Psoriasis: Targets and Therapy

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ORIGINAL RESEARCH

Effectiveness and Safety of Tildrakizumab in Elderly and Frail Elderly Psoriatic Patients Up to 2 years

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Purpose: Elderly patients with age ≥65 years represent an increasing percentage of the population with moderate-severe psoriasis. The definition of "frail elderly" is not easily framed, generally meaning a patient with unstable homeostasis. To date, there is no study in the literature examining possible differences between frail and non-frail elderly with psoriasis being treated with tildrakizumab.

Patients and Methods: The present multicentre retrospective study evaluated the effectiveness, drug survival and safety up to 2 years of treatment with tildrakizumab in the elderly (≥65 years) comparing frail and non-frail patients. Frail patients were defined as those with: i) 2 major comorbidities, or 1 major comorbidity and low economic level ii) and/or 2 of the following 5 parameters: weight loss, weakness, sluggishness, low activity level, and exhaustion.

Results: A total of 217 patients aged ≥65 years were enrolled, of whom 89 (41%) were grouped in the frail patient category. In the entire population, 2-year drug survival was ≥80%, and PASI 90 and ≤2 was achieved in 75% and 87.5% of patients, respectively. No difference in effectiveness or safety was found between frail and non-frail populations. Adjusting for baseline characteristics at Cox-regression, frail patients did not show a greater risk of discontinuation (HR 0.51, p=0.091).

Conclusion: Tildrakizumab showed good safety and effectiveness at 2 years in the elderly population with or without frailty, confirming it as a possible treatment of choice in psoriatic patients with significant comorbidities and older frail patients who deserve systemic treatments.

Keywords: psoriasis, tildrakizumab, elderly, safety, real-life

Introduction

Psoriasis is a chronic inflammatory skin condition affecting 2–4% of the population in Western countries.[1] Therapeutics targeting the interleukin (IL)- 23/IL- 17 axes have shown good efficacy and safety.[2] The humanized monoclonal antibody tildrakizumab, targeting the IL-23p19 subunit, is a systemic treatment approved for adult patients with moderate-to-severe plaque psoriasis.[3] Tildrakizumab has demonstrated efficacy and a favourable safety profile in the treatment psoriasis in large-scale randomized controlled Phase III trials (RCT) (reSURFACE 1 and reSURFACE 2) on long

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term.[3] Patients enrolled in RCTs often display different characteristics from daily practice: higher baseline disease severity and fewer comorbidities, such as cardiovascular disease.[2]

Patients with age ≥ 65 years) represent an increasing proportion of patients with psoriatic disease and 15% have moderate-to-severe disease.[4] Multiple comorbidities and a high number of medications, along with infections and oncological conditions, often make therapeutic management of psoriasis difficult in this specific population.[4] To date, there are no shared guidelines on the therapeutic management of the elderly patient.[1,4]

Biologic drugs are often used in the elderly even though data on safety and efficacy are limited; in fact, patients older than 65 years are often excluded from clinical trials.[4] Results from real-world studies confirm the safety of IL-23 inhibitors in a wide population of patients with psoriasis, including older patients, those who failed multiple biologics, and those with comorbidities such as obesity, metabolic syndrome, cardiovascular disease, dyslipidemia, diabetes, hypertension, inflammatory bowel disease, and psoriatic arthritis.[5] Real-life studies that have evaluated the effectiveness and safety of tildrakizumab in the elderly population are scarce.[1] The first report on elderly patients in clinical practice was reported by Ruggiero et al.[6] This study evaluated only 6 individuals, and reported outcomes that were similar to those of RCTs.[7] In a recent pharmacovigilance analysis, tildrakizumab, among IL-23 inhibitors, appeared to be associated with fewer side effects.[8]

Depending on the number of illnesses, economic conditions, and the general state of the patient, the elderly population may be quite heterogeneous.[9] According to L. Fried, an elderly person who reports weight loss, weakness, sluggishness, low activity level, and exhaustion is to be considered frail.[10] According to Clegg et al, in frailty one must consider weight loss >5% per year, exhaustion, reduced gait speed, reduced grip strength, and low energy expenditure.[11] The definition of "frail elderly" is not easily framed, but generally means a patient with unstable homeostasis, vulnerable to external damage, associated with increased hospitalization, institutionalization, falls, and death.[12] The frail patient also may be characterized by low income, deteriorating cognitive function, and progressive social isolation.[9]

To date, there is no study in the literature analyzing possible differences between frail and non-frail elderly patients with moderate-severe psoriasis undergoing treatment with biologic agents.

Materials and Methods

The present multicenter study involved 7 secondary and tertiary Italian dermatology centers aiming to analyze the effectiveness and safety of tildrakizumab in the elderly population (≥65 years) and to compare frail elderly and non-frail elderly patients for up to 2 years.

Population

All consecutive patients with moderate-severe psoriasis, aged ≥65 years treated or being treated with tildrakizumab with data retrievable from medical records from Dec 1, 2019 to May 31, 2023 were retrospectively analyzed.

This study was conducted as part of the SS-Dermo-20 protocol, approved by CET (internal review board) Interaziendale AOU Città della Salute e della Scienza di Torino. The patients signed written informed consent.

Demographic and disease characteristics at baseline were collected: age at enrollment, age at psoriasis onset, age at first biologic treatment, sex, smoking, education, weight, height, body mass index (BMI), type of psoriasis, joint involvement, special site involvement, and comorbidities. Medication history of the disease was also collected: previous biologic therapy, systemic therapy prior to tildrakizumab, and concomitant topical therapy with tildrakizumab.

Primary Objectives

Analysis of effectiveness outcomes derived from absolute PASI (Psoriasis Area Severity Index) at 12–16 (T1), 24–28 (T2), 48–52 (T3), 76–80 (T4), and 102–106 (T5) weeks: PASI ≤2 at any time point, PASI 90 at any time point, and PASI 100 at any time point.

Analysis of QoL (Quality of Life) outcomes derived from the DLQI (Dermatology Life Quality Index) at baseline, 48–52 weeks (T3), 76–80 weeks (T4), and 102–106 weeks (T5): DLQI 0/1 at any time point.

Analysis of drug survival (DS) was also evaluated.

Secondary Objectives

The above-described outcomes were compared between frail vs non-frail patients.

Frail patients were defined as those with: i) 2 major comorbidities, or 1 major comorbidity and low economic level (ie 9360 eur family income per year according to past Italian legislation for admission to "basic income pay"); ii) and/or 2 of the following 5 parameters: weight loss, weakness, sluggishness, low activity level, and exhaustion.

Statistical Analysis

Continuous variables were reported as mean±standard deviation (SD) or median and range, based on the distribution of each variable. For categorical variables, counts and frequencies were provided. Percentages were based on the number of non-missing values. The categorical variables were analyzed using a chi-square test and Fisher's exact test when appropriate, while continuous variables were tested using the Shapiro–Wilk test to investigate the normality of the distribution. The Student's *T*-test was used to compare dichotomous normal distributions, and non-normal distributions were tested using the Mann–Whitney *U*-test. The Kruskal–Wallis test was used to analyze more than two distributions. Imputation of non-responders was not conducted, and only observed cases were evaluated.

To analyze retention rate, survival analysis with a Kaplan Meier model was employed. The event was defined as drug discontinuation for any reason, while the time of observation was calculated as the time between the date of the last follow-up and the date of tildrakizumab start.

Cox (Proportional Hazards) Regression was used to evaluate baseline predictive factors associated with risk of interruption. Statistical analysis was conducted with STATA 15.1 SE (Stata Corp., 2017). All tests were two-sided and the statistical significance was set to $\alpha = 0.05$.

Results

A total of 217 (59.9% male) patients were enrolled. Baseline and demographic characteristics are summarized in Table 1. The mean age of access to first biologic treatment was 70.4 years (SD 4), or 21.6 years after the onset of the first sign of

Table 1 Baseline Characteristics of Patients, Mean Follow-Up, and Concomitant Topical Treatment

No. of patients	217
Mean Age, (SD) Median (Q1-Q3)	73 (6.2) 72 (68–77)
Mean BMI, (SD) Median (Q1-Q3)	26.7 (4) 26 (24–28.9)
Mean age of onset, (SD)	48.6 (18.3)
Median (Q1-Q3)	51 (35–63)
Sex (M), N°/%	130/59.9%
Mean age at first biologic, (SD)	70.4 (7.2)
Median (Q1-Q3)	70 (48–89)
Years between psoriasis onset and first biologic, (SD)	21.6 (16.8)
Median (Q1-Q3)	19 (7–32.8)
Vulgar psoriasis, N°/%	208/95.9%
Pustular psoriasis, N°/%	4/1.8%
Guttate psoriasis, N°/%	9/4.1%

(*Continued*)

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Table 1 (Continued).

Inverse psoriasis, N°/%	16/7.4%
Erythrodermic psoriasis, N°/%	1/0.5%
Smoking habit (17 missing), N/% Smokers Ex-smokers Non-smokers	200/100% 58/29% 56/28% 86/43%
Education (56 missing), N/% Primary first -degree Primary second-degree Secondary University	161/100% 29/18% 43/26.7% 68/42.2% 21/13%
Difficult-to-treat areas, N/%	128/59%
PsA, N/%	44/20.3%
Cardiovascular disease, N/%	61/28.1%
GI disease, N/%	25/11.5%
T2D, N/%	55/25.3%
Oncological diseases, N/%	30/13.8%
Autoimmune diseases, N/%	8/3.7%
Metabolic syndrome, N/%	52/24%
Obesity, N/%	46/21.2%
Frail patients, N/%	89/41%
Bio-naïve, N/%	145/66.8%
Adalimumab, N/%	35/16.1%
Etanercept, N/%	15/6.9%
Infliximab, N/%	9/4.2%
Ustekinumab, N/%	11/5.1%
Secukinumab, N/%	12/5.5%
Ixekizumab, N/%	4/1.8%
Brodalumab, N/%	4/1.8%
Multi-failure, N/%	4/1.8%
Topical treatment, N/% Emollients Combination therapies Steroids Calcineurin inhibitors	145/66.8% 105/48.4% 83/38.2% 22/10.1% 2/0.9%
Mean FU under tildrakizumab, (SD) Median (Q1-Q3)	16.9 (9.2) 16 (0–41)
Tildrakizumab STOP N/%	27/12.4%

(*Continued*)

Table 1 (Continued).

Cause of interruption N/%	27/100%
Primary failure	4/14.8%
Secondary failure	12/44.4%
Adverse event	2/7.4%
Death (not related to treatment)	3/11.1%
Other	6/22.2%

Abbreviations: SD, standard deviation; Q, quartile; N, number; PsA, psoriatic arthritis; BMI, Body Mass Index; M, Male; GI, gastrointestinal; T2D, Diabetes Mellitus, type II; FU, follow-up.

psoriasis. Most patients had psoriasis vulgaris (208, 95.9%), 59% of patients had at least one difficult-to-treat area (scalp, nails, genitals, palmoplantar regions), and 20.3% reported joint involvement. The most frequently reported comorbidity was hypertension (n=131), followed by diabetes mellitus (n=55); the remaining comorbidities are listed in Supplementary Table 1. A total of 61 patients (28.1%) reported a major cardiovascular comorbidity, 25 (11.5%) a gastrointestinal comorbidity, 30 an oncologic disease (13.8%), 8 an autoimmune disease (3.7%), 52 patients suffered from metabolic syndrome (24%), 46 were obese (21.2%), and 22 patients had no comorbidities (10.1%). According to the definition adopted, 89 patients (41%) were considered frail.

At tildrakizumab initiation, 145 patients were bio-naive (66.8%), and 145 patients applied concomitant topical therapy (66.8%), half of patients used emollients (105, 48.4%), and calcipotriene plus betamethasone combination therapy was used by 83 patients (38.2%).

Median PASI decreased from 12 (10–18.25) to 3 (1–5) as early as T1 visit (16 weeks) maintaining a progressive reduction until T5 when a median PASI of 0 was reached. Progressive achievement of relative outcomes was equally observed with PASI 100 being achieved by 70% of patients at T5, PASI 90 by 75%, and residual PASI ≤2 by 88%. Median DLQI decreased from 15 (10–22) at baseline to 0 (0–3) at T3 and 0 (0–1) at T5, with the attainment of DLQI 0/1 in 65.6% and 83.3% at the same time points (Figure 1 and Table 2).

Comparing the frail elderly patient population with the remaining elderly population, the latter was found to have a lower mean age at enrollment [72.3 (SD 6.3) vs 74 (SD 5.9) years, p=0.015] and a lower mean BMI [26 kg/m^2 (SD 3.4) vs 27.7 (SD 4.6) kg/m^2, p=0.005], while no differences between the two cohorts were observed concerning sex, mean age at onset, and bio-naive status (Supplementary Table 2).

Concerning effectiveness outcomes, no significant difference was observed in the reduction of mean PASI, as well as in the achievement of relative outcomes; and the proportions of those achieving PASI 90, PASI 100, and PASI ≤2 in the fragile population were higher at almost all time points (Table 3). Similar considerations are possible considering DLQI (Figure 2 and Table 3).

After a median follow-up of 16 months (0–41), 27 patients permanently discontinued treatment (12.4%). The leading cause of discontinuation was secondary failure (44.5%), while 4 patients discontinued for primary failure (14.8%) and only 2 for treatment-related adverse events (7.4%) (1 for unknown event and 1 for elevation of blood creatinine and urea); 3 patients died for reasons related to their comorbidities and not to treatment (11.1%), and 6 patients discontinued for other causes (22.2%). In all, 10 patients reported mild to moderate side effects that did not lead to treatment discontinuation: 2 patients reported upper respiratory tract infection, 1 chronic rhinitis, 1 nausea and vomiting, 1 eczematisation after 1 year of treatment, 1 increase in glycemia, 1 anti-HBC increase, 1 flushing, 1 headache, and 1 weight gain. No substantial differences were observed between the two categories: 4 frail patients reported AEs vs 6 non-frail patients.

The estimated retention rate in patients at risk of discontinuation was 89.6% at 12 months and 80% at 24 (Figure 3). Frail patients showed lower drug survival (p=0.042) (Figure 3) without considering possible confounding factors. In

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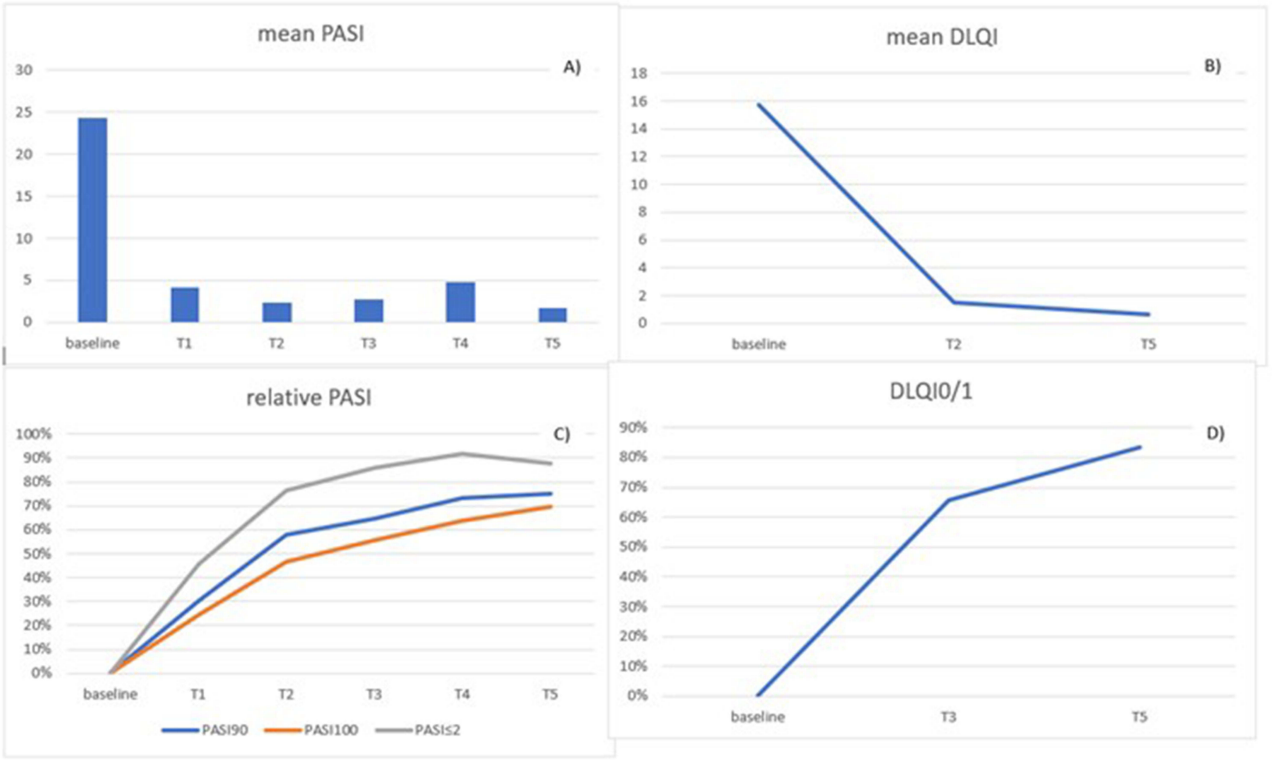

Figure 1 (**A**) Mean PASI reduction of observed patients at any time point [baseline, (T1), 24–28 (T2), 48–52 (T3), 76–80 (T4), and 102–106 (T5) weeks]. (**B**) Mean DLQI reduction of observed patients at baseline, T3, and T5. (**C**) Relative PASI achievement in observed patients at any time point (baseline, T1, T2, T3, T4, and T5). (**D**) Relative DLQI 0/1 achievement in observed patients at baseline, T3, and T5.
Abbreviations: PASI, Psoriasis Area Severity Index; DLQI, Dermatology Life Quality Index.

contrast, at multivariate analysis considering age, age of onset, sex, naïve status, and difficult site involvement the frail population did not show a greater risk of discontinuation (HR 0.51, p=0.091, CI 0.23–1.11); BMI was not included in the analysis because obesity (BMI ≥30 kg/m^2) has been considered as a possible defining factor of "frailty" (Supplementary Table 3).

Table 2 Mean PASI Reduction of Observed Patients at any Time Point

	Baseline	T1	T2	T3	T4	T5
No. of patients observed	217	187	179	165	86	56
Mean PASI (SD) Median (Q1-Q3)	24.36 (38.8) 12 (10–18.25)	4.09 (6.6) 3 (1–5)	2.35 (5.7) 1 (0–2.5)	2.8 (8.1) 0 (0–2)	4.8 (24.5) 0 (0–1)	1.7 (4.8) 0 (0–1)
PASI 90	0%	31%	58%	65%	73%	75%
PASI 100	0%	25%	46%	56%	64%	70%
PASI ≤2	0%	46%	77%	86%	92%	88%
Mean DLQI (SD) Median (Q1-Q3)	15.7 (8.1) 15 (10–22)			1.5 (2.2) 0 (0–3)		0.7 (1.2) 0 (0–1)
DLQI 0/1	0%			65.6%		83.3%

Notes: Baseline, (T1), 24-28 (T2), 48-52 (T3), 76-80 (T4), and 102-106 (T5) weeks, mean DLQI reduction of observed patients at baseline, T3, and T5, relative PASI achievement by observed patients at any time points (baseline, T1, T2, T3, T4, and T5), relative DLQI 0/1 achievement by observed patients from baseline to T3 and T5.
Abbreviations: N, number; SD, standard deviation; Q, quartile; PASI, Psoriasis Area Severity Index; DLQI, Dermatology Life Quality Index.

Table 3 Achievement of Outcomes by Frail Patients and Non-frail Patients.

	Baseline			T1			T2			T3			T4			T5		
	Frail	Non-Frail	p-value	Frail	Non-Frail	p-value	Frail	Non-Frail	p-value	Frail	Non-Frail	p-value	Frail	Non-Frail	p-value	Frail	Non-Frail	p-value
No. of patients	89	128		76	111		71	108		65	100		36	50		23	33	
Mean PASI, (SD)	25.4 (42.8)	23.68 (36)	0.576	4.2 (8.8)	4 (4.6)	0.707	2.2 (6.7)	2.5 (4.9)	0.286	2.9 (9.8)	2.7 (6.8)	0.791	3.9 (20.3)	5.4 (27.3)	0.643	1.5 (5.2)	1.9 (4.6)	0.823
PASI90	0%	0%		34%	28%	0.359	65%	54%	0.141	69%	62%	0.342	75%	72%	0.757	74%	76%	0.875
PASI100	0%	0%		25%	24%	0.916	51%	44%	0.346	55%	56%	0.938	67%	62%	0.657	70%	70%	0.992
PASI≤2	0%	0%		47%	44%	0.615	80%	74%	0.338	88%	85%	0.626	94%	90%	0.457	96%	82%	0.124
Mean DLQI (SD)	16.95 (8)	14.8 (8.2)	0.088							1.3 (1.9)	1.6 (2.4)	0.708				0.9 (1.3)	0.5 (1.1)	0.279
DLQI 0/1	0%	0%								67%	64%	0.734				85%	81%	0.776

Notes: Significant p-value <0.05. Mean PASI reduction at any time point [baseline, (T1), 24–28 (T2), 48–52 (T3), 76–80 (T4), and 102–106 (T5) weeks]. Mean DLQI reduction at baseline, T3, and T5. Relative DLQI 0/1 achievement from baseline, to T3 and T5. PASI 90 achievement at any time point (baseline, T1, T2, T3, T4, and T5). PASI ≤2 achievement at any time point (baseline, T1, T2, T3, T4, and T5). PASI 100 achievement at any time point (baseline, T1, T2, T3, T4, and T5).

Abbreviations: SD, standard deviation; PASI, Psoriasis Area Severity Index; DLQI, Dermatology Life Quality Index.

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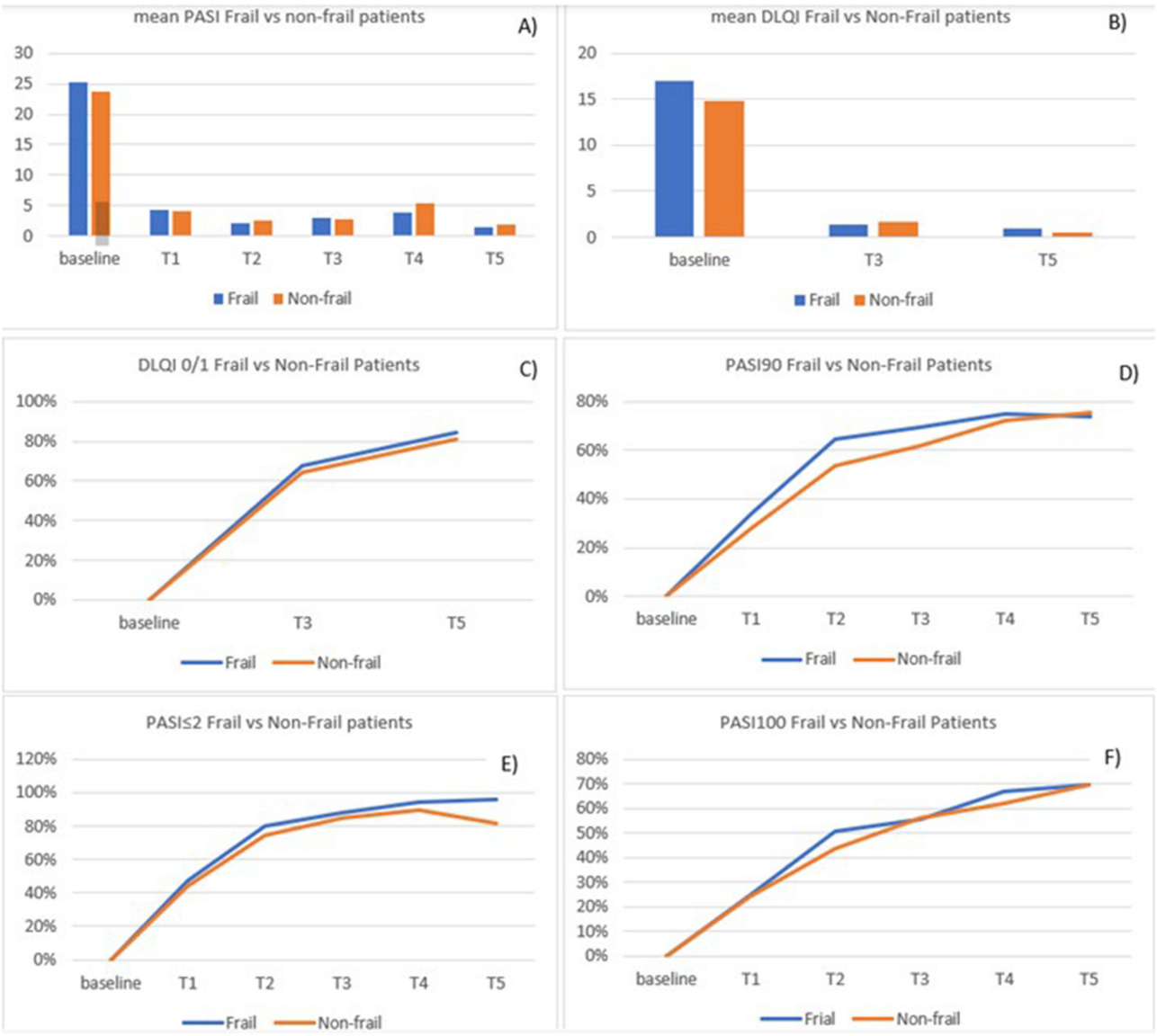

Figure 2 Comparative achievement of outcomes between frail and non-frail patients. Significant p-value <0.05. (**A**) Mean PASI reduction at any time point [baseline, (T1), 24–28 (T2), 48–52 (T3), 76–80 (T4), and 102–106 (T5) weeks]. (**B**) Mean DLQI reduction at baseline, T3, and T5. (**C**) Relative DLQI 0/1 achievement from baseline, to T3 and T5. (**D**) PASI 90 achievement at any time point (baseline, T1, T2, T3, T4, and T5). (**E**) PASI ≤2 achievement at any time point (baseline, T1, T2, T3, T4, and T5). (**F**) PASI 100 achievement at any time point (baseline, T1, T2, T3, T4, and T5).
Abbreviations: PASI, Psoriasis Area Severity Index; DLQI, Dermatology Life Quality Index.

Discussion

The increasing number of patients with ≥ 65 years having moderate to severe psoriasis in daily practice is a challenge for the clinician.[4] Evidence in this patient population is available for limited biological agents and small molecule inhibitors.[4] Some clinicians feel not comfortable prescribing biological agents to elderly patients, considering the high amount of comorbidities, immunosenescence, and cognitive decline.[13] These factors can alter the risk-to-benefit ratio of biological agents in this special population, requiring a closer examination of the evidence for these agents in older patients.[13]

In our population, almost 9 of 10 patients had at least one comorbidity. The most frequent major comorbidity was cardiovascular, affecting more than one-fourth of patients.

In our population, 41% of our patients fit the definition of frail elderly. Previous evidence has documented equal efficacy of anti-TNFalpha, ustekinumab, and secukinumab in the elderly and nonelderly populations.[13]

The present analysis is one of the first to report on the effectiveness and safety of tildrakizumab in elderly populations and compare frail and non-frail elderly patients.

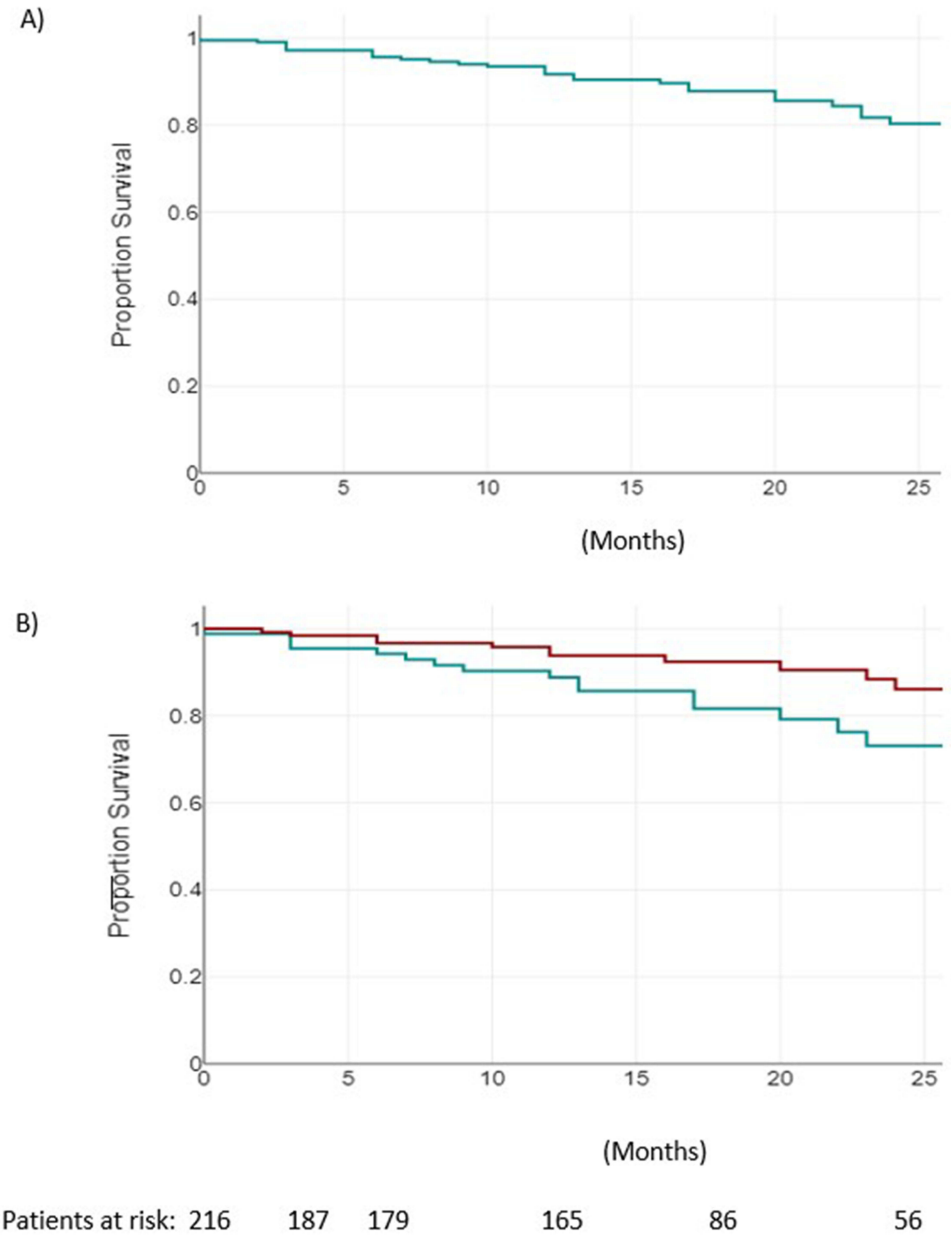

Figure 3 (**A**) Drug Survival of patients at risk of discontinuation up to 24 months by Kaplan-Meier estimator. (**B**) Comparative drug survival between frail (green) and non-frail (red) patients at risk of discontinuation up to 24 months by Kaplan-Meier estimator. Significant p-value <0.05.

In the present study, tildrakizumab was effective and safe in the treatment of moderate-severe psoriasis for up to 2 years of treatment in both elderly and frail elderly patients. Our study is also one of the few reporting on concomitant topical treatment during biological therapy. In our population, almost half of patients used at least emollients, with more than one-third using a topical agent such as the combination of calcipotriene plus betamethasone. The use of such agents can improve the overall response to biological therapies, facilitating achievement of PASI outcomes. Only 2 of the 12 reported AEs led to drug discontinuation. The nature of these AEs was generally mild with minimal impact on health. We observed three deaths, all occurring in the frail population, and none related to tildrakizumab treatment.

Regardless of the age of the population analyzed, real-life effectiveness data for up to 2 years of treatment with tildrakizumab are scarce.[14,15] In the study by Drerup et al, 58 patients treated with tildrakizumab for up to 76 weeks were observed, and 58% of these achieved PASI ≤1 and 80% PASI ≤3, which is lower than what we observed at the same time point in 86 patients considering, however, the achievement of PASI ≤2 (92%).[14] This observation, also considering the

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different mean initial PASI between our study and the German study (24.36 vs 8.6), might suggest a greater efficacy of tildrakizumab in the elderly population.[13]

There is robust real-life evidence of the effectiveness of tildrakizumab at 52 weeks.[15–20]

In the Italian multicenter study by Narcisi et al, achievement of PASI 100, PASI 90, and PASI ≤2 was seen in 58.68%, 73.55%, and 85.95% of cases, respectively;[16] these results are similar to our observations for the same outcomes: 56%, 65%, and 86%, respectively. The population in that study, started from a mean initial PASI of 14.45, and a mean age of 48.6 years, confirming the efficacy of tildrakizumab regardless of age and disease severity.[16] Campione et al reported in a cohort of 59 patients the attainment of PASI 100 and PASI 90 in 77% and 90.2% of the observed population, which is far higher than what we observed (56% and 65%, respectively).[17] Such differences lie not only in the different sample sizes, but also in the mean age of 51 years versus 73 years in our population, along with the lower mean initial PASI.[17] In contrast, two other Italian studies have reported results similar to ours at 52 weeks.[18–20] Our patients performed better than the large population observed in the multicenter TILOT study, which reported a PASI ≤3 at 52 weeks in 74.6% of cases, compared with 86% attainment of PASI ≤2 in our population.[21]

Regarding the 2-year drug survival in the literature, in the study by Gargiulo et al on 488 patients the estimated number of psoriatic patients on treatment at 2 years was 87%, which is higher than our observation of 80%;[15] Torres et al reported a 1-year drug survival of 90%, similar to the 91.7% seen herein.[22]

Regarding the elderly population (age ≥65) treated with tildrakizumab, the study by Ruggiero et al showed PASI 90 and PASI 100 attainment in 60% and 30% of the observed population, respectively, compared with 58% and 46% in our study.[6] The same group showed lower effectiveness compared with risankizumab for both outcomes and compared with guselkumab for PASI 100.[6] The ESTER study reported an achievement of PASI 75, PASI 90, and PASI 100 in 77.5%, 60%, and 45.2% of patients with age > 65 years at 28 weeks. The same study highlighted the effectiveness of tildrakizumab on palmoplantar areas, scalp, fingernails, and genitals affected by psoriasis in the elderly.[23]

Fukasawa et al recently highlighted that it is easier for the elderly to achieve PASI ≤2 at 7 months compared to patients with age <65 years.[24] The authors further highlighted that in the elderly population Treg lymphocytes were reduced in number and were less functional, and that tildrakizumab was able to restore their proper function.[24] Tildrakizumab also improved nail fold bleeding and enlarged capillaries, which are known risk factors for psoriatic arthritis in the elderly, and the authors suggested that the drug may inhibit progression to psoriatic arthritis, effect shared with other IL-23 inhibitors.[24]

Given the complex definition of frailty in the elderly patient, except for the pilot study by Rosset et al, there are no reports investigating biologic treatments in frail elderly patients with psoriasis.[1]

Tildrakizumab has been shown to be safe in a population with comorbidities and elderly patients in some post hoc analyses of registrational studies, and in real-life experiences.[25,26] Fernandez et al observed that metabolic syndrome does not lead to a significant increase in adverse events in the population treated with tildrakizumab nor does it affect the efficacy of the treatment compared to the population without metabolic syndrome, confirming previous observations by Menter et al who did not detect an increase in cardiometabolic risk factors in this population.[27,28] Recently, Cacciapuoti et al observed a significant reduction in adipokines, resistin, and leptin in patients treated with tildrakizumab who showed a rapid response to treatment, suggesting the value of a rapid response as a proxy for a reduction in factors associated with increased risk of metabolic syndrome.[29] Ter Haar et al reported a higher proportion of musculoskeletal, metabolic, and vascular disorders in elderly treated with tildrakizumab.[4] In any case, patients over 65 years did not show less efficacy at 28 and 244 weeks than younger patients and the safety profile was comparable.[4]

Recently Al-Yafeai et al in an FDA adverse event reporting system (FAERS) analysis, reported that compared with other interleukin inhibitors tildrakizumab was less associated with cardiovascular events considering pericarditis, atrial fibrillation, and cardiac ischemic events.[30]

In our population, the presence of severe comorbidities did not impact the effectiveness and safety of the tildrakizumab. There were no significant differences even considering patients with severe comorbidities and an overall frail condition.,Of note, these patients had also a higher mean age at baseline and a higher mean initial PASI.

The limitations of the present study are inherent in its real-life and retrospective nature. Another limitation is the absence of a shared definition for the frail patient, even if our definition was derived from different literature sources.

In any case, our study has a large sample size of a specific population, while also providing effectiveness and safety data at 2 years, a time point that is still poorly explored in the literature.

Conclusions

Literature data and our study confirm the effectiveness and safety of tildrakizumab in the elderly and frail elderly for up to 2 years of therapy. The presence of severe comorbidities should not be considered as a barrier to the introduction of tildrakizumab in this population. Some pilot studies suggest a protective effect of tildrakizumab on possible risk factors for metabolic syndrome, and the drug does not appear to be associated with different rates of major cardiovascular events than other interleukin inhibitors. The frail elderly patient may benefit from tildrakizumab with comparable treatment survival to a more fit population.

Collaborators

Collaborators from the working group for Frail-PsO Group: Angela Fico and Fabio Artosi. Both are affiliated with Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy and Dermatology Unit, Fondazione Policlinico Tor Vergata, Rome, Italy.

Disclosure

M. Galluzzo declare to have acted as speakers and/or consultants for AbbVie, Almirall, Eli-Lilly, Janssen-Cilag, LeoPharma, Novartis and Sanofi, outside the submitted work. E Campione served as a consultant for Almirall, BMS, Amgen, and UCB. Paolo Gisondi has been a consultant and/or speaker for AbbVie, Almirall, Amgen, Janssen, Leopharma, Eli Lilly, Novartis, Pierre Fabre, Sandoz, Sanofi, UCB. A.V. Marzano reports consultancy/advisory board disease-relevant honoraria from AbbVie, Amgen, Boehringer Ingelheim, Leopharma, Novartis, Pfizer, Sanofi, Incyte, Bristol Myers Squibb and UCB. The other authors report no conflicts of interest in this work.

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