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ORIGINAL RESEARCH ARTICLE

Drug Survival, Safety, and Effectiveness of Biologics in Older Patients with Psoriasis: A Comparison with Younger Patients—A BioCAPTURE Registry Study

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Abstract

Background Psoriasis is a common inflammatory disease in any age group, but also in older patients (≥ 65 years of age). Since older patients are often excluded from clinical trials, limited data specifically on this growing population are available, e.g. regarding the safety and performance of biological treatment.

Aims We aimed to give insight into this specific population by comparing the drug survival and safety of biologics in older patients with that in younger patients.

Methods In this real-world observational study, data from 3 academic and 15 non-academic centers in The Netherlands were extracted from the prospective BioCAPTURE registry. Biologics included in this study were tumor necrosis factor (TNF)-α, interleukin (IL)-17, IL-12/23, and IL-23 inhibitors. Patients were divided into two age groups: ≥ 65 years and < 65 years. The Charlson Comorbidity Index (CCI) was used to measure comorbid disease status, and all adverse events (AEs) that led to treatment discontinuation were classified according to the Medical Dictionary for Regulatory Activities (MedDRA) classification. All AEs that led to treatment discontinuation were studied to check whether they could be classified as serious AEs (SAEs). Kaplan–Meier survival curves for overall 5-year drug survival and split according to reasons of discontinuation (ineffectiveness or AEs) were constructed. Cox regression models were used to correct for possible confounders and to investigate associations with drug survival in both age groups separately. Psoriasis Area and Severity Index (PASI) scores during the first 2 years of treatment and at the time of treatment discontinuation were assessed and compared between age groups.

Results A total of 890 patients were included, of whom 102 (11.4%) were aged ≥ 65 years. Body mass index, sex, and distribution of biologic classes (e.g. TNFα, IL12/23) were not significantly different between the two age groups. A significantly higher CCI score was found in older patients, indicative of more comorbidity ($p < 0.001$). The 5-year ineffectiveness-related drug survival was lower for older patients (44.5% vs. 60.5%; $p = 0.006$), and the 5-year overall (≥ 65 years: 32.4% vs. < 65 years: 42.1%; $p = 0.144$) and AE-related (≥ 65 years: 82.1% vs. < 65 years: 79.5%; $p = 0.913$) drug survival was comparable between age groups. Of all AEs ($n = 155$) that led to discontinuation, 16 (10.3%) were reported as SAEs but these only occurred in younger patients. After correcting for confounders, the same trends were observed in the drug survival outcomes. Linear regression analyses on PASI scores showed no statistical differences at 6, 12, 18, and 24 months of treatment between age groups.

Conclusions This study in a substantial, well-defined, prospective cohort provides further support that the use of biologics in older patients seems well-tolerated and effective. Biologic discontinuation due to AEs did not occur more frequently in older patients. Older patients discontinued biologic treatment more often due to ineffectiveness, although no clear difference in PASI scores was observed. More real-world studies on physician- and patient-related factors in older patients are warranted.

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Key Points

In this real-world observational study regarding biologic treatment for psoriasis, drug survival, effectiveness, and safety were mainly comparable between age groups (<65 years and ≥65 years).

Treatment of older patients with biologics appears a well-tolerated and effective therapeutic option.

1 Introduction

Psoriasis is a chronic immune-mediated disease associated with not only a physical but also a psychological burden. It affects 2–4% of the world's population and can occur at any age [1]. The combination of an aging world population and the chronic course of psoriasis results in an increase in the prevalence of older patients with psoriasis [1, 2]. As older patients are often excluded from clinical trials, only limited literature for this specific population is available regarding the effectiveness and safety of systemic anti-psoriatic treatments [3–5].

Biologics are the most recent addition to the arsenal of therapeutic options for psoriasis and appear to be more effective than conventional systemic therapies in older patients [3]. However, choosing the optimal type of treatment can be challenging in older patients, not only due to limited evidence on safety and effectiveness but also due to possibly complicating patient characteristics such as comorbidities, concomitant medication use, polypharmacy, functional status, and frailty. Therefore, it is possible that physicians are reluctant to prescribe certain systemic therapies such as biologics in older patients, which could lead to undertreatment of this patient group [6].

With this prospective observational real-world study in patients using biologics for psoriasis, we aimed to provide insight into the drug survival, safety, and effectiveness of biologics in older patients and compare outcomes with a younger population.

2 Materials and Methods

2.1 The BioCAPTURE Database

In this real-world cohort study, data were extracted from the prospective, multicenter Continuous Assessment of Psoriasis Treatment Use Registry with Biologics (BioCAPTURE registry; www.biocapture.nl). We used data on psoriasis patients treated with biologic therapy from 3 academic and 15 non-academic centers in The Netherlands (2005–2021). The biologics included in this study were tumor necrosis factor (TNF)-α, interleukin (IL)-17, IL-12/23, and IL-23 inhibitors (see Table 1). According to the regional Medical Ethics Committee, ethical approval was not necessary for this non-interventional study. Nevertheless, written informed consent is obtained from every included patient.

2.2 Data Collection

Data were collected from adult patients treated with biologics. Two age groups were compared: patients ≥ 65 years and < 65 years of age at the start of biological treatment. The 65 years of age threshold was chosen because it is widely used in psoriasis literature [3, 7, 8]. In this study, the first biologic treatment episode (TE) per patient in BioCAPTURE was included. A TE represents a continuous period of time in which a patient was treated with a certain biologic. If treatment was interrupted ≥ 90 days, the TE ended. The maximum follow-up duration was set at 5 years. Baseline patient characteristics were collected and calculated for every TE. To measure comorbid disease status, the International Classification of Diseases, Tenth Revision (ICD-10) version of the Charlson Comorbidity Index (CCI) was used [9, 10]. In addition to the CCI, depression and hypertension were added as these were regarded relevant comorbidities in the context of psoriasis. To assess the possibility that this cohort was comprised of relatively healthy older patients due to pre-selection on comorbidity in the context of biologic therapy initiation, a comparison of CCI scores with another Dutch psoriasis cohort including older adults (≥ 65 years) using all types of antipsoriatic therapy ($n = 230$) was performed (data available upon request). This study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) criteria [11].

2.3 Drug Survival Analysis

Drug survival up to 5 years of treatment was visualized using Kaplan–Meier survival curves. For the overall drug survival curve, discontinuation due to ineffectiveness, adverse events (AEs), ineffectiveness and AEs combined, other reasons, and death were considered an event. Additionally, we assessed drug survival according to reason for discontinuation (separately for ineffectiveness and AEs). Patients were censored when lost to follow-up, when still 'on drug' at the moment of data lock (with a maximum follow-up of 5 years), or when a patient reached the age of 65 years during treatment. For the analyses based on discontinuation reasons, patients were

Table 1 Patient and treatment characteristics of older patients, compared with younger patients, using biologic treatment

	< 65 years of age [*n* = 788]	≥ 65 years of age [*n* = 102]	All patients [*n* = 890]	*p* value[a]
Age at start of biologic treatment, years				NA
Mean ± SD	45.4 ± 11.1	70.3 ± 4.1	48.2 ± 13.2	
Median (range)	45.9 (19.1–64.8)	69.9 (65.1–82.5)	48.3 (19.1–82.5)	
Sex [*n* (%)][c]				0.515
Male	487 (62.6)	60 (58.8)	547 (62.2)	
Female	291 (37.4)	42 (41.2)	333 (37.8)	
Hospital type [*n* (%)]				0.437
Academic	526 (66.8)	64 (62.7)	590 (66.3)	
Non-academic	262 (33.2)	38 (37.3)	300 (33.7)	
Body mass index, kg/m^2 [c]				0.930
Mean ± SD	28.9 ± 6.1	28.5 ± 4.3	28.9 ± 5.9	
Median (range)	27.9 (16.4–69.9)	27.3 (21.4–42.6)	27.9 (16.4–69.9)	
Age at onset of psoriasis, years[c]				NA
Mean ± SD	24.8 ± 12.3	41.9 ± 18.8	26.7 ± 14.2	
Median (range)	22.0 (0–59)	47.0 (2–76)	23.0 (0–76)	
Duration of psoriasis until start of biologic, years[b,c]				0.001
Mean ± SD	20.0 ± 11.9	26.5 ± 18.5	20.7 ± 12.9	
Median (range)	18.2 (0.6–57.2)	17.4 (1.7–72.0)	18.2 (0.6–72.0)	
Biologic naive [*n* (%)]				0.827
Yes	510 (64.7)	65 (63.7)	575 (64.6)	
No	278 (35.3)	37 (36.3)	315 (35.4)	
Family history of psoriasis [*n* (%)][c]				0.311
Yes	472 (66.9)	50 (59.5)	522 (66.1)	
No	234 (33.1)	33 (40.5)	268 (33.9)	
Psoriatic arthritis [*n* (%)][c]				0.447
Yes	211 (32.0)	22 (27.2)	233 (31.5)	
No	448 (68.0)	59 (72.8)	507 (68.5)	
Baseline PASI score[c]				0.421
Mean ± SD	13.2 ± 7.7	12.3 ± 6.8	13.1 ± 7.6	
Median (range)	11.8 (0–45.2)	11.0 (0–36.2)	11.4 (0–45.2)	
Biologic treatment [*n* (%)]				0.291
TNFα	515 (65.4)	74 (72.5)	589 (66.2)	
Adalimumab	268 (34.0)	49 (48.0)	317 (35.6)	
Certolizumab	4 (0.5)	0 (0.0)	4 (0.4)	
Etanercept	234 (29.7)	25 (24.5)	259 (29.1)	
Infliximab	9 (1.1)	0 (0.0)	9 (1.0)	
IL-12/23 (ustekinumab)	182 (23.1)	21 (20.6)	203 (22.8)	
IL-17	60 (7.6)	3 (2.9)	63 (7.1)	
Brodalumab	3 (0.4)	1 (1.0)	4 (0.4)	
Ixekizumab	23 (2.9)	1 (1.0)	24 (2.7)	
Secukinumab	34 (4.3)	1 (1.0)	35 (3.9)	
IL-23	31 (3.9)	4 (3.9)	35 (3.9)	
Guselkumab	21 (2.7)	1 (1.0)	22 (2.5)	
Risankizumab	9 (1.1)	3 (2.9)	12 (1.3)	
Tildrakizumab	1 (0.1)	0 (0.0)	1 (0.1)	
No. of previously used biologics [*n* (%)]				0.737
0	510 (64.7)	65 (63.7)	575 (64.6)	
1	159 (20.2)	18 (17.6)	177 (19.9)	
2	59 (7.5)	11 (10.8)	70 (7.9)	

Table 1 (continued)

	< 65 years of age [$n = 788$]	≥ 65 years of age [$n = 102$]	All patients [$n = 890$]	p value[a]
3	30 (3.8)	5 (4.9)	35 (3.9)	
4	18 (2.3)	3 (2.9)	21 (2.4)	
≥ 5	12 (1.5)	0 (0.0)	12 (1.3)	
No. of previously used conventional systemics [n (%)]				0.070
0	4 (0.5)	1 (1.0)	5 (0.6)	
1	204 (25.9)	35 (34.3)	239 (26.9)	
2	301 (38.2)	35 (34.3)	336 (37.8)	
3	209 (26.5)	26 (25.5)	235 (26.4)	
4	70 (8.9)	5 (4.9)	75 (8.4)	
Type of prior conventional systemic				NA
Cyclosporin	303 (38.5)	22 (21.6)	325 (36.5)	0.001
Fumaric acid	442 (56.1)	45 (44.1)	487 (54.7)	0.026
Methotrexate	697 (88.5)	93 (91.2)	790 (88.8)	0.506
Systemic retinoid	242 (30.7)	40 (39.2)	282 (31.7)	0.090

Values might not add up due to missing values

SD standard deviation, *NA* not applicable, since the categorization of patients in the two age groups automatically leads to differences in age-related variables, *ANOVA* analysis of variance, *PASI* Psoriasis Area and Severity Index

[a]Pearson's Chi-square test was used for categorical outcomes, one-way ANOVA was used for continuous parametric distribution, and the Mann–Whitney U test was used for continuous non-parametric distribution

[b]Selection of biologic-naïve patients

[c]Missing sex: 10; missing body mass index: 117; missing age at onset: 76; missing duration until start of biologic: 76; missing family history of psoriasis: 100; missing psoriatic arthritis: 150; missing baseline PASI: 107

censored when they discontinued their biologic for a reason other than the reason of interest. Log-rank tests were performed to compare Kaplan–Meier curves between patient groups.

2.3.1 Correcting for Confounders

Baseline characteristics were compared between the two age groups; if baseline variables were different between groups, they were considered as confounders and were incorporated into the Cox regression model. Multiple imputation was used in the case of large amounts of missing data (> 15%). Imputed variables were created and pooled in the model 10 times, and were incorporated in the confounder-corrected model if the variable differed significantly between treatment groups or had a > 10% effect on model outcomes.

2.3.2 Variables Associated with Drug Survival

Additionally, Cox regression analyses with baseline variables were performed with a selection of patients < 65 years of age, and ≥ 65 years of age separately, to investigate associations with drug survival. Baseline variables were tested univariately and incorporated in the multivariable Cox regression model if their association with drug survival was considered clinically meaningful and the p value was < 0.1. Backward selection was used to identify relevant variables for the final model.

2.4 Adverse Events Leading to Treatment Discontinuation

All AEs that led to discontinuation of the biologic were collected and classified into categories according to the Medical Dictionary for Regulatory Activities (MedDRA). Patients could have more than one AE simultaneously leading to treatment discontinuation and these were counted as separate AEs in this study. Additionally, all AEs leading to discontinuation were studied to check if they could be classified as serious AEs (SAEs) according to the International Council for Harmonisation (ICH) E6 (R2) Good Clinical Practice Guidelines [12].

2.5 Psoriasis Area and Severity Index (PASI) Analysis

To be able to visualize treatment effectiveness in both age groups, the Psoriasis Area and Severity Index (PASI) scores were analyzed. In the PASI analysis, only TEs with a baseline PASI and at least one follow-up PASI within the first year of treatment were included. Since scheduling visits at the exact time points is not feasible in a clinical setting,

linear interpolation was used to estimate PASIs at the following time points: weeks 6, 12, 26, 39 and 52, and months 18 and 24. Interpolated PASI scores were used to calculate 1-year PASI ≤ 1 and ≤ 5 proportions. Additionally, PASI scores at the time of treatment discontinuation due to ineffectiveness were assessed. Linear regression analyses were performed, with age group as the independent outcome and PASI as the dependent outcome, at 6, 12, 18 and 24 months of treatment. Correction for possible confounders was applied in linear regression analyses.

In patients who discontinued treatment due to ineffectiveness and/or AEs, PASI scores at discontinuation were carried forward using the last observation carried forward (LOCF) method. With this method, PASI scores in the case of early discontinuation are carried forward, which ensures a more conservative approach [13].

2.6 Statistical Analysis

Analyses were performed in SPSS version 25.0 (IBM Corporation, Armonk, NY, USA). A p value < 0.05 was considered significant. Baseline patient and treatment characteristics for the first TE per patient and per biologic were displayed using descriptive statistics [mean ± standard deviation (SD), median (range), N (%)]. Continuous variables were compared between patient groups using one-way analysis of variance (ANOVA) for parametric distributions and Mann–Whitney U tests for non-parametric distributions, respectively. Pearson's Chi-square test was used for comparison of categorical variables.

3 Results

3.1 Patient Characteristics

We included a total of 890 patients, of whom 102 (11.5%) were 65 years of age or older at the start of biologic therapy compared with 788 (88.5%) patients aged under 65 years. In total, 2013 patient-years were observed: 206 years in patients ≥ 65 years of age and 1807 in patients < 65 years of age. The median follow-up duration was 19 months in patients ≥ 65 years of age versus 22 months in patients < 65 years of age. The median age at the start of biologic treatment was 48.3 years (19.1–82.5). Body mass index (BMI), sex, and the distribution of biologic classes prescribed (e.g. TNF, IL12/23) were not significantly different between the two groups (Table 1). The most frequently reported comorbidities in older patients were hypertension ($n = 45$, 44.1%) and diabetes mellitus ($n = 31$, 30.4%) [see Table 2]. The frequencies of other comorbidities were considerably lower. A significantly higher median CCI score was found in older versus younger patients (1 [0–7] vs. 0 [0–6]; $p < 0.001$). The median CCI scores of this older population and those of another Dutch psoriasis cohort including older patients were highly comparable (1 [0–7] vs. 1 [0–7]; $p = 0.380$) [data not shown].

3.2 Drug Survival

During the first 5 years of treatment, 220 (24.7%) patients discontinued treatment due to ineffectiveness, 90 (10.1%) due to AEs, and 60 (6.7%) for other reasons (mostly due to pregnancy [wish], patient's own initiative, or unknown reasons). Among those patients who discontinued treatment due to 'other reasons', three (0.3%) patients discontinued treatment due to the coronavirus disease 2019 (COVID-19) pandemic, all aged < 65 years. Crude drug survival rates are visualized using Kaplan–Meier curves (Fig. 1). The crude overall 5-year drug survival in older patients was 32.4% versus 42.1% in younger patients (log-rank test, $p = 0.144$). Specifically for ineffectiveness, the 5-year drug survival was lower for older patients than for younger patients (44.5% vs. 60.5%; $p = 0.006$), while the 5-year drug survival with regard to AEs was 82.1% in older patients versus 79.5% in younger patients ($p = 0.913$). An overview of the reasons for treatment discontinuation and drug survival per age group is given in Table 3.

3.2.1 Correcting for Confounders

No extensive confounder correction was performed as age groups had no statistical differences except for the CCI score and hypertension. When corrected for CCI score and hypertension, the hazard ratio (HR) for the variable 'age group' was not statistically significant for drug survival due to all discontinuation reasons and drug survival due to AEs. For drug survival due to ineffectiveness, the confounder-corrected HR for age group was 1.497 (95% confidence interval [CI] 1.053–2.129), indicating that older patients had more risk of discontinuing their biologic therapy due to ineffectiveness compared with younger patients.

3.2.2 Variables Associated with Drug Survival

When analysing univariable HRs in the two different age groups separately, sex, BMI, and treatment class were associated with discontinuation due to ineffectiveness, AEs, and 'all reasons' in the younger patient group; however, there were no statistically significant associations with discontinuation in older patients. The results of separate univariable and multivariable Cox regression analyses are presented in electronic supplementary Tables 1 and 2.

When implementing imputed data in univariable Cox regression analyses, HRs were pointing in the same direction, showing robustness of the results.

Table 2 Overview of comorbidities/medical history in older and younger patients using biologics

	< 65 years of age [*n* = 788]	≥ 65 years of age [*n* = 102]	All patients [*n* = 890]
Comorbidity/medical history			
Myocardial infarction[c]	30 (3.8)	11 (10.8)	41 (4.6)
Cardiac failure[c]	4 (0.5)	2 (2.0)	6 (0.7)
Peripheral vascular disease[c]	3 (0.4)	8 (7.8)	11 (1.2)
Cerebral vascular disease[c]	17 (2.1)	11 (10.8)	28 (3.1)
Diabetes mellitus[c]	69 (8.7)	31 (30.4)	100 (11.2)
Chronic pulmonary disease[c]	45 (5.7)	11 (10.8)	56 (6.3)
Connective tissue disorder[c]	9 (1.1)	1 (1.0)	10 (1.1)
Cancer[a,c]	15 (1.9)	14 (13.7)	29 (3.2)
Metastatic[c]	1 (0.1)	0 (0.0)	1 (0.1)
Chronic kidney disease[c]	9 (1.1)	0 (0.0)	9 (1.0)
Peptic ulcer[c]	13 (1.6)	6 (5.9)	19 (2.1)
Liver disease[c]	83 (10.5)	16 (15.7)	99 (11.1)
Dementia[c]	2 (0.2)	3 (2.9)	5 (0.6)
Paraplegia[c]	0 (0.0)	0 (0.0)	0 (0.0)
HIV[c]	0 (0.0)	0 (0.0)	0 (0.0)
Hypertension	157 (19.9)	45 (44.1)	202 (22.7)
Depression	66 (8.4)	7 (6.9)	73 (8.2)
CCI[b] [median (range)]	0 (0–6)	1 (0–7)	0 (0–7)[d]
0	598 (75.9)	42 (41.2)	640 (71.9)
1	140 (17.8)	32 (31.4)	172 (19.3)
2	31 (3.9)	13 (12.7)	44 (4.9)
≥ 3	19 (2.4)	15 (14.7)	34 (3.8)

Data are expressed as *n* (%) unless otherwise specified

CCI Charlson Comorbidity Index, *SD* standard deviation, *ICD-10* International Classification of Diseases, Tenth Revision

[a]Included all types of cancer other than non-melanoma skin cancer

[b]The CCI consists of 17 comorbidities and each comorbidity is given a separate weight

[c]Comorbidities scored in the CCI. In a few cases, specific comorbidities were not scored in the CCI calculation but are depicted here. For specific CCI definitions, see the ICD-10 codes reported by Sundararajan et al. [10]

[d]A significantly higher CCI was seen in older adults compared with younger patients ($p < 0.001$)

3.3 Adverse Events Leading to Treatment Discontinuation

Overall, 115 (12.9%) patients discontinued biologic treatment due to AEs, or AEs and ineffectiveness combined, with a maximum follow-up of years. In older patients, 12 (11.8%) patients discontinued biologic therapy due to AEs compared with 103 (13.1%) younger patients. In total, 155 AEs leading to treatment discontinuation were reported—16 AEs in older patients and 139 AEs in younger patients (see Table 4). Of all AEs, 16 were reported as serious, and these only occurred in younger patients. In both age groups, treatment discontinuation due to AEs was most frequently attributed to infectious causes (5/102 [4.9%] ≥ 65 years and 25/788 [3.2%] < 65 years). Upper respiratory infections/flu-like symptoms were the most frequently reported infections in both age groups.

3.4 PASI Analysis

The mean 2-year PASI course split according to age group is shown in Fig. 2. The median baseline PASI was 11.0 (0.0–36.2) in older patients and 11.8 (0.0–45.2) in younger patients. After 1 year of treatment, the median PASI in older and younger patients was 2.8 (0.0–11.5) and 2.6 (0.0–21.7), respectively. The proportion of patients ≥ 65 years of age who reached a PASI score of < 1 after 1 year of treatment was 20.0%, versus 24.6% in patients aged < 65 years. Furthermore, a PASI score of < 5 after 1 year of treatment was reached in 77.1% of patients aged ≥ 65 years, versus 75.4% in patients aged < 65 years. Linear regression analyses on PASI scores showed no statistical differences at 6, 12, 18, and 24 months of treatment, nor after confounder correction for CCI score and hypertension. After applying the LOCF method, similar PASI results were seen (see electronic supplementary text).

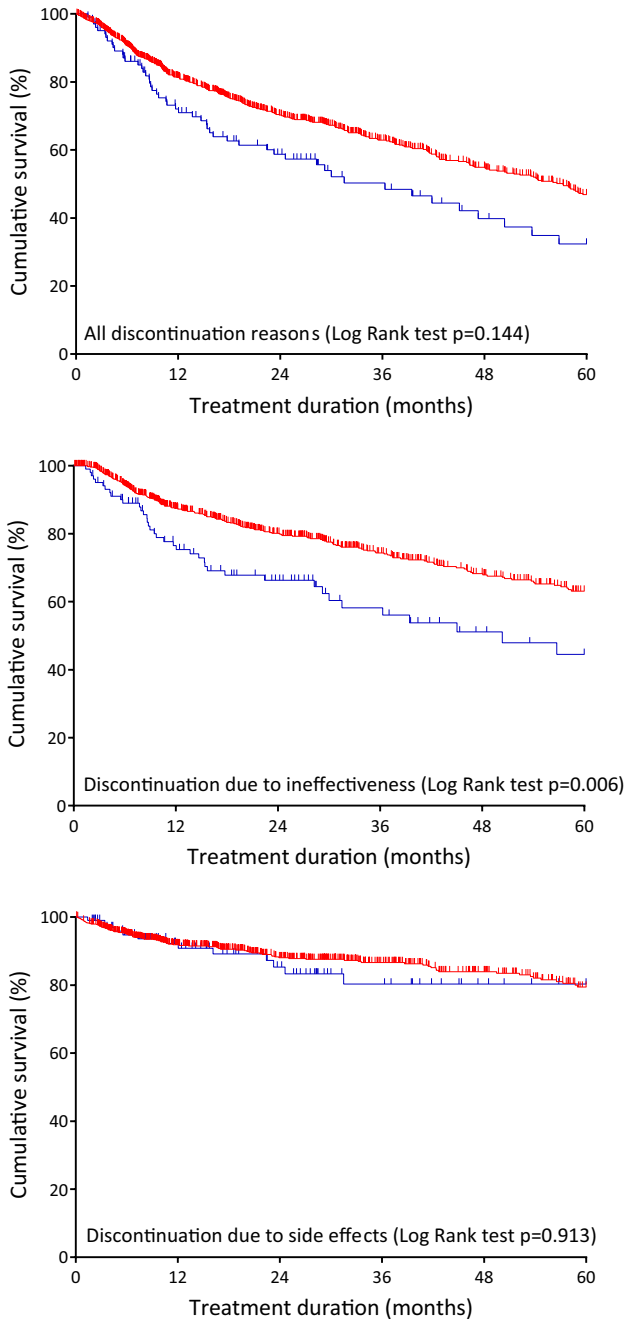

Fig 1 Five-year drug survival of older patients compared with younger patients using biologics treatment, split according to discontinuation reasons

In cases where patients discontinued treatment due to ineffectiveness, PASI scores at discontinuation were collected. In patients ≥ 65 years of age, the median PASI at discontinuation was 7.8 (2.6–14.8), compared with 9.6 (0.0–34.4) in patients < 65 years of age. This difference was not statistically significant ($p = 0.347$).

4 Discussion

In this prospective real-world psoriasis cohort study, we provide insights into the drug survival, safety, and effectiveness of biologics in older patients with psoriasis, and compare outcomes in younger patients. We set out to reduce the current knowledge gap and improve personalized care for older patients with psoriasis. In total, data of 890 patients were analyzed, of whom 102 were aged ≥ 65 years (11.5%). Overall, the two age groups (< 65 years and ≥ 65 years) were highly comparable regarding patient and disease characteristics. Comorbidities were more common in older patients at the start of biologic treatment, as expected and in line with previous research [14–16]. The overall 5-year drug survival of biologic treatment, including all reasons for treatment discontinuation, was comparable between age groups (≥ 65 years, 32.4%; < 65 years, 42.1%). A significant difference in 5-year drug survival was found only for ineffectiveness as the reason for treatment discontinuation; older patients had a lower ineffectiveness-related drug survival (44.5%) compared with younger patients (60.5%). Furthermore, no difference in 5-year AE-related drug survival between age groups was found (82.1% in older patients vs. 79.5% in younger patients). The number of reported AEs leading to treatment discontinuation in the first 5 years of treatment was low in both groups (≥ 65 years, 11.8%; < 65 years, 13.1%). The PASI course during the first 2 years of treatment was comparable between age groups.

Drug survival is a widely used measure that combines several aspects of treatment modalities (e.g., effectiveness and safety) [17–19]; however, literature on drug survival in older patients with psoriasis is sparse. We found a comparable overall drug survival between the age groups, before and after correction for confounding factors, as also reported for a period of 2 years by Osuna et al. [20]. The crude and confounder-corrected drug survival with regard to ineffectiveness was lower for patients aged ≥ 65 years. Remarkably, PASI scores at discontinuation were slightly lower in older patients, although this was not statistically significant (≥ 65 years, 7.8 [2.6–14.8] versus < 65 years, 9.6 [0.0–34.4]; $p = 0.347$). A possible explanation for the more frequent treatment discontinuation due to ineffectiveness in older patients is the difference in needs or treatment burden between these age groups. Treatment effectiveness in research is often based on disease severity outcome, however individual treatment goals, needs, and preferences can play a significant role in treatment decision making. Although limited literature is available on the needs and treatment goals of older psoriasis patients, some distinct differences have been reported compared with those of younger patients [21, 22]. Older patients found it more important to be free of scaling and redness and to have complete clearance of psoriasis

Table 3 Reasons for treatment discontinuation and drug survival in older patients compared with younger patients

	All patients [$n = 890$]	< 65 years of age [$n = 788$]	≥ 65 years of age [$n = 102$]	p value[a]
Reasons for treatment discontinuation [n (%)]				
Ineffectiveness	220 (24.7)	185 (23.5)	35 (34.3)	
Adverse events	90 (10.1)	82 (10.4)	8 (7.8)	
Ineffectiveness and adverse events	25 (2.8)	21 (2.7)	4 (3.9)	
Other	60 (6.7)	57 (7.2)	3 (2.9)	
Lost to follow-up	46 (5.2)	42 (5.3)	4 (3.9)	
Survival functions (Kaplan–Meier analyses)[b]				
1-year (%)				
All reasons	75.5	75.9	72.0	0.475
Ineffectiveness	84.0	85.0	76.5	0.036
Adverse events	91.0	90.2	92.2	0.613
5-year (%)				
All reasons	41.1	42.1	32.4	0.144
Ineffectiveness	58.7	60.5	44.5	0.006
Adverse events	79.7	79.5	82.1	0.913

[a]Log-rank tests were performed to compare Kaplan–Meier curves of patients aged <65 years and ≥65 years

[b]The percentage of patients calculated using Kaplan–Meier analysis who are still on drug after 1–5 years of treatment, split according to discontinuation reasons

lesions than their younger counterparts. Furthermore, minimization of different treatment modalities such as the use of topical treatment, injections, and tablets or capsules, as well as reducing hospital visits and laboratory assessments, were valued significantly higher by older patients [21]. This may indicate that the treatment burden is experienced as higher, possibly due to aging-related factors such as comorbidity, polypharmacy, functional impairment, and low confidence in psoriasis therapy due to more extensive treatment history [22–25]. Another possible influential factor on drug survival differences is treatment adherence; however, evidence regarding the influence of age on treatment adherence in psoriasis is scarce [26]. One study described a modest relation between older age and higher levels of treatment adherence in patients using traditional systemic and biologic treatment [27].

In general, older patients are more at risk of AEs using systemic medication due to comorbidity, polypharmacy, and drug metabolism alterations [28]. We found no difference in 5-year drug survival with regard to AEs between age groups and no SAEs were reported as the reason for treatment discontinuation in older patients. Infections are the most frequently reported AEs in older patients using biologics [14, 29–31]; however, a recent systematic review on systemic therapies in older patients with psoriasis described no significant association with infection occurrence and age [3]. In our study, infections were the most frequently reported AEs that led to treatment discontinuation in both age groups. Nevertheless, absolute numbers were comparable and low. Conflicting evidence has been reported regarding the occurrence of neoplasms in older patients using biologics [32]; we only report one neoplasm leading to treatment discontinuation. Note that we focused only on neoplasms as the reason for discontinuation, and not on absolute rates of neoplasms during therapy in both groups.

The PASI course in this study was highly comparable between age groups, implicating a comparable treatment response. This trend has previously been described for adalimumab and etanercept regarding PASI outcomes and older age [33–35]. A recent systematic review concluded that effectiveness in older patients is in line with that of younger patients [3]. Studies evaluating the effectiveness of IL-17 and IL-23 inhibitors in older patients are scarce and would be of added value in the future.

Studies regarding older patients using biologics often have limited sample sizes and focused mainly on separate biologics. Furthermore, studies describing drug survival in this population are lacking. Our study is an addition to the current scarce body of evidence in older patients; however, more evidence regarding older patients with psoriasis is being published [20, 36–38]. A strength of this study is its high external validity, due to its real-world practice nature, and multicenter, prospective design. When evaluating eligibility for biologic treatment, there is a chance that patients with high comorbid disease status are more often excluded. Therefore, the chance of selection bias regarding comorbidity was assessed. The CCI score of our older population was compared with that of another

Table 4 Adverse events leading to treatment discontinuation of biologic therapy in older patients compared with younger patients

Adverse events (MedDRA classification)	< 65 years of age [*n* = 103]	≥ 65 years of age [*n* = 12]	All patients [*n* = 115]
All AEs	139	16	155
Cardiac disorders	5 (3.6)	0 (0.0)	5 (3.2)
Endocrine disorders	1 (0.7)	0 (0.0)	1 (0.6)
Eye disorders	2 (1.4)	0 (0.0)	2 (1.3)
Gastrointestinal disorders	5 (3.6)	0 (0.0)	5 (3.2)
General disorders and administration site conditions	18 (12.9)	1 (6.3)	19 (12.3)
Fatigue	6 (4.3)	1 (6.3)	7 (4.5)
Fever	4 (2.9)	0 (0.0)	4 (2.6)
Oedema	3 (2.2	0 (0.0)	3 (1.9)
Malaise	2 (1.4)	0 (0.0)	2 (1.3)
Other[a]	3 (2.2)	0 (0.0)	3 (1.9)
Immune system disorders	10 (7.2)	2 (12.5)	12 (7.7)
Infections and infestations	25 (18.0)	5 (31.3)	29 (18.7)
Upper respiratory infections/flu-like symptoms	9 (52.0)	2 (12.5)	11 (7.1)
Pneumonia	4 (2.9)	1 (6.3)	4 (2.6)
Skin infections[b]	3 (2.2)	1 (6.3)	4 (2.6)
Urinary tract infections	2 (1.4)	0 (0.0)	2 (1.3)
Sepsis	1 (0.7)	0 (0.0)	1 (0.6)
Other[c]	6 (4.3)	1 (6.3)	7 (4.5)
Investigations	4 (2.9)	0 (0.0)	4 (2.6)
Musculoskeletal and connective tissue disorders	12 (8.6)	1 (6.3)	13 (8.4)
Neoplasms benign, malignant, and unspecified	8 (5.8)	1 (6.3)	9 (5.8)
Nervous system disorders	13 (9.4)	1 (6.3)	14 (9.0)
Psychiatric disorders	6 (4.3)	1 (6.3)	7 (4.5)
Renal and urinary disorders	1 (0.7)	0 (0.0)	1 (0.6)
Respiratory, thoracic, and mediastinal disorders	8 (5.8)	1 (6.3)	9 (5.8)
Skin and subcutaneous tissue disorders	12 (8.6)	1 (6.3)	14 (9.0)
Surgical and medical procedures	4 (2.9)	1 (6.3)	5 (3.2)
Vascular disorders	2 (1.4)	0 (0.0)	2 (1.3)
Unknown	3 (2.2)	1 (6.3)	4 (2.6)

Data are expressed as *n* (%)

Percentages are calculated using the total amount of AEs in the age groups

Twenty-seven patients (24 younger patients and 3 older patients) had more than one AE simultaneously, leading to treatment discontinuation

For the MEDRA classification categories blood and lymphatic system disorders; ear and labyrinth disorders; hepatobiliary disorders; injury, poisoning and procedural complications; metabolism and nutrition disorders; reproductive system; and breast disorders, no AEs that led to treatment discontinuation were reported

AEs adverse events, *MedDRA* Medical Dictionary for Regulatory Activities

[a]Included throat complaints, cough, and pain on the chest after biologic injection

[b]Included wound infections, infection of eczema, condylomata

[c]Included latent tuberculosis infection, recurrent infections, toe infection, oral candidiasis, ear infection, gingivitis, fungal infection

Dutch psoriasis cohort, showing no significant difference and implicating a limited influence of pre-selection.

A limitation of this study is the smaller number of older patients. Furthermore, the 65-year age threshold is arbitrary, as chronological age does not always reflect health status. However, to be able to make a comparison between age groups, this cut-off value was chosen in accordance with existing psoriasis literature [3, 21, 36, 39].

To conclude, in this real-world observational study on biologic treatment in older (≥ 65 years of age) and younger

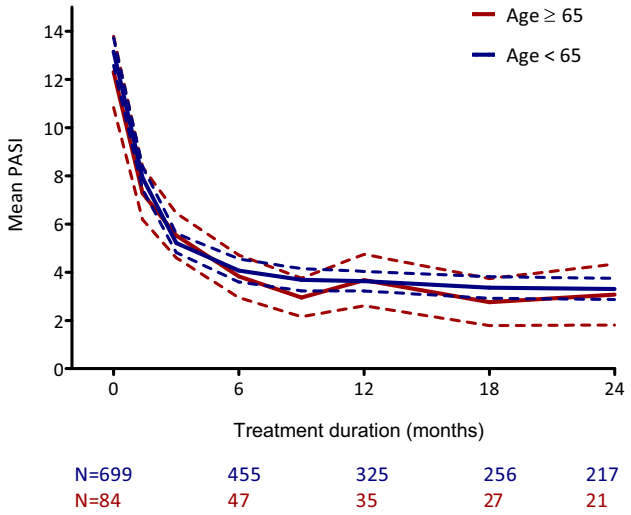

Fig 2 Mean 2-year PASI course + 95% confidence intervals of patients using biologics, comparing age groups. *PASI* Psoriasis Area and Severity Index

(< 65 years of age) patients, drug survival regarding discontinuation for all reasons and AEs was high and comparable in older and younger patients. Older patients discontinued biologic treatment more often due to ineffectiveness. This may indicate a difference in needs or treatment burden between age groups, possibly related to aging factors such as extensive comorbid disease status, polypharmacy, or functional impairments. Biologic discontinuation due to AEs did not occur more frequently in older patients and no SAEs leading to treatment discontinuation in older patients were reported. Therefore, treatment of older patients with biologics appears a well-tolerated and effective therapeutic option.

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Declarations

Conflict of interest E.L.M. ter Haar has carried out investigator-initiated research with financial support from Almirall and has carried out clinical trials for Novartis. All funding is not personal but goes to the independent research fund of the Department of Dermatology, Radboud University Medical Center Nijmegen (Radboudumc), The Netherlands. S.E. Thomas carries out clinical trials for Janssen and Novartis. All funding is not personal but goes to the independent research fund of the Department of Dermatology, Radboud University Medical Center Nijmegen, The Netherlands. M.E. Otero has acted as a consultant for Eli Lilly. P.P.M. van Lümig has received research funding from Wyeth; has carried out clinical trials for Abbott and Janssen-Cilag; has received speaking and consulting fees from Wyeth and Schering-Plough; has received reimbursement for attending a symposium from Schering-Plough and Pfizer; and has attended advisory boards for Abbvie, Leo Pharma, Novartis and UCB. W.P. Arnold has been a consultant, advisory board member, and/or speaker for AbbVie and UCB. S.R.P. Dodemont has attended advisory boards for Abbvie, Janssen and Leo Pharma, and has received a congress fee from Abbvie. M.S. de Bruin-Weller has been a consultant, advisory board member, and/or speaker for AbbVie, Almirall, Arena, Aslan, Eli Lilly, Galderma, Janssen, Leo Pharma, Pfizer, Regeneron, and Sanofi-Genzyme. R.A. Tupker has attended advisory boards for Leo Pharma, UCB Pharma, and Eli Lilly Netherlands. E.M.G.J. de Jong has received research grants for the independent research fund of the Department of Dermatology, Radboud University Medical Center Nijmegen, The Netherlands, from AbbVie, BMS, Janssen Pharmaceutica, Leo Pharma, Novartis, and UCB for research on psoriasis; has acted as a consultant and/or paid speaker for, and/or participated in research sponsored by, companies that manufacture drugs used for the treatment of psoriasis or eczema, including AbbVie, Amgen, Almirall, Celgene, Galapagos, Janssen Pharmaceutica, Lilly, Novartis, Leo Pharma, Sanofi and UCB. All funding is not personal but goes to the independent research fund of the Department of Dermatology, Radboud University Medical Center Nijmegen, The Netherlands. J.M.P.A. van den Reek has carried out clinical trials for AbbVie, Celgene and Janssen; has received speaking fees/attended advisory boards from AbbVie, Janssen, BMS, Almirall, LEO Pharma, and Eli Lilly; and has received reimbursement for attending a symposium from Janssen, Pfizer, Celgene, and AbbVie. All funding is not personal but goes to the independent research fund of the Department of Dermatology, Radboud University Medical Center Nijmegen, The Netherlands. S.F.K. Lubeek has received research grants for investigator-initiated research by Almirall, and has acted as a consultant and/or paid speaker for Janssen, LEO Pharma, Almirall, Sanofi Genzyme, and Sunpharma. All funding is not personal but goes to the independent research fund of the Department of Dermatology, Radboud University Medical Centre Nijmegen, The Netherlands. M.D. Njoo, P.M. Ossenkoppele, E.N. Kop, J.E.M. Körver, A.L.A. Kuijpers, R.J. Lindhout, J.M. Mommers, M.A.M. Berends, M.I.A. Koetsier, M.B. Visch, and M.M. Kleinpenning have no conflicts of interest to report.

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Ethics approval Ethical review and approval were waived for this study in consultation with our regional Medical Ethics Committee due to the non-interventional design of the study.

Consent to participate Informed consent was not necessary due to the non-interventional design of this study; however, written informed consent is obtained from every patient included in the study.

Consent for publication Not applicable (see the Consent to participate section).

Data availability statement The data that support the findings of this study are not publicly available as participants of this study did not agree for their data to be shared publicly.

Code availability Not applicable.

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and JMPAvdReek. Investigation: ELMtH and SET. Resources: MEO, MDN, PMO, ENK, SD, JEMK, ALAK, RJL, RAT, JMM, MAMB, MIAK, MSdB, BV, WPA, PPvL, MMK. Data curation: MEO, ELMtH and SET. Writing—original draft preparation: ELMtH and SET. Writing—review and editing: JMPAvdR, EMGJdJ and SFKL, MEO, MDN, PMO, ENK, SD, JEMK, ALAK, RJL, RAT, JMM, MAMB, MIAK, MSdB, BV, WPA, PPvL, MMK. Visualization: ELMtH, SET. Supervision: JMPAvdR, EMGJdJ and SFKL. Project administration: JMPAvdR, EMGJdJ and SFKL. Funding acquisition: MEO, JMPAvdR, EMGJdJ.

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