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Research Article

Dactylitis and Enthesitis in Psoriatic Arthritis: 10-Year Experience with Adalimumab in Real World Clinical Practice

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Keywords

• Dactylitis; Enthesitis; Psoriatic arthritis; Adalimumab; Remission

Abstract

Objective: To evaluate the efficacy of adalimumab (ADA) on enthesitis and dactylitis in psoriatic arthritis (PsA), and to assess the prognostic role of dactylitis and enthesitis as expressed by the correlation with remission and low disease activity (LDA) achieving.

Methods: Retrospective, 10-year, observational study of 273 consecutive patients with PsA treated with ADA, 40 mg/every other week, combined with methotrexate in 123 (45.5%) or in monotherapy in 150 (54.95%). ADA was administered as first- or second-line therapy in 200 (73.3%) and 73 (26.7%) patients, respectively. Primary outcome measures: intention to treat analysis of the number of clinically detectable enthesitis in any site according to Leeds Enthesitis Index (LEI), and the number of any digit with dactylitis (0 to 20) at the end of follow-up. Secondary outcome measure: the correlation between the occurrence of dactylitis and enthesitis and remission and MDA.

Results: At baseline, dactylitis and enthesitis were present in 88 (32.2%) and 127 (46.7%) patients, respectively. Dactylitis resolution was recorded in 86,2% patients ($p<0.001$) and enthesitis in 83.3%, ($p<0.001$), with LEI change from 2.9 ± 1.2 to 0.20 ± 0.3 ($p< 0.001$). Patients with dactylitis and enthesitis were more likely not to achieve the remission or LDA (adjusted OR of 2.02; 95% CI 1.56-4, 11; p= 0.039 for dactylitis, and 1.88; 95% CI 1.51-4.34; p= 0.039 for enthesitis). No significant differences of efficacy between ADA first-line and second-line and between ADA mono- or combo-therapy groups resulted.

Conclusion: ADA efficacy resulted comparable with other anti-TNF- and non-anti-TNF targeted biologics. Dactylitis and enthesitis represented poor prognostic markers.

INTRODUCTION

Psoriatic arthritis (PsA) is a multifaceted inflammatory disease characterized by different clinical manifestations including arthritis, spondylitis, tenosynovitis, enthesitis, dactylitis, uveitis and cardiovascular adverse events [1]. As recommended by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) [2], and the European League against Rheumatism (EULAR) [3], the treatment of PsA includes the use of traditional disease modifying antirheumatic drugs (tDMARDs) and, in case of failure or intolerance, biologic agents and apremilast is indicated. Over the last 15 years, data from clinical trials and real life clinical practice evidenced the efficacy of anti-TNF targeted biologics for the treatment of PsA, and more recently, biologics inhibiting the IL-12/23 and IL-17 pathways, and apremilast, a non-biologic drug inhibiting the intracellular phosphodiesterase-4, have been licensed[4].

Enthesitis and dactylitis are hallmarks of PsA with an estimated frequency of 60% to 80% and at least 30% of the patients, respectively [1,4]. Regarding the therapeutic approach to enthesitis and dactylitis, given the limited efficacy of tDMARDs methotrexate (MTX), sulphasalazine and leflunomide [5,6], biologics are recommended in resistant cases[2].

However, though these manifestations are frequent and often disabling, the efficacy of different treatments on enthesitis and dactylitis in PsA has been mainly assessed as secondary end-points or by sub-analyses of randomized clinical studies (RCT) chiefly designed to evaluate the joints and psoriasis outcomes [7-9]. In addition, in the oldest RCTs, namely those evaluating the efficacy of etanercept [10-13] and adalimumab (ADA) [14-17], dactylitis and enthesitis outcomes were not assessed. More recently, in RCTs of anti-TNF agents golimumab [18] and certolizumab pegol [19], and of non-anti-TNF targeted biologics ustekinumab [20-22] and secukinumab [23-25], the efficacy on dactylitis and enthesitis was evaluated as secondary end-point, with response rates for both features ranging from 50% to 80% of the cases.

Primary end-point of present study was to evaluate the efficacy of ADA on enthesitis and dactylitis in a large cohort of patients with PsA observed over a 10-year follow-up period. Secondary end-Points were the assessment of dactylitis and enthesitis as prognostic factors as expressed by the association with the risk of not achieving the remission and low disease activity (LDA), and the safety profile of ADA therapy.

PATIENTS AND METHODS

Setting

The study was conducted at the Rheumatology Department of the Azienda USL Toscana Centro, Prato Hospital that serves an area of around 1.700.000 people and covers the three levels of care for patients with rheumatic disorders. In addition, due the specific expertise in spondyloarthritis, many patients are referred from other Tuscany hospitals and from other Italian regions.

Study design

Retrospective review of the medical records of all patients with PsA treated with ADA over a 10-year period.

Data extraction

A computed database of all patients with rheumatic disorders was operating in Prato center since the year 2000. All clinical records of consecutive patients meeting the CASPAR classification criteria for PsA [26], treated with first- or second-line ADA between January 2007 and December 2016 were extracted from the database.

Definitions

-Peripheral PsA: Presence of at least one swollen and tender joint, without clinical evidence of axial involvement.

-PsA spondylitis: Patients meeting the modified New York criteria for ankylosing spondylitis [27]

-PsA mixed pattern: Patients with both peripheral and axial involvement.

-Dactylitis: diffuse tenderness and swelling of the entire digit assuming sausage aspect.

-Enthesitis: Tenderness and swelling at sites of tendon, ligament and joint capsule insertion into bone.

-Disease remission: The remission was evaluated by DAS28-CRP ≤ 2.6 [28], and BASDAI ≤ 4 [29].

-LDA: Patients with PsA peripheral pattern achieving a DAS28-CRP between >2.6 and ≤ 3.2.

-Non-responders: patients failing to achieve or maintain a DAS28-CRP ≤ 3.2 in peripheral PsA and a BASDAI ≤ 4 in PsA spondylitis.

-Relapse: Patients were considered as relapsing in the case of recurring of any articular or extra-articular clinical manifestation, independently on the acute-phase reactants values.

Outcome measures

At baseline and at every follow-up visits all patients were evaluated for the following outcome measures:

Primary: the number of clinically detectable enthesitis in any site according to Leeds Enthesitis Index (LEI) [30], and the number of any digit with dactylitis (0 to 20).

Secondary: the percentage of patients achieving and maintaining the clinical remission and LDA for at least 2 consecutive visits as expressed by DAS28-CRP ≤ 2.6 or between >2.6 and ≤ 3.2, and BASDAI ≤ 4, respectively.

The safety was assessed by recording the number and type of adverse events occurring during the treatment.

Treatment regimen

A standardized therapeutic approach was adopted in our department since the year 2003, when anti-TNF agents infliximab and etanercept were licensed by the Italian Health Authorities. Adalimumab was licensed in late 2005. PsA patients presenting with mono-oligoarthritis were initially treated with NSAIDs, and, when indicated, local infiltrative corticosteroid (CS) therapy. Short-term, low-dose CS was added in resistant patients with oligoarthritis. Non-responders were given MTX at the dose of 10–15 mg/week added to NSAIDs for at least 6 months. Switching to CsA was done in case of intolerance to MTX, and CS was permitted in case of resistance to therapy.

PsA patients presenting with polyarthritis were scheduled to start MTX and NSAIDs at diagnosis. Non-responders were treated with the same schedule described earlier. Patients with both peripheral patterns who were non-responders to therapy with tDMARDs received an anti-TNF agent. In case of MTX intolerance, anti-TNF was given in monotherapy. Over the following years patients could also receive other anti-TNFs, including golimumab and certolizumab pegol, and more recently ustekinumab, and secukinumab. As regards the specific therapy for enthesitis and dactylitis, one course of local corticosteroid infiltrative therapy was usually done in patients with one-site enthesitis and/or one digit dactylitis at diagnosis. In patients requiring second-line therapy with biologics the occurrence of one or both features during the follow-up was infiltrated with CS if isolated, otherwise, if concomitant to other clinical manifestations of disease relapse the switch to another biologic was done.

ADA was given at the dose of 40 mg/every other week, subcutaneously. In patients achieving a stable remission of at least 12-month duration, ADA dose reduction up to 40 mg/4 weeks was attempted, and in patients maintaining the remission with the reduced dose for at least 12 months, the drug was interrupted.

Follow-up

Patients were followed by the same rheumatologist, and follow-up visits were scheduled at baseline, after 2 months, and every 4-6 months thereafter. Control visit intervals were shortened in the case of urgent clinical problems, and all patients were instructed to call the center in presence of worsening of previous arthritis, additional joint involvement, extra-articular manifestations onset and adverse events (AEs).

At every visit, patients had a complete physical examination including all previously listed outcome measures. Moreover, routine blood examinations including ESR, CRP, RF, complete blood cell count with differential count, renal and liver function tests and ANA were carried out. Radiological examination of involved joints was done in all study patients at baseline and every 2 years. Patients with additional clinically involved joints underwent to radiological examination at symptom onset and

every 2 years. All clinical and laboratory data were recorded in a computed patients' chart.

Adverse events

At every visit, all patients were monitored for clinical and laboratory evidence of AEs defined as mild (transient and easily tolerated), moderate (subject discomfort with interruption of usual activities) and severe (incapacitating or life-threatening). The end of follow-up was extended to December 2016.

As usually done in our center before biologic therapy starting, a written informed consent was signed by all patients.

Ethics approval for this type of study was not required in accordance with the policy of our institution.

Statistical analysis

Groups of treatment were defined at the baseline visit and, following an intention to treat principle, and comparisons among different treatments did not take into account any treatment switching. Data are summarized as mean ± standard deviation for continuous variables, and absolute frequency and percentage for categorical variables. Univariate comparisons among groups were evaluated for statistical significance using Chi-square test for categorical variables and one-way analysis of variance or Mann-Whitney test for continuous variables. Finally, to evaluate the independent association between diagnosis/treatments and clinical characteristics/outcomes, multilevel regression models (i.e. linear for continuous variables and logistic for dichotomous variables) were performed considering the visit as a cluster variable. The associations of dactylitis and enthesitis with remission and LDA achievement were assessed with logistic regression models with calculation of adjusted odds ratios (ORs) and 95% confidence intervals (CIs) to estimate the risk of not achieving remission or LDA. The following variables were analysed: age, gender, disease duration, body mass index (BMI), number of involved joints, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values, corticosteroids and tDMARDs use, prior biologic therapies. ADA survival was analysed by Kaplan–Meier estimates and log-rank test.

A p value of <0.05 was considered statistically significant. All analyses were performed using Stata for Windows (version 13.0) by importing data from Microsoft Excel (2010 version) files.

RESULTS

As shown in Table 1, during the 10-year period, 273 consecutive patients with PsA, 106 (38.8%) males and 167 (61.2%) females with a mean age at diagnosis of 50.69 ± 12.69 years, and with a mean disease duration of 59,05 ± 64.5 months, started ADA 40 mg/every other week, combined with methotrexate in 123 (45.5%) or in monotherapy in 150 (54.95%). ADA was administered s first-line biologic therapy in 200/273 (73.3%) patients, while 73 (26.7%) patients switched from another anti-TNF. As regards the PsA clinical patterns, 139 (50.9%) had peripheral PsA, 95 (34.8%) PsA spondylitis, and 39 (14.3%) mixed. The mean DAS28-CRP and BASDAI were 4.52 ± 0.92 and 6.90 ± 1.04, respectively.

Primary end-point results

At baseline, dactylitis and enthesitis were present in 88

Table 1: Baseline demographic and clinical characteristics of PsA patients treated with adalimumab.

Feature	Number (Percentage)
Overall number	273
Male/Females	106 (38.8)/167(61.2)
Age at diagnosis; years; mean±SD	50.89±12.69
Age at ADA starting; years; mean±SD	54.42±17.75
Disease duration; months; mean±SD	59.05±64.50
B-27 positive*	58 (21.25)
BMI; mean±SD	26±6.36
Peripheral PsA	139 (50.9)
PsA spondylitis	95 (34.8)
Mixed PsA pattern	39 (14.3)
Biologic naïve	200 (73.3)
Previous biologic therapy; N (%)	
-Overall	73 (26.7)
-Etanercept	40 (54.8)
-Infliximab	28 (38.4)
-Etanercept+Infliximab	3 (4.1)
-Golimumab	2 (2.7)
ADA monotherapy	150 (54.95)
ADA+MTX	123 (45.05)
ESR mm/h; mean±SD	32.55±15.07
CRP mg/dl; mean±SD	1.82±1.52
Tender joints; mean±SD	5.84±4.87
Swollen joints; mean±SD	2.91±2.67
Dactylitis	88 (32.3)
Enthesitis	127 (46.5)
Anterior uveitis	67 (24.5)
-LTBI positive	6 (2.2)
DAS28-CRP; mean±SD †	4.52±0.92
BASDAI; mean±SD ǂ	6.90±1.04
PGA; mean±SD #	77.08±8.24
PhGA; mean±SD #	71.34±8.44
Comorbidities	
-Overall	137 (50.2)
-Metabolic syndrome	42 (15.4)
-Diabetes ##	54 (19.8)
-Hypertension ##	57 (20.9)
-Dyslipidaemia ##	57 (20.9)
-Obesity ##	48 (17.6)
-CV events	20 (6.6)
-Osteoporosis	17 (6.2)
-IBD	5 (1.8)
-COPD	5 (1.8)

Symbols: * B-27 typing was missing in 44 (16.12%) patients; † Calculated on 178 patients with peripheral and mixed PsA. ǂ Calculated on 134 patients with PsA spondylitis and mixed. # Visual analogue scale 0-100. ## Including patients with metabolic syndrome.
Abbreviations. BMI: Body Mass Index; ADA: Adalimumab; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; SD: Standard Deviation; PGA: Patient Global Assessment; PhGA: Physicia global Assessment; CV events: Cardiovascular Ischemic Events; IBD: Inflammatory Bowel Disease; COPD: Chronic Obstructive Lung Disease; LTBI: Latent Tuberculosis Infection.

(32.2%) and 127 (46.7%) patients, respectively. Dactylitis was recorded in 62 (44,6%) out of 139 patients with peripheral PsA, in 14 (14.7%) of 95 patients with spondylitis, and in 12 (30.7%) of 39 with mixed pattern, and affected 1 digit in 46 (52.3%) cases, 2 digits in 26 (29.5%), 3 digits in 13 (14.8%), and 4 digits in 3 (3.4%).

Enthesitis involved 1 site in 33 (26%) cases, 2 sites in 62 (48.9%), 3 sites in 26 (20.5%), 4 sites in 3 (2.4%) and 5 sites in 3 (2.4%), with a resultant LEI of 2.9 ± 1.2. Enthesitis was concomitant with dactylitis in 39 (30.7%) patients.

Table 2 shows the results of ADA treatment. At final visit dactylitis was absent in 75 (86,2%) out of 88 patients (p<0.001), with 5 (6%) episodes of isolated dactylitis relapse treated with local CS infiltration. ADA efficacy was rapid with resolution of dactylitis in 83 (94.3%) and of enthesitis in 111 (87.4%) patients at 6-month visit.

At final visit, enthesitis remission was observed in 106 (83.3%) out of 127 patients (p<0.001). Isolated enthesitis relapse episodes, resolved with local CS infiltration, were recorded in 9 (8.5%) out of 106 patients. The LEI dropped from 2.9 ± 1.2 at baseline to 0.20 ± 0.3 (p< 0.001) at the end of follow up.

No significant differences of efficacy on dactylitis and enthesitis were observed between ADA first-line and second-line and between ADA mono- or combo-therapy groups.

Secondary end-points results

Logistic regression revealed that both patients with dactylitis and enthesitis were more likely not to achieve the remission or LDA with unadjusted OR of 2.13 (95% CI 1.67-4.23; p=0.043) and adjusted OR of 2.02 (95% CI 1.56-4,11; p= 0.039) for dactylitis, and unadjusted OR of 1.98 (95% CI 1.56-4.45; p= 0.045) and adjusted OR of 1.88 (95% CI 1.51-4.34; p= 0.031) for enthesitis.

As shown in Table 2, at the end of follow-up 172 (63%) patients were still receiving ADA. The dose reduction up to 40 mg/every 4 weeks was recorded in 82 (30%). Of these, 76 (92.6%) maintained the remission at the end of follow up. ADA was interrupted in 25 (9.15%) who maintained a stable remission after dose reduction up to the final visit. Overall remission/LDA was observed in 222 (81.3%) of the patients.

Remission rate was significantly higher in patients treated with ADA as first-line therapy as compared with second-line (84.5% vs 72.6; p: 0.04), while no differences were recorded between ADA mono or combo-therapy both for remission and LDA. The mean follow-up was 45.11 ± 30.5 months.

ADA interruption and AEs

The drug was withdrawn in 42 (15.4%) patients for primary or secondary failure. Moderate to severe AEs requiring the interruption of therapy occurred in 34 (12.4%) out of 273 patients. Of these, pneumonitis occurred in 7 (2.6%) patients, severe cutaneous rush in injection site in 10 (3.7%), alopecia in 3 (1.1%), pregnancy in 4 (1.5%), cytomegalovirus posterior uveitis in 1 (0.4%), anal fistula in 1 (0.4%) patient with concomitant Crohn's disease, multiple urinary infections in 2 (0.7%), and malignancy in 4 (1.5%) including 2 intestinal, 1 lung, and 1 breast cancers. Two patients, with an history of acute myocardial infarction died for sudden coronary death.

DISCUSSION

Local corticosteroid injections and NSAIDs are recommended as first intervention in patients with enthesitis [2,3], while therapy with tDMARDs is suggested only for patients with dactylitis, due to the absence of efficacy data in those with enthesitis [2]. In case of unresponsiveness to local infiltrative therapy and tDMARDs, biologics are indicated, even if the evidence of efficacy of biologics results from the respective RCTs as secondary end-point outcome measure [18-25].

Though assessed by different enthesitis outcome measures, studies on biologics show level 1b evidence of efficacy for infliximab, golimumab, certolizumab, ustekinumab, and secukinumab, with percentages of resolution of enthesitis ranging from 40% to 80% [2,31]. A comparable degree of evidence of the efficacy of these biologics on dactylitis is available [32]. Notably, among anti-TNFs, the efficacy data of etanercept on enthesitis and dactylitis in adults with PsA are reported only in one RCT of 752 patients randomized to receive the drug at the dose of 50 mg once or twice weekly [33]. At week 24, 81% reduction of enthesitis sites and 84% of dactylitis score (on a 0 to 60 scale) were recorded. Similarly to etanercept, ADA studies were chiefly focused on the efficacy on joint and skin manifestations of PsA, while enthesitis and dactylitis response rates were rarely evaluated. To date, the efficacy of ADA in PsA was investigated in two RCTs, the ADEPT trial [14] and its long-term extension studies [15,16], and in 100 patients with inadequate response to previous DMARD treatment [34]. Furthermore, ADA efficacy in PsA was reported in five open studies [17,35-38], and in two RCTs of ixekizumab and tofacitinib [39,40].

Enthesitis and dactylitis outcomes were reported only in the 12 week, open-label ACCLAIM trial of ADA in 127 PsA patients [38], showing a significant reduction of the baseline percentage of patients with dactylitis (from 33.9% to 11%; p<0.001) and enthesitis (from 29.9% to 14.2%; for Achilles tendonitis; p=0.004, and from 24.4% to 11% for plantar fasciitis p= 0.008). However, in this study only patients with active dactylitis in ≥ 4 digits and only those with involvement of two enthesitis sites were assessed.

In 101 PsA patients treated with ADA who served as active comparator arm in a 24-week RCT of ixekizumab, a complete resolution of dactylitis was recorded in 78% of the patients, and a LEI=0 resulted in 33% at the end of follow-up [39]. Similarly, a significant reduction of baseline mean LEI and dactylitis scores (LEI: -1.6 ± 0.2; dactylitis: -6.1 ± 0.7) was recorded in ADA arm of 106 patients included in a 12-month RCT of tofacitinib [40]. The two RCTs were not designed as head to head studies, but an analysis of the efficacy on enthesitis and dactylitis in ADA arms show comparable results with the study drug arms.

Differently from all previously quoted studies, in present study the efficacy of ADA on enthesitis and dactylitis was evaluated as primary end-point. In our 10-year cohort of 273 patients with PsA treated with ADA, at the end of a mean follow-up of 45.11 ± 30.5 months, dactylitis and enthesitis resolution was respectively recorded in 75 (85.2%), and in 106 (83.3%) patients,

Table 2: Clinical response to ADA treatment in 88 PsA patients with dactylitis and 127 patients with enthesitis.

	Baseline	Month 6	Month 12	End of follow-up	P
Overall patients in treatment N (%)	273 (100)	259 (94.8)	223 (81.7)	197 (72.2)*	0.001
ADA first-line N (%)	199 (72.9)	191 (69.9)	165 (60.4)	153 (56)	0.002
ADA second-line N (%)	74 (27.1)	72 (26.3)	58 (21.2)	44 (16.1)	0.049
ADA monotherapy group N (%)	150 (54.9)	142 (94.7)	121 (80.7)	109 (72.7)	0.026
ADA combo therapy group N (%)	123 (45.1)	117 (95.1)	102 (82.9)	88 (71.5)	0.038
Total ADA withdrawal N (%)				76 (27.8)	
Patients with dactylitis N (%)	88 (32.2)	5 (1.83)	0		<0.001
Dactylitis in ADA withdrawal N (%)		3 (21.4)	3 (8.3)	4 (1.8)	
Overall non-responder dactylitis N (%)**				13 (14.8)	
Overall responder dactylitis N (%)				75 (85.2)	
First-line vs second-line ADA groups N (%)	66 (75)/22 (25)	4 (6.1)/ 1(4.5)	0/0	0/0	0.988
ADA monotherapy vs combo-therapy groups N(%)	50 (56.8)/ 38 (43.2)	2 (4)/ 3 (7.9)	0/0	0/0	0.954
Patients with enthesitis N (%)	127 (46.5)	16 (6.2)	2 (0.7)	2 (0.7)	<0.001
Enthesitis in ADA withdrawal N (%)		6 (46.1)	8 (22.2)	11 (8.7)	
Overall non-responder enthesitis N (%)				21 (16.5)	
Overall responder enthesitis N (%) ł				106 (83.3)	
LEI	2.9±1.2	1.25±0.9	0.06±0.7	0.20±0.3	<0.001
First-line vs second-line ADA groups N (%)	96 (48.2)/ 31 (41.8)	12 (12.5)/ 4 (12.9)	0 (0)/ 2 (6.4)	2 (2.1)/ 0 (0)	0.453
ADA monotherapy vs combo-therapy groups N (%)	75 (59.1)/ 52 (40.9)	8 (10.6)/ 8 (15.3)	2 (2.7)/ 0 (0)	1 (1.3)/ 1 (1.9)	0.897
Overall remission/LDA*				222 (81.3)	
Overall remission in ADA first-line and second-line N (%) *				169(84.5)/53(72.6)	0.04
Overall remission in ADA mono-/combo- therapy groups*				128(85.3)/94 (76.4)	0.08
Overall duration of remission/LDA; months; mean±SD				29.7±14.4	
Correlation with the risk of not achieving					
remission/LDA					
Dactylitis					
Unadjusted OR (95% CI)				2.13(1.67-4.23)	0.043
Adjusted OR (95% CI)				2.02 (1.56-4,11)	0.039
Enthesitis					
Unadjusted OR (95% CI)				1.98 (1.56-4.45)	0.045
Adjusted OR (95% CI)				1.88 (1.51-4.34)	0.031
Follow-up duration; months; mean±SD				45.11±30.5	

Symbols. *Including ADA interruption in 25 patients in stable remission. **Sum of dactylitis number in ADA withdrawal and the 3 episodes requiring CS local infiltrative therapy. † Sum of non-responder enthesitis in ADA withdrawal and 9 episodes requiring CS local infiltrative therapy.

with a significant reduction of LEI to 0.20 ± 0.3 (p<0.001). For both manifestations no significant differences of efficacy were observed among groups receiving ADA as first- or second-line therapy, and mono- or combo-therapy. These response rates are similar with those reported in other studies of the efficacy of anti-TNFs [41,42], though this comparison results problematic due to the use of different enthesitis and dactylitis scoring measures. Two recent RCTs of anti-IL12-23 ustekinumab [21], and anti-IL17 secukinumab [24,25] evaluated the efficacy on dactylitis and enthesitis as secondary end-points. In ustekinumab RCT dactylitis was assessed in 20 digits of hand and feet by using a severity scale 0 to 3, and enthesitis by PsA-modified MASES score [43]. At week 100, dactylitis was absent in 144 (68.2%) out of 200 patients, and enthesitis resolved in 177 (52.2%) of 296 patients [21]. The 2-year extension phase of secukinumab RCT demonstrated 84.2% resolution rate for dactylitis, and 80% for enthesitis. In this trial dactylitis was assessed as presence/absence in 20 digits, while enthesitis was evaluated as presence/absence in 4 sites (right and left lateral epicondyle humerus and right and left proximal Achilles). Hence, the results of our 10-year retrospective study are comparable with those of non-anti-TNF targeted biologics ustekinumab and secukinumab.

Overall, at the end of follow up, ADA retention rate was 63% and overall remission/LDA were recorded in 222 (81.3%), with a mean duration of remission/LDA of 29.7 ± 14.4 months. As expected, a significant higher rate of remission was observed in patients receiving ADA as first-line therapy (p: 0.04) while no differences resulted between mono- or combo-therapy. These results are similar to those reported in other studies from real world clinical practice [44]. Confirming other reports [45,46], in present cohort of PsA patients, the presence of dactylitis

and enthesitis represented a poor prognostic indicator with a significant lower probability to achieve the remission and LDA. Regarding the safety, ADA was generally well tolerated with no new safety alerts.

The retrospective design and data missing on psoriasis severity at baseline and during the follow-up may limit the relevance of the results of present study. Regarding the lack of data of cutaneous lesions, in our current clinical practice the dermatologist was consulted for the initial psoriasis diagnosis, and the follow-up evaluation of skin involvement was limited to the most severe cases.

CONCLUSION

In our large PsA cohort treated with ADA, dactylitis and enthesitis resolution was recorded in more than 80% of the cases. The response rates were comparable with those observed with other anti-TNF- and non-anti-TNF targeted biologics. Finally, patients with dactylitis and enthesitis were more likely not to achieve the remission and LDA.

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