Persistence, effectiveness and safety of ustekinumab compared to TNF inhibitors in psoriatic arthritis within the Italian PsABio cohort

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Abstract

Objective

To compare real-world persistence, effectiveness and tolerability of ustekinumab versus TNF inhibitors (TNFi) in psoriatic arthritis (PsA).

Methods

One-year data from Italian subjects enrolled in the PsABio study (PsA patients receiving 1st- to 3rd-line treatment with ustekinumab or TNFi) were evaluated. Treatment persistence was analysed using Kaplan-Meier curves; hazard ratios (HR) of stopping treatment, and the corresponding 95% confidence intervals (CI), were computed through Cox regression models. Proportions of patients reaching clinical effectiveness endpoints were analysed using logistic regression, including propensity score (PS) adjustment for imbalanced baseline covariates, and non-response imputation if treatment was stopped/switched.

Results

Among 222 participants with follow-up data (effectiveness set), 101 received ustekinumab and 121 TNFi. In the ustekinumab group, 74.3% continued treatment up to 12±3 months compared to 63.6% in the TNFi group. Ustekinumab showed better persistence than TNFi, overall and in specific subgroups (females, monotherapy without methotrexate, BMI <25 or >30 kg/m², patients receiving ustekinumab as 2nd-line treatment instead of a second TNFi). Overall, the PS-adjusted HR of treatment discontinuation was 0.46 (95% CI: 0.26–0.82) for ustekinumab vs. TNFi. cDAPSA LDA/remission was achieved in 43.5% of ustekinumab and 43.6% of TNFi-treated patients, while MDA was achieved in 24.2% and 28.0% of patients, respectively. After PS adjustment, odds ratios of clinical effectiveness did not differ significantly. Both treatments showed an acceptable safety profile.

Conclusion

This prospective, real-life study found a better persistence of ustekinumab than TNFi in PsA patients. At 1 year, both treatments showed similar effectiveness.

Key words

persistence, effectiveness, safety, observational studies, TNF inhibitors, ustekinumab, psoriatic arthritis

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Competing interests on page 742.

Introduction

Psoriatic arthritis (PsA) is a complex, heterogeneous and potentially severe disease involving a large spectrum of manifestations, including the musculoskeletal system, skin, nails and, less frequently, eyes and gut (1).

The European League Against Rheumatism (EULAR) recommendations for the management of PsA address non-steroidal anti-inflammatory drugs, local glucocorticoid injections and conventional synthetic disease-modifying anti-rheumatic drugs (csDMARD) as initial treatments for active PsA (1). An increasing number of effective treatment options are available for moderate-to severe PsA not responding to csDMARDs. These options include biologics as tumour necrosis factor (TNF) inhibitors, interleukin (IL)-12/23, IL-23 and IL-17 inhibitors, and small molecules as PDE4 and JAK inhibitors (1-3). The IL-12/23 inhibitor, ustekinumab, was the first new biologic drug for PsA to be developed after TNFi (4). The phase III PSUMMIT 1 and 2 trials demonstrated a greater clinical response at 24 weeks with ustekinumab compared to placebo in patients with PsA (5, 6).

However, data from RCTs generally lack external validity because of stringent inclusion and exclusion criteria, and only real-life observations can provide indications on long-term effectiveness and safety in everyday clinical settings. Moreover, further clinical outcomes are used in real-life studies, for example treatment persistence, *i.e.* a comprehensive outcome involving effectiveness and safety, mixed with patient and doctor satisfaction and preferences (7-9). For these reasons, real-world studies are central to integrate evidence from RCTs, as it was shown in Registry-based studies of patients with psoriasis and spondyloarthritis (SpA) (10-13).

The PsABio study is an international, prospective, observational cohort study aimed to evaluate the persistence, effectiveness, and safety of 1st/2nd/3rd-line ustekinumab *versus* TNFi in a real-life setting of adult PsA patients. The study was conducted in 8 European countries enrolling 991 patients between December 2015 and June 2018 in 92 study sites. Participants were treated according to standard clinical practice in each country, with the choice of treatment (ustekinumab or any approved TNFi) being at the discretion of the treating Rheumatologist. The main findings at 6 months and at the 1-year follow-up of the PsABio study – full population – have been recently published (14, 15). Because Italian sites contributed a significant number of patients to this study, a country analysis of 1-year data was performed.

Materials and methods

Study design

The PsABio study (registered at http://www.clinicaltrials.gov: NCT02627768) is an observational study of adult PsA patients fulfilling the Classification Criteria for Psoriatic Arthritis - CASPAR (16). The methods of the PsABio study have been described in-depth in earlier reports (14, 15). The current interim analysis at month 12 (±3 months) is based on the Italian PsABio cohort alone, involving 15 sites that enrolled a total of 238 consecutive PsA patients. Before data collection, all patients signed an informed consent form allowing data collection and source data verification, in agreement with Italian regulations and trial sponsor policy. The study was approved by the Ethics Committees of the Italian participating centres and was conducted according to the principles of the Declaration of Helsinki and the Good Clinical Practice guidelines.

Participants were screened consecutively, and all those meeting the eligibility criteria were offered enrolment into the study. Treatment decision was taken by each investigator prior to, and independently of the patient inclusion in the study, following Italian standard clinical practice and regulations. TNFi therapies included any PsA approved TNFi (*i.e.* adalimumab, etanercept, golimumab, infliximab, certolizumab pegol), including biosimilars. Patients received biological DMARD (bDMARD) in addition to other co-medications as treatment for PsA (*e.g.* methotrexate, steroids, NSAIDs, etc.) or psoriasis (*e.g.* systemic therapy, phototherapy) according to local standard clinical

practice. After the study entry, patients were visited regularly by their treating rheumatologists according to clinical practice (at least every 6 months ±3 months), and could be switched to any other approved bDMARD (or to other classes of medications), changed recommended dosing schedules or stopped therapy, in accordance with physician's decision. This notwithstanding, data collection continued if the patient did not withdraw from the study.

Data collection at baseline and at the following visits included information available as for clinical practice, *i.e.* those related to demographic and clinical characteristics, PsA disease features (including 66/68 swollen/tender joint count, enthesitis, dactylitis, psoriasis, psoriatic nail disease, presence of back pain and/or chronic widespread pain assessed by the Fibromyalgia Rapid Screening Tool), previous TNFi and csDMARDs usage, medical history, other concomitant PsA medication, treatment persistence, clinical response outcomes (including the proportions of patients reaching minimal disease activity [MDA], very low disease activity [VLDA], clinical Disease Activity index for PSoriatic Arthritis [cDAPSA] low disease activity [LDA] or remission, ≥50% improvement in Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]), safety of therapies (*i.e.* occurrence of adverse events, serious adverse events, etc.), Patient-Reported Outcomes (PROs), data on comorbidities, use of concomitant medications, hospitalisations and resource utilisation. Given the real-world study setting, cDAPSA was used instead of DAPSA. The two indexes previously showed consistent results (17, 18). Due to the observational nature of the study, axial disease was clinically defined by the investigator-treating rheumatologist and no imaging and/or HLA-B27 results were required. Patients could have either pure axial disease (*i.e.* no signs of peripheral joint involvement) or combined peripheral and axial disease.

Primary outcomes of this interim analysis in the Italian cohort were 1-year treatment persistence and proportions of patients reaching effectiveness endpoints as MDA, VLDA, cDAPSA LDA/remission and cDAPSA remission. Secondary outcome was the number of participants with adverse events and serious adverse events. Adverse events were summarised under the initial treatment line as well as under all treatments started within a 91-day safety period after the initial treatment line prior to the adverse event.

Table I. Main demographic and clinical characteristics at baseline of the PsABio Italian cohort, overall and according to treatment type (effectiveness set).

Characteristic	UST (n=101)	TNFi (n=121)	Overall (n=222)
Age			
<40	12 (11.9%)	27 (22.3%)	39 (17.6%)
40–50	34 (33.7%)	31 (25.6%)	65 (29.3%)
50–60	34 (33.7%)	35 (28.9%)	69 (31.1%)
60–65	8 (7.9%)	11 (9.1%)	19 (8.6%)
≥65	13 (12.9%)	17 (14.0%)	30 (13.5%)
Mean (SD)	51.4 (11.3)	49.9 (12.9)	50.6 (12.2)
Sex			
Female	61 (60.4%)	76 (62.8%)	137 (61.7%)
BMI*			
<25	35 (35.7%)	48 (42.9%)	83 (39.5%)
25–30	39 (39.8%)	40 (35.7%)	79 (37.6%)
>30	24 (24.5%)	24 (21.4%)	48 (22.9%)
Mean (SD)	28.1 (6.2)	26.7 (5.4)	27.4 (5.8)
Time since diagnosis (years), mean (SD)	6.2 (6.9)	5.9 (6.4)	6.0 (6.6)
Line of biological treatment			
First line	44 (43.6%)	64 (52.9%)	108 (48.6%)
Second line	39 (38.6%)	40 (33.1%)	79 (35.6%)
Third line	18 (17.8%)	17 (14.0%)	35 (15.8%)
Type of PsA¥			
Presence of axial involvement	32 (31.7%)	42 (35.0%)	74 (33.5%)
Presence of enthesitis	39 (38.6%)	51 (42.1%)	90 (40.5%)
Presence of dactylitis	9 (8.9%)	12 (10.0%)	21 (9.5%)
MTX use at baseline	32 (31.7%)	45 (37.2%)	77 (34.7%)
BSA*,¥			
<3%	41 (51.3%)	69 (67.0%)	110 (60.1%)
3–10%	29 (36.3%)	27 (26.2%)	56 (30.6%)
>10%	10 (12.5%)	7 (6.8%)	17 (9.3%)
cDAPSA, mean (SD)	26.3 (15.4)	23.5 (12.3)	24.8 (13.9)
Extra-articular manifestations			
Uveitis	1 (1.0%)	3 (2.5%)	4 (1.8%)
IBD	5 (5.0%)	4 (3.3%)	9 (4.1%)

*The sums do not add up to the total because of some missing data.
¥ Psoriasis skin involvement.
BMI: Body Mass Index; BSA: body surface area; cDAPSA: Clinical Disease Activity Index for Psoriatic Arthritis; CI: confidence interval; IBD: inflammatory bowel disease; MTX: methotrexate; SD: standard deviation; UST: ustekinumab; TNFi: tumour necrosis factor inhibitor.

Statistical methods

Data validation, development of a detailed analysis plan and all statistical analyses were performed by or under the authority of the sponsor (Janssen Pharmaceutica, Beerse). Analyses of treatment persistence and effectiveness were based on the effectiveness set, including all patients with baseline data and any effectiveness follow-up data. A detailed description of statistical methods, including handling of missing data and propensity score (PS) analysis, was previously given (14, 15).

As the analysis was exploratory, no predefined hypotheses were tested and no adjustment for multiplicity was applied. Hence, and in consensus with recent recommendations (19), within- and between-group differences included the 95% CI, rather than by *p*-values, which provide no information about the variability of an estimated association.

Treatment persistence was calculated as the time from the initiation of the bDMARD at enrolment, up to the

last injection of this bDMARD (plus one dispensing interval), or start of subsequent bDMARD, or withdrawal from the study, or data cut-off date for subjects who remained on their initial treatment.

In addition to descriptive analyses, comparative effectiveness analyses were performed to investigate between-cohort differences. In this analysis, the month-12 effectiveness data of patients who switched/stopped their original treatment during the one-year follow-up period, were imputed as non-responders.

The difference in risk for stop/switch of initial treatment (persistence) was analysed by means of a Cox proportional hazards model including the PS, presenting the PS-adjusted hazard ratios (HRs). The difference in one-year effectiveness endpoints MDA/VLDA, cDAPSA LDA and remission, was analysed using logistic regression models including the PS, and presenting the PS-adjusted odds ratios (OR). All ratios are presented including the 95% CI.

The safety analysis included descriptive statistics of UST or TNFi treatment emerging adverse events.

Results

The main demographic and clinical characteristics at baseline are showed in Table I. Out of 222 patients in the effectiveness set, 101 (45.5%) were treated with ustekinumab and 121 (54.5%) with TNFi drugs. There were 137 women (61.7%) and 85 men (38.3%) enrolled. Forty-eight subjects (22.9%) were obese, 24 in each treatment group. At baseline, 108 patients (48.6%) started for the first time a bDMARD treatment, 79 (35.6%) started a second-line and 35 (15.8%) a third-line biologic therapy. About one-third of patients had peripheral PsA with axial involvement clinically diagnosed by the treating Rheumatologist; 40.5% had enthesitis and 9.5% dactylitis. Methotrexate was used by 34.7% of patients at baseline. There were some imbalances in baseline demographic/disease-related covariates between ustekinumab and TNFi groups: in the ustekinumab group, patients under 40 years were 11.9%, while in the TNFi cohort they were 22.3%; PsA patients were more frequently overweight or obese in the ustekinumab (64.3%) than TNFi (57.1%) group; first-line biological treatment was less frequent in the ustekinumab group (43.6% *vs.* 52.9% in the TNFi group); and MTX at baseline was used less frequently in the ustekinumab group (31.7% *vs.* 37.2% in the TNFi group). The mean (standard deviation) baseline cDAPSA was 26.3 (15.4) for ustekinumab and 23.5 (12.3) for TNFi.

Of patients starting ustekinumab and TNFi, 75/101 (74.3%) and 77/121 (63.6%), respectively (*p*-value from log-rank test = 0.047), persisted with treatment at one-year follow-up visit (12 months ± 3 months). The observed mean persistence was 410 days for ustekinumab and 363 days for TNFi, and time to reach the 75% percentile of the treatment persistence probability curve was 430 days (95% CI: 332-not estimable) for ustekinumab and 259 days (95% CI: 189–333) for TNFi. One out of 101 patients in the ustekinumab group switched/stopped initial treatment early, *i.e.* before week 12 (due to effectiveness reasons), while 9 out of 121 patients switched/stopped initial treatment early in the TNFi group (4 due to effectiveness and 5 due to safety

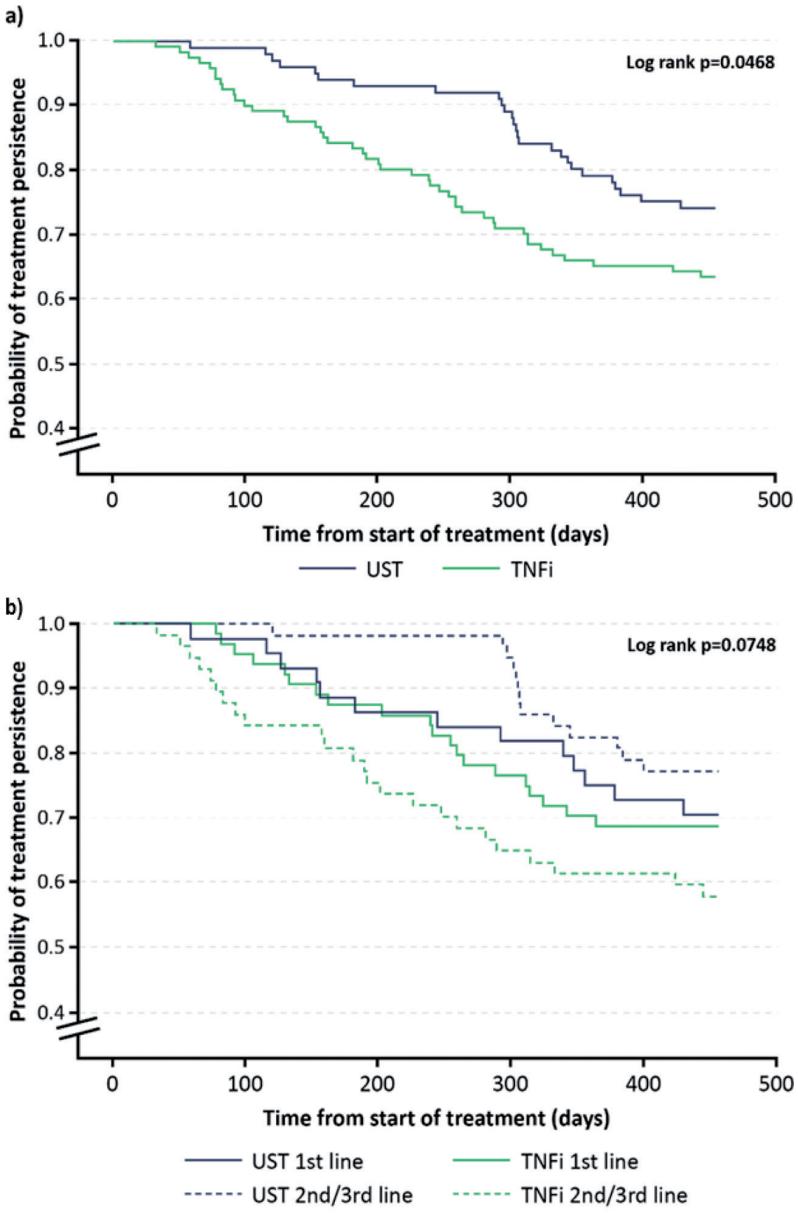

Fig. 1. Kaplan-Meier estimates of treatment persistence for ustekinumab and TNFi in the PsABio Italian cohort, overall (**A**) and by line of treatment (**B**).

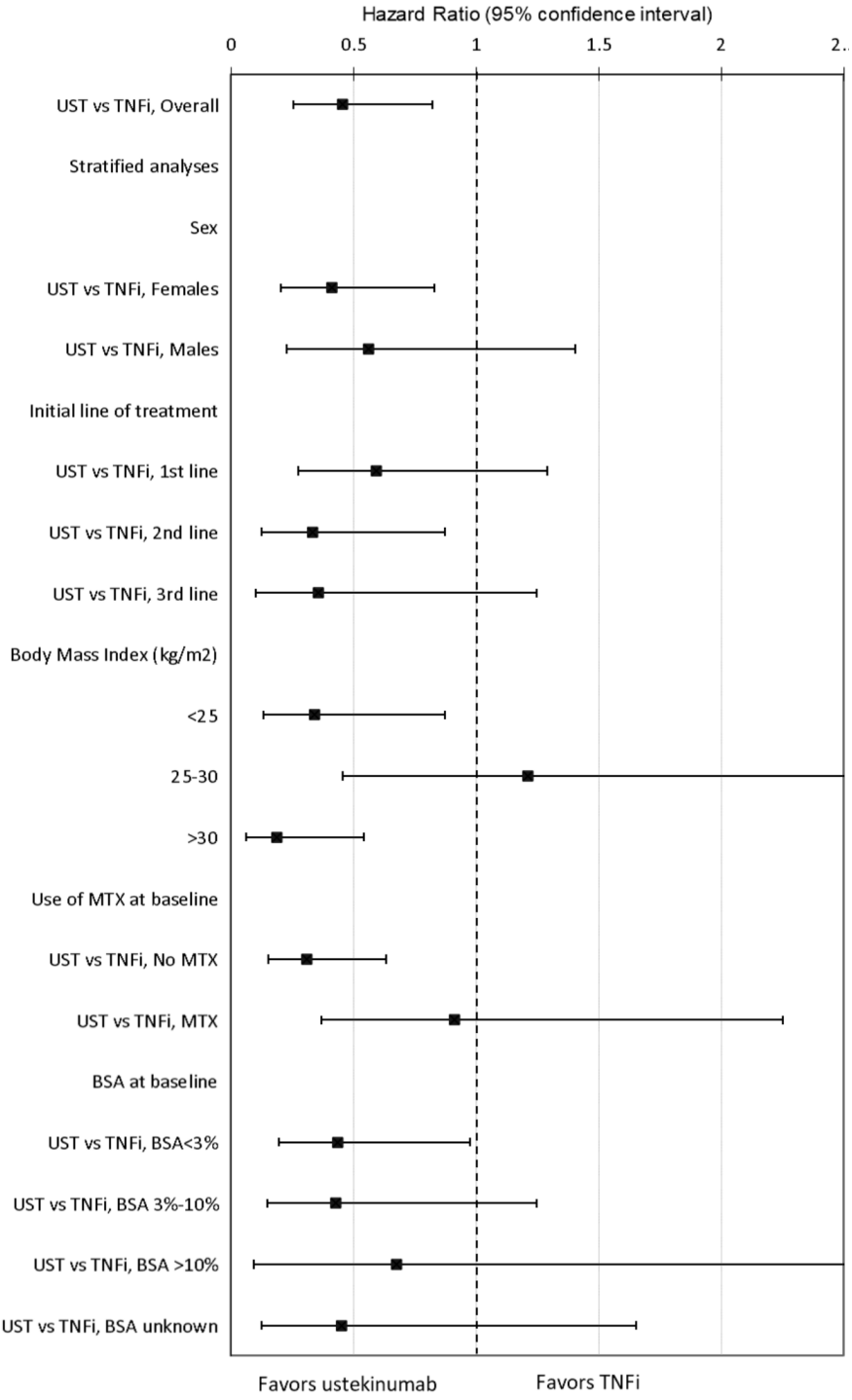

Fig. 2. PS-adjusted hazard ratios of discontinuation of treatment, and corresponding 95% confidence intervals, for ustekinumab and TNFi in the PsABio Italian cohort, overall and by selected covariates. BSA: body surface area; MTX: methotrexate; PS: propensity score; TNFi: tumour necrosis factor inhibitor; UST: ustekinumab.

reasons). Figure 1 presents Kaplan-Meier curves of treatment persistence up to 15 months for ustekinumab and TNFi, overall (**A**) and by line of treatment (**B**).

In the Cox proportional hazards model which included the PS, treatment and several factors of interest, the overall PS-adjusted HR for discontinuation showed significantly lower risk of discontinuation (HR [95% CI]) (so higher persistence) for ustekinumab versus TNFi (0.46 [0.26; 0.82]) (Fig. 2). In addition to this, the model showed better persistence of ustekinumab compared to TNFi in patients receiving biologic monotherapy (HR 0.31 [0.15; 0.63]), in females (0.41 [0.20; 0.83]), in patients with body mass index (BMI) <25 kg/m^2 (0.34 [0.14; 0.87]) or >30 kg/m^2 (0.19 [0.06; 0.54]), in patients receiving second-line bDMARD (0.33 [0.13; 0.87]) and in those with baseline BSA <3% (0.44 [0.19; 0.98], borderline finding). Of other factors included in the Cox regression model (enthesitis Yes/No, axial involvement, oligo- or polyarticular PsA), no significant effect was shown.

Clinical DAPSA LDA/remission (cDAPSA≤13) was achieved by 43.5% of ustekinumab and 43.6% of TNFi-treated patients. The corresponding PS-adjusted OR of cDAPSA LDA/remission was 1.08 (95% CI: 0.54–2.15) for ustekinumab as compared to TNFi treatment (Fig. 3). Clinical DAPSA remission (cDAPSA ≤4) was reached in 19.6% of ustekinumab and 17.9% of TNFi-treated patients, with corresponding PS-adjusted OR of 0.80 (95% CI: 0.35–1.85). MDA was reached in 24.2% of patients treated with ustekinumab and in 28.0% of those treated with TNFi (PS-adjusted OR=0.96; 95% CI: 0.45–2.05). The corresponding proportions of patients achieving VLDA were 12.5% and 10.2%, respectively (PS-adjusted OR=0.99; 95% CI: 0.35–2.76). Supplementary Figure 1 reports the same clinical outcomes, but referred only to patients with PsA and axial involvement (*i.e.* n=32 in the ustekinumab and n=42 in the TNFi group), and includes also improvement of at least 50% in BASDAI score as compared to baseline.

Safety data are reported in Table II. There were 23/113 (20.4%) patients reported with at least 1 treatment emergent adverse event (TEAE) with ustekinumab and 30/135 (22.2%) with TNFi. These events led to withdrawal of bDMARD in 6 (5.3%) patients treated with ustekinumab and 10 (7.4%) with TNFi. Two patients (1.8%) treated with ustekinumab had treatment emergent serious adverse events: 1 (0.9%) had skin infection and 1 (0.9%) had malignant parathyroid tumour; for TNFi, serious adverse events occurred in 1 patient (0.7%), who had pneumonia.

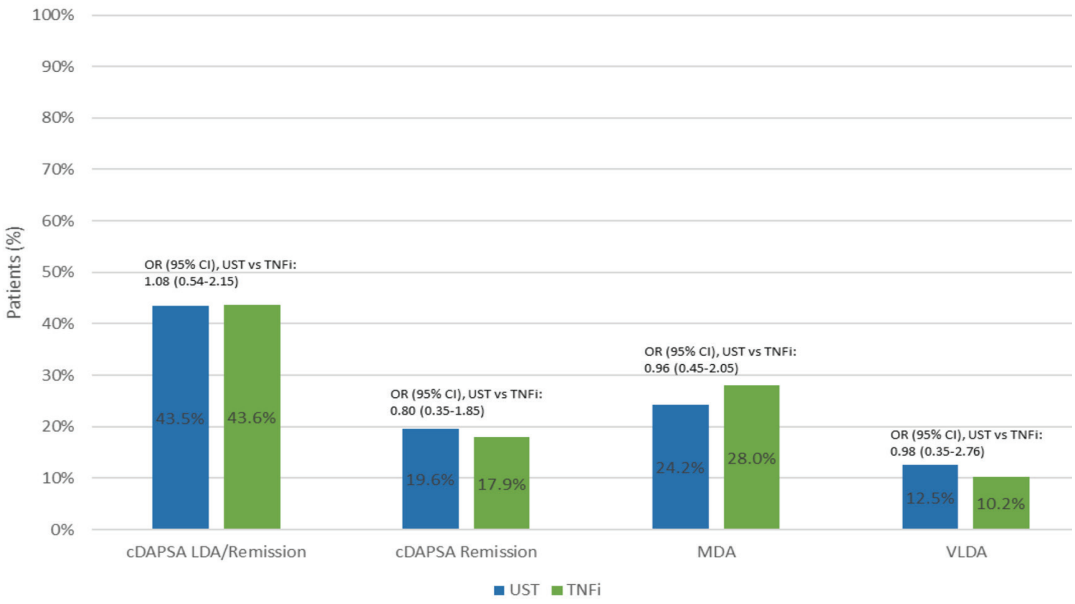

Fig. 3. Proportion of patients achieving cDAPSA LDA/remission and MDA/VLDA at one-year follow-up for ustekinumab and TNFi in the PsABio Italian cohort and corresponding PS-adjusted odds ratios (95% confidence intervals). cDAPSA: clinical Disease Activity index for PSoriatic Arthritis; CI: confidence interval; LDA: low disease activity; MDA: minimal disease activity; OR: PS-adjusted odds ratio; PS: propensity score; TNFi: tumour necrosis factor inhibitor; UST: ustekinumab; VLDA: very low disease activity.

Discussion

This is an exploratory interim analysis of real-life data on the use of ustekinumab and TNFi in clinical practice, restricted to the Italian cohort only of the European PsABio study, thus important limitations to the quality and relevance of the data are acknowledged. In particular, the study has a relatively short follow-up period, thus sample size and related statistical power are not particularly high and did not allow to provide results separately for each TNFi. Other limitations of this analysis are those typical of real-life studies, *e.g.* lack of patient randomisation, potential information or selection bias and presence of missing data. For example, presence at follow-up visits and completeness of data may be higher in compliant patients, treatment groups may be unbalanced at baseline for relevant characteristics, etc., leaving the analysis open to potential biases. To try to overcome at least part of these limits, we performed a preliminary PS analysis, and adjusted treatment effects for the estimated PS.

Our findings showed a better persistence of ustekinumab compared to TNFi in PsA patients followed up to 15 months. Persistence was also higher for ustekinumab than TNFi in specific subgroups of patients *i.e.* females, those without methotrexate use, those with BMI >30 kg/m^2, and those receiving second-line ustekinumab instead of a second TNFi. The clinical effectiveness - measured by cDAPSA responses, a measure of articular response only, and MDA/VLDA achievement, which cover also the skin, enthesis and PROs – was similar in both groups, with more than 40% of patients achieving cDAPSA LDA/remission at one year. Both treatments showed an acceptable safety profile.

During the last few years, an increasing number of studies have considered the real-world persistence of various biological drugs in PsA patients (20). However, comparative, prospective, observational studies like ours are scarce. Recently, an analysis of the multi-country PsABio full population after 1 year of treatment demonstrated a comparable overall persistence of ustekinumab and TNFi in presence – as observed in our Italian cohort – of a better drug persistence of ustekinumab in selected subgroups of patients (15). Further, published studies of ustekinumab in real-life clinical practice showed the effectiveness of this drug on different domains of PsA, with a good safety profile. The proportion of patients reaching MDA was between 30 and 70% (7, 21-24). Therefore, results in these terms indicate similar magnitudes of response *versus* TNFi, with some advantages for ustekinumab in case of concomitant psoriasis and/or enthesitis (1). In a recent analysis of Swedish population-based registry data, including a total of 3918 PsA patients, ustekinumab had a favorable treatment persistency profile as compared to adalimumab in both biologic-naïve (HR=0.48; 95% CI: 0.33–0.69) and biologic-experienced (HR=0.65; 95% CI: 0.56–0.76) patients (25). Favourable outcomes were also observed in an Italian real-life prospective multicentric study of ustekinumab treatment after 24 months of follow-up, where patients with PsA showed significant improvements in PASI, DAPSA, Leeds Enthesitis Index (LEI) and several other clinical and serologic features (22). In Italy, ustekinumab persistence and effectiveness in PsA was examined also in a regional registry-based study in Southern Italy (Apulia region) including 160 treated patients (7). The authors reported a 12-month ustekinumab drug survival of 74%, similar to our finding. On the other hand, in contrast to our data, treatment persistence in that registry study was higher in bDMARD naïve (87%) than in previously TNFi-treated patients (68%). Another Italian study of 34 PsA patients treated with ustekinumab after failure or inadequate response to csDMARDs or TNFi, reported achievement of MDA in 70.5% of subjects at month 24 (23), and maintenance of low or minimal disease activity status has been recently shown to have a great influence on patients' quality of life and perception of their clinical condition (26).

A recent European multinational registry-based study, the EuroSpA research

Table II. Treatment emergent adverse events occurring in the PsABio Italian cohort, by treatment (safety dataset)*.

	UST* (n=113)	TNFi* (n=135)
no. of patients with ≥1 TEAE	23 (20.4%)	30 (22.2%)
System organ class/Preferred term		
Infections and infestations	12 (10.6%)	9 (6.7%)
Skin and subcutaneous tissue disorders	4 (3.5%)	8 (5.9%)
General disorders and administration site conditions	4 (3.5%)	5 (3.7%)
Gastrointestinal disorders	0	4 (3.0%)
Nervous system disorders	2 (1.8%)	2 (1.5%)
Musculoskeletal and connective tissue disorders	2 (1.8%)	1 (0.7%)
Neoplasms (benign, malignant and unspecified)	2 (1.8%)	1 (0.7%)
Vascular disorders	1 (0.9%)	2 (1.5%)
Cardiac disorders	1 (0.9%)	1 (0.7%)
no. of patients with ≥1 bDMARD agent related TEAE	7 (6.2%)	15 (11.1%)
no. of patients with ≥1 serious TEAE	2 (1.8%)	1 (0.7%)
System organ class/Preferred term		
Infections and infestations	1 (0.9%)	1 (0.7%)
Pneumonia	0	1 (0.7%)
Skin infection	1 (0.9%)	0
Neoplasms (benign, malignant and unspecified)	1 (0.9%)	0
Parathyroid tumour malignant	1 (0.9%)	0
no. of patients with ≥1 bDMARD agent-related serious TEAE	0	0
no. of patients with ≥1 TEAE leading to withdrawal of bDMARD drug	6 (5.3%)	10 (7.4%)
no. of patients with ≥1 bDMARD agent-related TEAE leading to withdrawal of bDMARD drug	5 (4.4%)	7 (5.2%)
no. of patients with ≥1 TEAE leading to permanent discontinuation of study	1 (0.9%)	0
no. of patients with ≥1 bDMARD agent-related TEAE leading to permanent discontinuation of study	0	0
no. of deaths	0	0

*Adverse events were summarised under the initial treatment line as well as under all treatments that started within a 91-day safety period after the initial treatment line prior to the adverse event. Therefore, the sum of subjects is higher than the total number in the safety set (n=237).
bDMARD: biological disease-modifying anti-rheumatic drug; TEAE: treatment emergent adverse event; UST: ustekinumab; TNFi: tumour necrosis factor inhibitor.

collaboration network (EuroSpA RCN), examined data of over 14,000 patients with PsA starting a first anti-TNF drug (27). The study, published by Brahe *et al*., found a 12-month treatment persistence ranging between 68% and 90% in different countries/registries, with a median of 77%. Our data on first-line TNFi treatment are generally consistent with these findings – though the persistence proportion is closer to the lowest than to the median estimate of EuroSpA. Based on the same research collaboration network, Michelsen *et al*. (28) have recently published the real-life evaluation at 12-months of secukinumab in 2,017 PsA patients. This demonstrated a 76% retention rate, similar to the median persistence observed by Brahe *et al*. in first-line TNFi users as well as to ustekinumab ones in our cohort.

Our findings on treatment persistence were consistent across several subgroups, including sex, use of concomitant methotrexate, and initial line of treatment, with a clear advantage for ustekinumab in patients receiving the drug as a first switch instead of a second TNFi.

In PsA patients, the best option for second-line biologic treatment after first-line TNFi failure is still uncertain and open to discussion (29). Both approaches of switching to a second TNFi or swapping to a biological drug with a different mechanism of action are possible (30-32), and comparative studies were advocated (33). A RCT including 300 patients with rheumatoid arthritis who were assigned, after insufficient response to a first TNFi drug, to a non-TNF biologic or to a second TNFi, found a more than doubled likelihood of response for patients in the swap (*i.e*. non-TNFi) *vs*. those in the switch (*i.e*. second TNFi) strategy (34). However, to our knowledge, no similar studies are available in PsA. Many factors should be considered to optimise second-line biologic therapy in PsA, including disease characteristics, comorbidities, cardiometabolic risk factors, treatment history, and patient preferences. As reported by Merola *et al*., switching between TNFis can be effective for many patients, but bDMARDs with different mechanisms of action may be superior alternatives (31). In this setting, the severity of psoriasis, the predominance of enthesitis and the risk of developing concomitant IBD may drive the choice towards ustekinumab (1, 3, 35).

Taking into consideration other factors related to drug response, our data confirmed that female gender and obesity adversely affect persistence in therapy in patients treated with TNFi (36-38), but not in those treated with ustekinumab.

Providing data from one specific country – besides the limitations that have already been acknowledged – has the advantage of a more homogeneous setting, with the consequence to obtain results closer to the real Italian clinical practice in managing PsA. Other strengths of this investigation are the prospective, predefined collection of data and the availability of information for both specific clinical effectiveness and safety outcomes and treatment persistence.

In conclusion, our analysis provided comparative real-life information on treatment persistence and effectiveness of biological drugs with different mechanisms of action, in an Italian cohort of adult PsA patients followed up to 15 months. In this setting, ustekinumab showed better persistence than TNFi, overall and in specific subgroups (females, monotherapy without methotrexate, BMI <25 or >30 kg/m^2, patients receiving ustekinumab as second-line treatment instead of a second TNFi), whereas clinical effectiveness, as measured by cDAPSA responses and MDA/VLDA achievement, and safety were similar.

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