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POS0077

SEX DIFFERENCES IN EFFECTIVENESS OF FIRST-LINE TUMOR NECROSIS FACTOR INHIBITORS IN PSORIATIC ARTHRITIS; RESULTS FROM THIRTEEN COUNTRIES IN THE EUROSPA RESEARCH COLLABORATION NETWORK

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Background: Evidence demonstrates sex differences in disease presentation, physical function, treatment response and drug retention in patients with psoriatic arthritis (PsA). Data from observational cohort studies indicate female sex is associated with reduced effectiveness of tumor necrosis factor inhibitors (TNFis)[1,2]. Although, conflicting results are also reported[3,4]. We sought to validate prior studies using data from a large multinational cohort based on real-life clinical practice.
Objectives: To investigate sex differences in treatment response and drug retention rates in clinical practice among patients with PsA, treated with their first TNFi.
Methods: Data from biologic-naïve PsA patients initiating a TNFi in the EuroSpA registries were pooled. In the primary analysis, propensity-score weighting was applied to assess the causal effect of sex on low disease activity (LDA) according to DAS28-CRP at 6 months. A generalized linear regression model was used to estimate the causal risk difference (RD) and relative risk (RR) of sex on LDA. Possible covariates influencing the outcome were determined a priori and selected based on availability in the database (<20% missing). The final covariates included were country, age, conventional synthetic disease-modifying antirheumatic drug use at baseline and TNFi start year. In the secondary analysis, drug retention was assessed over 24 months of follow-up by Kaplan-Meier curves and log-rank test.
Results: In total, 7,679 PsA patients with available data on DAS28-CRP at 6 months were assessed for treatment response. Baseline characteristics are shown in the Table 1. In the adjusted analysis, the probability for females to have LDA was 17% (RR, 0.83; 95% confidence interval [CI], 0.81 to 0.85) lower compared to males and the difference in probability for having LDA was 13 percentage points (RD, 0.13; 95% CI, 0.11 to 0.15). The survival analysis included 18,599 PsA patients with available data on retention rates. The TNFi 6/12/24-month retention rates were significantly lower in females (81%/68%/56%) compared to males (89%/80%/69%), see Figure 1.

Table 1. Baseline characteristics of all biologic-naïve PsA patients treated with their first TNFi and available DAS28-CRP at 6 month, data pooled across all countries

	Female	Male
	Mean (SD), median [IQR] or percentages	Mean (SD), median [IQR] or percentages
Age (years)	49.7 (12.5)	47.8 (11.9)
Disease duration (years)	4.0 [1.0, 10.0]	4.0 [1.0, 10.0]
TNFi start year		
1999-2009	29%	29%
2010-2013	26%	27%
2014-2016	25%	24%
2017-2020	20%	20%
Concomittant csDMARD	75%	77%
DAS28-CRP	4.4 (1.2)	4.2 (1.2)
DAPSA28	32 (16)	29 (16)
CRP (mg/L)	7.0 [3.0, 17.0]	8.0 [3.3, 19.0]
SJC (0-28)	3.0 [1.0, 6.0]	3.0 [1.0, 6.0]
TJC (0-28)	6.0 [2.0, 10.0]	4.0 [2.0, 9.0]
VAS pain, mm	61 (23)	55 (23)
VAS fatigue, mm	62 (26)	53 (27)

Data are as observed, mean (SD), median [IQR] or percentage. TNFi, tumor necrosis factor inhibitor; csDMARD, Conventional synthetic disease-modifying antirheumatic drugs; DAS28-CRP, Disease Activity Score 28-joint count C reactive protein; DAPSA28, Disease Activity in PsA 28; CRP, C-reactive protein; SJC, swollen joint count; TJC, tender joint count.

Conclusion: Treatment efficacy and retention rates are lower among female patients with PsA initiating their first TNFi. Females presented with higher 28-tender joint count and higher scores on patient reported outcomes at baseline, reflecting differences in disease expression. Recognizing these sex differences is of relevance for customized patient care and may improve patient education.

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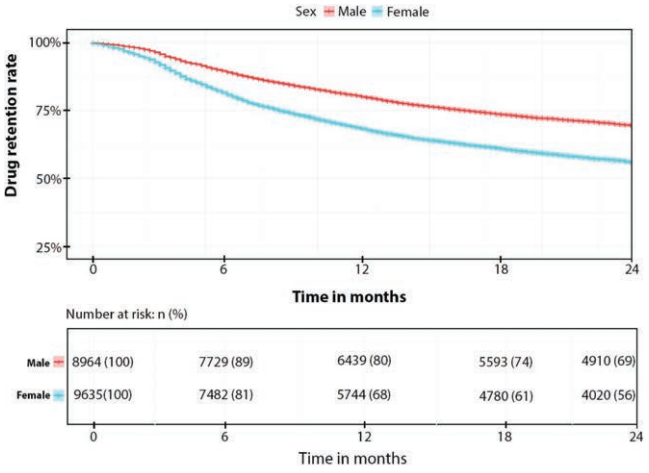

Figure. Sex differences in 24-month retention rates in first-line tumor necrosis factor inhibitors in patients with psoriatic arthritis in EuroSpA (Kaplan-Meier, log-rank test; p<0.001).

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POS0078 COMPARING METHOTREXATE MONOTHERAPY WITH METHOTREXATE PLUS LEFLUNOMIDE COMBINATION THERAPY IN PSORIATIC ARTHRITIS: A RANDOMISED, PLACEBO-CONTROLLED, DOUBLE-BLIND CLINICAL TRIAL (COMPLETE-PSA)

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Background: Conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) are the cornerstone first-line treatment in psoriatic arthritis (PsA), although there is a paucity of evidence for the effectiveness of csDMARDs and especially their combination. Assessing the efficacy and safety of combinations of csDMARDs compared with csDMARD monotherapy has been prioritized on the EULAR research agenda. We hypothesized that combining csDMARDs might be more effective than csDMARD monotherapy.

Objectives: We aimed to investigate whether a combination of methotrexate (MTX) and leflunomide (LEF) is superior to MTX monotherapy on improvement in disease activity in patients with PsA.

Methods: Patients with a clinical diagnosis of PsA and active disease (≥2 swollen joints) were included in this randomised, placebo-controlled, double-blind trial. Patients were randomised (1:1) to MTX plus LEF or MTX plus placebo. Patients received MTX 15 mg/week for four weeks and thereafter 25 mg/week, combined with two LEF 10 mg tablets or two placebo tablets daily. The primary outcome was the difference between the MTX plus LEF group and the MTX plus placebo group on the psoriatic arthritis disease activity score (PASDAS) at week 16 adjusted for baseline PASDAS. Key secondary outcomes included safety and the achievement of minimal disease activity (MDA) criteria and PASDAS low disease activity (LDA) (≤3.2).

Results: A total of 78 PsA patients (MTX + LEF n=39; MTX + placebo n=39) were included. The mean age was 53.1 (SD=12.8) years and 36% (n=28) of the patients were female. The mean PASDAS at baseline was 4.9 (SD=1) in both treatment groups. Table 1 shows that MTX plus LEF was superior to MTX plus placebo at week 16 (PASDAS 3.1, SD=1.4 vs 3.7, SD=1.3; treatment difference= -0.6, 90% CI -1.0 to -0.1, one-sided P-value=0.025). Similar and significant results were found for achievement of MDA criteria (59% vs 33%, one-sided P-value=0.013) and PASDAS LDA (59% vs 35%, one-sided P-value=0.019) (Figure 1 and Table 1). Other favorable and significant outcomes for the MTX plus LEF group included -among others- the improvement in swollen joint count (SJC) (median [IQR] = -3 [-5, -2] vs -2 [-4, 0], one-sided P-value=0.039) and the proportion of patients with active psoriasis (i.e. body surface area score >0) at week 16 (44% vs 68%, one-sided P-value=0.014). Generally mild adverse events and treatment discontinuation (MTX+LEF n/N=10/39; MTX + placebo n/N=3/39) occurred more frequently in the MTX plus LEF group.

Table 1. Primary and secondary outcomes at week 16

	MTX + LEF (N=39)	MTX + placebo (N=38)*	Absolute difference [90% CI]	P-value One-sided
Primary endpoint				
PASDAS at week 16	3.1 (1.4)	3.7 (1.3)	-0.6 [-1.0, -0.1]	**0.025**
Selected secondary endpoints				
Fulfilling PASDAS LDA, N (%)	23 (59)	13 (35)	24% [6, 42]	**0.019**
Fulfilling MDA criteria, N (%)	23 (59)	12 (33)	26% [7, 44]	**0.013**
SJC66, change from baseline, median (Q1, Q3)	-3 (-5, -2)	-2 (-4, 0)	..	**0.039**
TJC68, change from baseline, median (Q1, Q3)	-2 (-4, 0)	-2 (-5, 0)	..	0.457
VAS physician global, change from baseline, mean (SD)	-22.0 (21.9)	-12.2 (19.7)	-9.8 [-17.7, -1.9]	**0.021**
VAS patient global, change from baseline, mean (SD)	-20.9 (24.4)	-13.9 (28.3)	-7.0 [-17.0, 3.0]	0.124
Active psoriasis, N (%)	17 (44)	26 (68)	-25% [-43, -7]	**0.014**

* One patient in the MTX + LEF group was excluded from the efficacy analysis due to change of diagnosis.

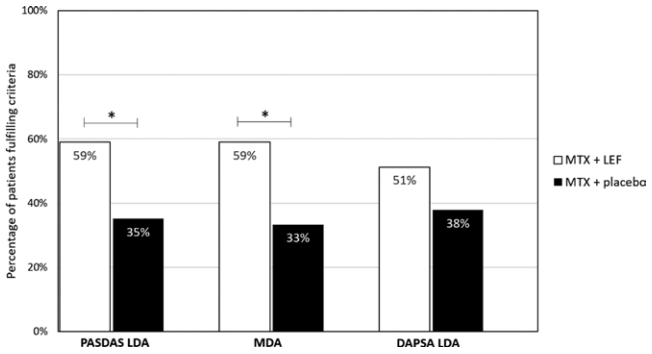

Figure 1. Proportion of patients meeting different PsA responder criteria for low disease activity at week 16* = one-sided P-value <0.05DAPSA = Disease Activity in Psoriatic Arthritis

Conclusion: MTX plus LEF combination therapy resulted in a significantly greater improvement in disease activity according to PASDAS and MDA than treatment with MTX monotherapy in patients with PsA after 16 weeks. In addition, a greater improvement in psoriasis was found for the combination group. However, there are indications that MTX plus LEF combination is less well tolerated than MTX monotherapy.

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POS0079 DOES METHOTREXATE IMPACT USTEKINUMAB IMMUNOGENICITY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS? A POST HOC ANALYSIS OF SAMPLES FROM A RANDOMIZED, PLACEBO-CONTROLLED TRIAL.

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Background: The formation of antidrug-antibodies (ADA) may reduce treatment efficacy or provoke discontinuation due to adverse reactions. Subsequent alterations in the drugs' pharmacodynamics, pharmacokinetics, safety, and efficacy are often unpredictable and can impede clinical discourse. Recent studies gave us some insights regarding the role of ADA formation against the monoclonal IL-12/-23 antibody ustekinumab (UST) and the impact of concomitant MTX treatment on immunogenicity in psoriatic arthritis (PsA) patients [1,2]. Valid measurement of ADA, particularly of neutralizing ADA (nADA) is essential to understand UST-associated immunogenicity and may help to predict clinical outcomes.

Objectives: To examine the impact of concomitant MTX on UST-immunogenicity in patients with active psoriatic arthritis (PsA).

Methods: Plasma samples were collected from a randomized controlled trial in patients with active PsA, treated with open UST and placebo-controlled methotrexate over a 52 weeks. We compared samples of 112 patients treated with