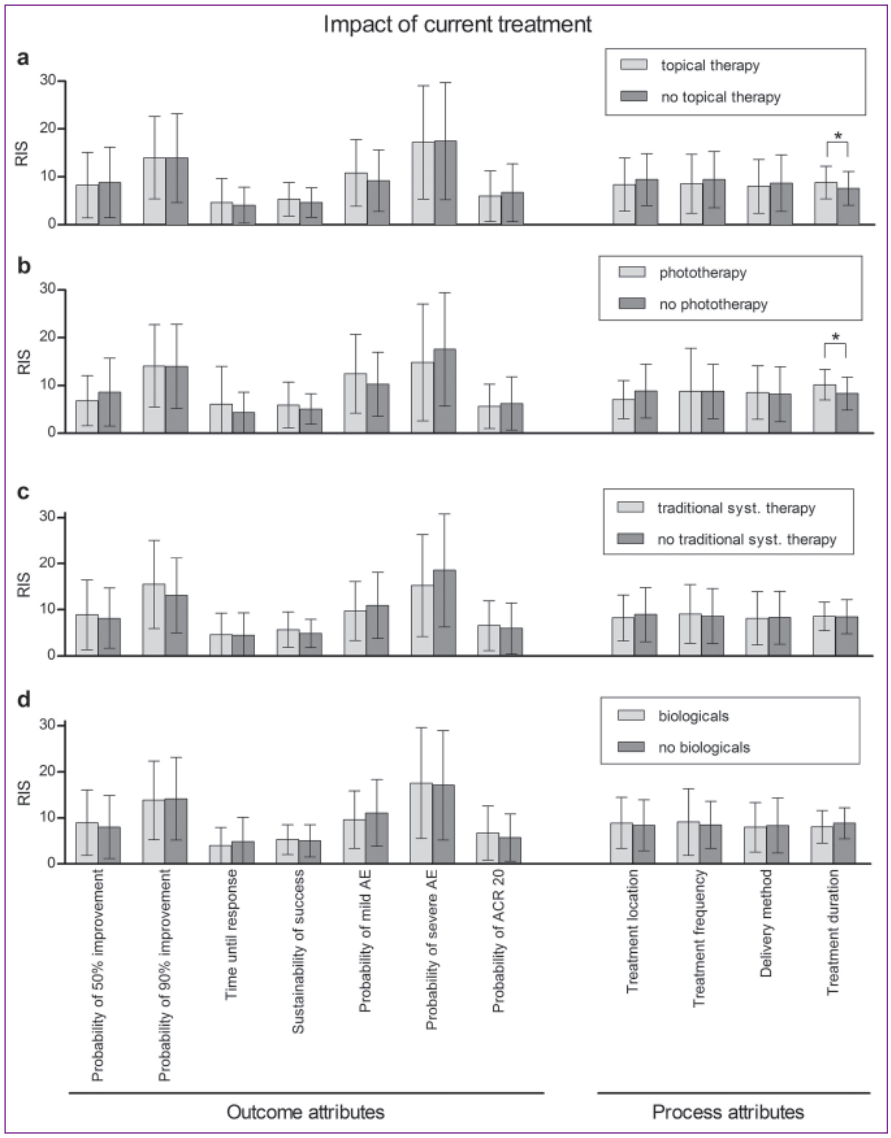

Figure 1 Impact of current treatments on patient preferences. Participants receiving topical therapy (a) or phototherapy (b) attached greater importance to treatment duration than others. Current use of traditional systemic agents (c) or biologicals (d) had no significant impact on preferences. Differences in Relative Importance Scores (RIS) were tested for significance with ANOVA (analysis of variance). Bars: Means with standard deviations. AE: adverse events. *p ≤ 0.05.

Process attributes (treatment location, frequency, duration, and delivery method) received RIS between 8.2 and 8.8 [22].

When the study population was stratified according to current treatment, respondents currently being treated with topical therapy or phototherapy attached significantly greater importance to treatment duration than those not using these modalities (RIS = 8.78 vs. 7.58, p = 0.02 for topical therapy, RIS = 10.13 vs. 8.32, p = 0.032 for phototherapy) (Figure 1a, b). As it is debatable whether skin care products containing urea should be counted as topical treatment, analyses were repeated without those participants who were merely using urea (n = 29; 14.5 %). However, the results turned out to be very similar, and the impact on treatment duration remained significant (RIS = 8.91 vs. 7.82; p = 0.03). Neither current use of traditional systemic medications nor current use of biologicals had a significant effect on preferences (Figure 1c, d).

In subgroup analyses based on previous treatments, preferences of participants with a history of topical therapy or phototherapy did not significantly differ from preferences of respondents without any experience with these modalities (data not shown). Individuals who had previously received traditional systemic medication set greater value on sustainability of success and treatment frequency than others (RIS = 5.45 vs. 4.28, p = 0.028 for sustainability, RIS = 9.27 vs. 7.26, p = 0.012 for frequency) (Figure 2a). Similarly, participants previously treated with biologicals were significantly more interested in sustainability (RIS = 5.59 vs. 4.82, p = 0.044) (Figure 2b). Previous treatment at a hospital (inpatient) or day hospital did not significantly impact preferences (data not shown).

When preferences were analyzed based on the number of different traditional systemic treatments ever used,

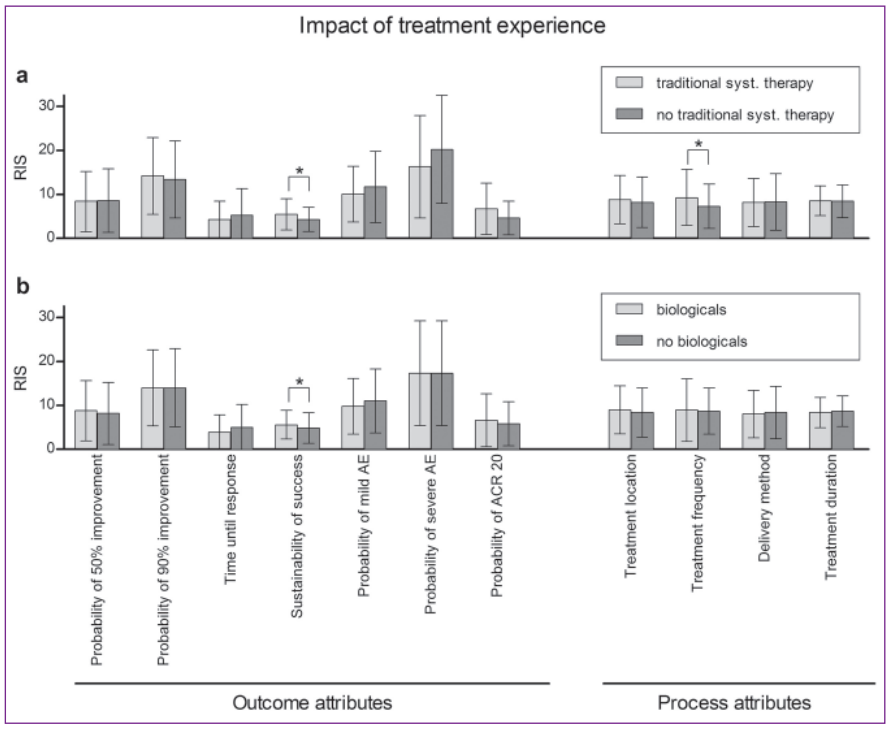

Figure 2 Impact of treatment experience on preferences. Participants previously treated with traditional systemic agents set greater value on sustainability of success and treatment frequency than others (a). Similarly, respondents experienced with biologicals appreciated sustainability (b). Differences in Relative Importance Scores (RIS) were compared with ANOVA (analysis of variance). Bars: Means with standard deviations. AE: adverse events. *p ≤ 0.05.

sustainability of success (PC = 0.159, p = 0.025) and treatment frequency (PC = 0.175, p = 0.013) became increasingly important in correlation with an increase in the number of traditional medications (Figure 3a). By contrast, the probability of severe AE became less relevant (PC = −0.150, p = 0.035). The number of biologicals ever administered did not significantly influence preferences (Figure 3b). However, there was a correlation between the increase in the overall number of any kind of systemic antipsoriatic medications ever prescribed and greater appreciation of sustainability (PC = 0.166, p = 0.019) (Figure 3c). Multivariate regression analyses revealed that this effect was independent of age, gender, PASI, DLQI, disease duration, and TSQM (β = 0.151, p = 0.045) (Table 2). In addition, regression models suggested that a greater number of systemic therapies ever used was associated with a rising interest in the probability of an ACR 20 response (β = 0.157, p = 0.038) (Table 2).

Compatible with the notion that experienced participants appreciate sustainability, longer disease duration was correlated with a greater importance attached to sustainability (PC = 0.167, p = 0.018; β = 0.133, trend with p = 0.082 in multivariate regression models) (Table 2) (Figure 4a).

Correlation between preferences and treatment satisfaction revealed significant associations between higher TSQM scores and greater prioritization of the probability of 50 % improvement (PC = 0.219, p = 0.002) (Figure 4b). Based on multivariate regression analysis, this association was independent of all other variables included in the models (β = 0.177, p = 0.028) (Table 2).

The impact of age, gender, and DLQI on preferences has previously been reported and discussed in detail [22], and is confirmed in the regression models presented herein. Briefly, women attached less value to the probability of 50 % and 90 % improvement than men. Older participants were less interested in efficacy, time until response, and treatment frequency than younger individuals yet more concerned about severe AE. Participants with greater impairment in quality of life put more importance on treatment duration [22] (Table 3).

Discussion

Integrating patients' preferences into shared decision-making is essential in order to improve treatment satisfaction, adherence, and outcome [32]. In our previous CA, which assessed patients' preferences for psoriasis treatment with biologicals, we demonstrated that – averaged across the study sample – safety and efficacy were rated as the most important parameters [22]. Here, we show that preferences vary significantly depending on treatment experience. Individuals exclusively treated with topical therapy or phototherapy at the time of the survey attached greater importance to treatment duration than those on traditional systemic therapy or biologicals. This finding is not surprising considering that both topical therapy and phototherapy may be very time-consuming. In a study by Dubertret et al., approximately one-half of the participants

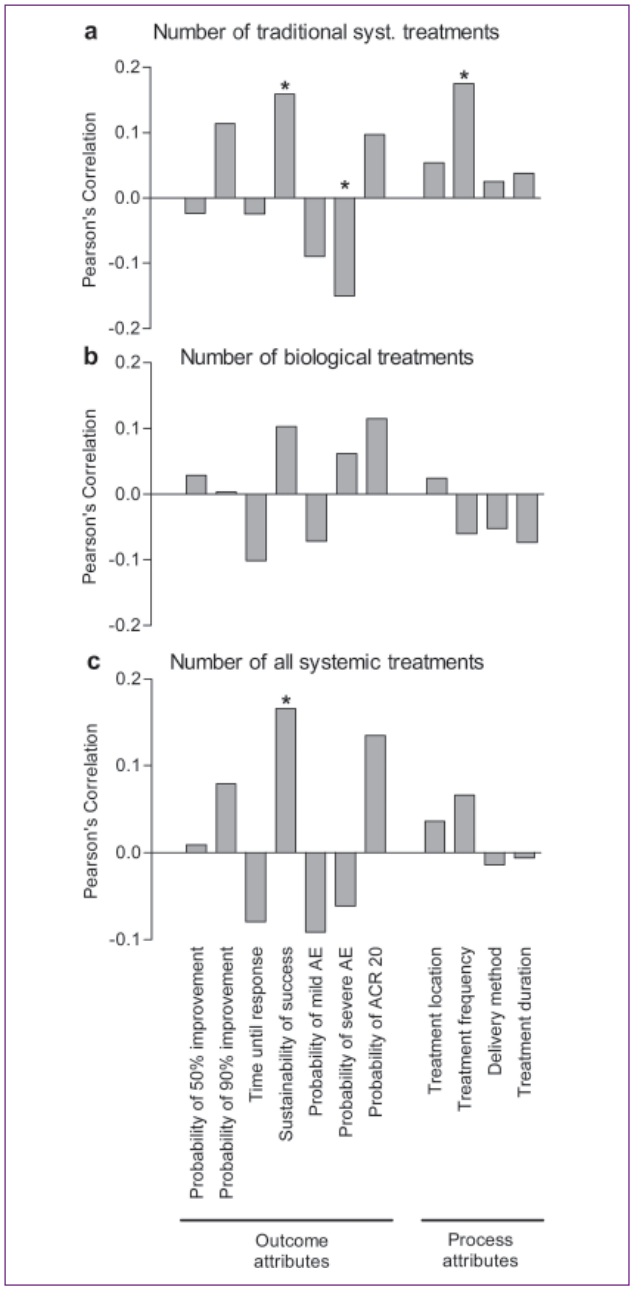

Figure 3 Impact of the number of different systemic treatments on preferences. An increasing number of traditional systemic agents ever used correlated with lower prioritization of severe adverse events (AE) but greater emphasis on sustainability of success and treatment frequency (a). The number of biologicals ever received did not influence preferences (b). An increasing number of any kind of systemic agents ever used, including traditional antipsoriatic drugs and biologicals, was associated with greater appreciation of sustainability (c). Impact on Relative Importance Scores (RIS) was tested for significance with two-tailed t-tests. Bars: Pearson's correlation (PC). *p ≤ 0.05.

identified expenditure of time as the most troublesome aspect of disease management [33]. Time consumption was perceived as even more disturbing than inefficiency and AE.

An important finding of our study is that preferences shift depending on prior experience with systemic antipsoriatic treatment. Participants with a history of using traditional systemic agents and/or biologicals set greater value on sustainability than others. Interest in sustainability was found to rise with an increasing number of previous systemic treatments as well as longer disease duration. Several studies have shown that patients with psoriasis prefer systemic therapies to topicals or phototherapy [11, 15, 19]. Compared to the latter, systemic treatment is associated with better quality of life, both due to its effectiveness and due to a more convenient method of administration [11–13]. Nevertheless, because of primary or secondary treatment failure or AE, many patients are forced to switch systemic therapies over the course of their disease. Such experiences are likely to intensify the desire for more sustainable treatment. When we previously analyzed patients' preferences for all kinds of psoriasis treatments, including topical treatments, phototherapy, traditional systemic medications, and biologicals, we found that patients pretreated with > 3 different therapies as well as patients with long disease duration were particularly interested in long-lasting benefits [14], which is in keeping with the results of the present study.

With respect to drug survival rates of biologicals in psoriasis, there have been conflicting reports, and long-term data is relatively scarce [34–37]. Van den Reek et al. demonstrated one-year drug survival rates of 85 % for ustekinumab, 74 % for adalimumab, and 68 % for etanercept [38], results that are largely in accordance with data published by Clemmensen et al. [39]. Another group even observed a one-year drug survival rate of 96.7 % for ustekinumab, compared to 79.7 % for adalimumab and 73.3 % for infliximab [40]. A recent study investigating > 1,800 treatment series with biologicals also revealed a significantly longer drug survival for ustekinumab than for TNF antagonists [35]. According to that study, drug survival was shortest for etanercept, whereas maintenance rates for adalimumab and infliximab were comparable [35]. In a study evaluating four-year drug survival of TNF antagonists, maintenance rates ranged from 70 % for infliximab to 40 % for etanercept or adalimumab [36]. Levine and colleagues identified infliximab as the biological with the longest sustainability, and ustekinumab as the biological with the lowest failure rate [41]. This data is at odds with findings published by Brunasso et al. who showed a lower four-year drug survival rate for infliximab than for etanercept and adalimumab [42], and also with an Italian study according to which maintenance was longest for etanercept, followed by infliximab and adalimumab [34]. Discrepancies in drug survival rates may in part be explained by the heterogeneity

Table 2 Multivariate regression models investigating the impact of socio-demographic characteristics, disease severity and duration, number of systemic antipsoriatic treatments and treatment satisfaction on RIS of outcome attributes.

Outcome attributes														
Characteristic	Probability of 50 % improvement		Probability of 90 % improvement		Time until response		Sustainability of success		Probability of mild AE		Probability of severe AE		Probability of ACR 20 response	
	β	*p*	*β*	*p*	*β*	*p*	*β*	*p*	*β*	*p*	*β*	*p*	*β*	*p*
Female[a]	***−0.149***	***0.034***	***−0.210***	***0.004***	0.057	0.432	0.011	0.883	0.069	0.340	0.031	0.666	0.063	0.378
Age	***−0.152***	***0.032***	*−0.140*	*0.052*	***−0.190***	***0.010***	0.073	0.310	0.088	0.232	***0.168***	***0.022***	0.128	0.077
PASI	0.002	0.984	−0.029	0.708	−0.035	0.655	0.076	0.325	0.095	0.224	0.023	0.762	−0.027	0.730
DLQI	−0.097	0.267	0.035	0.694	0.067	0.455	0.121	0.173	0.044	0.627	−0.138	0.125	0.076	0.396
No. of syst. therapies[b]	−0.013	0.864	0.055	0.466	−0.038	0.616	***0.151***	***0.045***	−0.024	0.757	−0.103	0.173	***0.157***	***0.038***
Disease duration	−0.074	0.318	0.021	0.783	−0.002	0.982	0.133	0.082	−0.100	0.200	0.017	0.828	0.050	0.513
TSQM score	***0.177***	***0.028***	0.010	0.903	0.013	0.877	0.075	0.358	0.025	0.766	−0.059	0.472	−0.092	0.260

The RIS was defined as dependent variable; gender, age, PASI, DLQI, number of systemic therapies, disease duration (in years), and TSQM score as predictors. β represents the standardized regression coefficient. For the binary variable gender, a positive β-value indicates greater importance of this attribute in women compared to men. For metric variables (all others), a positive β signifies that the attribute gains importance with an increase of the characteristic, whereas a negative β indicates loss of importance with an increase of the characteristic. Significant findings are highlighted in bold.

[a]The reference group for "female" was male.

[b]"No. of syst. therapies" designates the number of different systemic antipsoriatic therapies ever used, including traditional systemic medications and biologicals.

Abbr.: DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; TSQM, Treatment Satisfaction Questionnaire for Medication; RIS, Relative Importance Score.

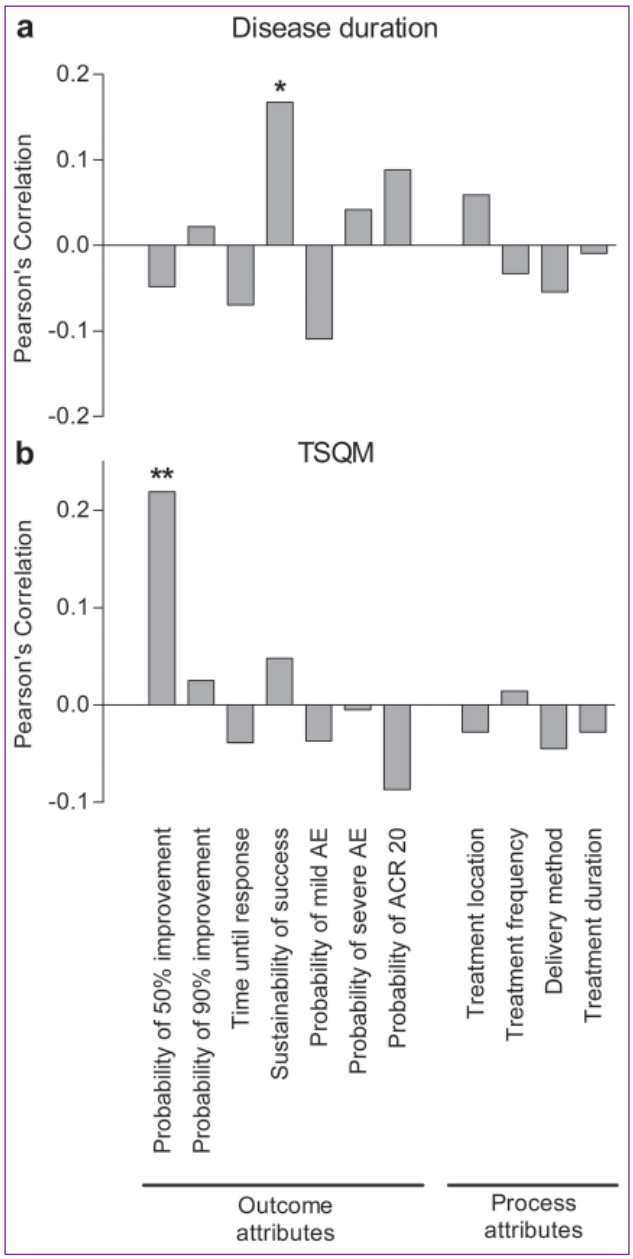

Figure 4 Correlation between disease duration, respectively TSQM (Treatment Satisfaction Questionnaire for Medication), and preferences. Participants with longer disease duration placed greater importance on sustainability of success (a). Higher TSQM scores correlated with greater emphasis on the probability of 50 % improvement (b). Impact on Relative Importance Scores (RIS) was assessed with two-tailed t-tests. Bars: Pearson's correlation (PC). AE: adverse events. * $p \leq 0.05$.

of the various studies. First, some were monocenter studies [40, 41], while others examined drug survival rates in large nationwide cohorts [34–38]. Secondly, inclusion and exclusion criteria as well as observation periods were heterogeneous. Thirdly, drug survival rates may differ between prospective [35, 36, 38–40] and retrospective studies [34, 41]. Fourthly, it is a safe assumption that drug survival is significantly impacted by the dose and the administration interval of each medication, which were individually adjusted in some studies. Last but not least, decisions for drug discontinuation and switching of medications are largely investigator-dependent. Several studies have identified inefficacy to be the main reason for treatment discontinuation [34, 36–38, 40, 41].

Biologicals are sometimes prescribed off-label in combination with methotrexate [43]. It has been shown – for infliximab in particular – that such a combination may increase drug survival [31]. Thus, it would be interesting to study the impact of combination regimens on preferences. However, such analyses would require larger-scale studies.

Remarkably, an increasing number of previous traditional systemic treatments correlated with fewer concerns about severe AE. Traditional systemic treatments such as fumaric acid esters, methotrexate, cyclosporine, and acitretin are associated with the risk of various mild and severe AE. However, given proper patient selection and careful monitoring, AE may often be avoided or well controlled [44]. Our findings suggest that most participants perceived the safety profile of their systemic treatments as favorable and the AE experienced as well manageable. Unfortunately, it was impossible to assess individual AE as well as their number and severity in the present study because participants had experienced a multitude of different AE during the course of their disease, which could not all be remembered and classified.

Regression analysis revealed that the greater the number of previous systemic treatments had been, the more pronounced was the interest of patients in an ACR 20 response. Subgroup analyses based on the presence or absence of psoriatic arthritis confirmed that individuals with psoriatic arthritis were significantly more interested in an ACR 20 response than those with sole cutaneous psoriasis, as was expected [23]. It is quite conceivable that participants with concomitant psoriatic arthritis had received a greater number of systemic therapies over the course of their disease than individuals without arthritis; hence, the presence of psoriatic arthritis was a confounding factor.

We chose the probability of 50 % and 90 % improvement as outcome attributes, instead of the PASI 75 response rate – the most common primary endpoint of clinical trials – because 50 % and 90 % improvement is easier to envisage for patients than a PASI 75 response. Ninety percent improvement rates of biologicals currently available – roughly reflecting PASI 90 response rates – show greater variability than their PASI 75 rates. In addition, we wanted to investigate whether 50 % improvement is a desirable therapeutic goal in patients' perception. Since the time of data collection, the

Table 3 Multivariate regression models assessing the influence of socio-demographic characteristics, disease severity and duration, number of systemic antipsoriatic treatments and treatment satisfaction on RIS of process attributes.

Process attributes								
Characteristic	**Treatment location**		**Treatment frequency**		**Delivery method**		**Treatment duration**	
	β	***p***	*β*	***p***	*β*	***p***	*β*	***p***
Female[a]	−0.003	0.968	0.123	0.088	0.031	0.670	0.073	0.304
Age	−0.134	0.070	***−0.163***	***0.026***	−0.102	0.169	0.119	0.100
PASI	−0.089	0.257	−0.025	0.750	−0.070	0.374	0.124	0.107
DLQI	−0.023	0.798	0.085	0.345	0.035	0.703	***0.192***	***0.031***
No. of syst. therapies[b]	0.005	0.945	0.103	0.174	0.022	0.777	0.085	0.257
Disease duration	0.080	0.302	−0.009	0.912	−0.028	0.721	−0.007	0.931
TSQM score	−0.063	0.452	0.055	0.504	−0.034	0.686	0.080	0.323

For explanations and abbreviations, see Table 2.

first representative of a novel class of biologicals, the interleukin 17 antibody secukinumab, has been approved for treatment of psoriasis. It is quite conceivable that, with rapidly improving therapeutic options, expectations and attitudes of patients are quickly changing, too, and may be influenced by therapies currently available. With the introduction of interleukin 17 antagonists and other novel agents, an increasing percentage of patients are likely to achieve a PASI 90 response [45]. One may therefore expect PASI 90 to replace PASI 75 as primary treatment goal in the near future. Our results underscore that patients highly appreciate this new goal. Nevertheless, the present study also shows that, for some patients, a PASI 50 response still remains a valuable target. In addition, we demonstrate that patients who appreciate a PASI 50 response – instead of expecting 90 % improvement – are likely to be more satisfied with the prescribed treatment.

Limitations of our study include the rather small sample size and the monocenter setting. Thus, the findings presented herein will have to be verified in larger and more diverse patient cohorts and in a multicenter setting. Our participants were characterized by a long disease history and extensive treatment experience; in addition, they were treated at a specialized psoriasis center. Clearly, long disease duration implies an increased risk of recall bias with respect to previous treatments.

Treatment preferences may be affected by a variety of different factors, including socio-demographic characteristics and disease severity (as confirmed in our regression models and as previously discussed in more detail [22]), but also by comorbidities such as psoriatic arthritis, cardiovascular disease, and diabetes [23]. The latter could not be taken into account in the regression analyses presented herein, given that the number of variables included in the models had to be limited. Furthermore, the extent of available information about the disease – obtained from physicians, patient organizations, or Internet platforms – might have an impact on preferences.

In summary, the present study shows that patients experienced with multiple systemic treatments as well as those with long disease duration particularly value sustainability. For these severely affected individuals, it is essential to identify highly effective therapies, marked by a favorable risk-benefit profile and long drug survival.

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Conflict of interest

Mr. Kromer has received honoraria for presentations from Janssen-Cilag. Prof. Ludwig-Peitsch has served as investigator for Abbvie, Eli Lilly, Janssen-Cilag, Merck, Novartis, Pfizer and UCB Pharma; has been on the advisory board of MSD and Novartis; has received honoraria from ALK-Abello, Abbvie, Janssen-Cilag, MSD and Novartis; and has received support for conferences from Abbvie, ALK-Abello, Alma Lasers, ARC Lasers, Asclepion, BMS, GSK, Janssen-Cilag, L'Oreal, LEO Pharma, Medac, Merck, MSD, Novartis, P&M Cosmetics, Pfizer and Roche. Dr. Schmieder has conducted clinical trials for Abbvie and Pfizer and has received support for conferences from Celgene, Abbvie, Janssen-Cilag

and Pfizer. Dr. Schaarschmidt has conducted clinical trials for Abbvie, Eli Lilly, Merck, Novartis and UCB Pharma; has received honoraria from Janssen-Cilag as well as financial support for participation in conferences from Abbvie, ALK-Abello, Biogen Inc., Janssen-Cilag and MSD. Mr. Herr and Dr. Sonntag have no conflict of interest to declare. The study presented herein was not supported by any pharmaceutical company.

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