Objectives: To investigate the risk of cancer in TNFi treated PsA patients compared with standardized rates from the general population in Denmark, Finland, Iceland and Sweden.

Methods: TNFi-treated PsA patients were followed from first registration with TNFi-treatment in ARTIS (Sweden), DANBIO (Denmark), ICEBIO (Iceland) or ROB-FIN (Finland) and linked to the national Cancer Registry in each country. Patients with a cancer history prior to start of follow-up were excluded. We investigated the risk of primary cancer among TNFi-treated PsA patients compared with general population cancer rates standardized to age, sex and calendar period within each country. Standardized incidence ratios (SIRs) were estimated for each country and pooled SIRs were subsequently calculated for both any cancer and site-specific cancers of interest.

Results: A total of 5218, 2039, 270 and 526 patients were registered as ever TNFi-treated in ARTIS, DANBIO, ICEBIO and ROB-FIN, respectively, contributing a total of 44 041 patient years of follow-up across all 4 countries.

For all cancers, the SIRs of TNFi-treated patients from ARTIS, DANBIO, ICEBIO and ROB-FIN were 0.94 (0.80 to 1.10), 0.99 (0.77 to 1.26), 1.71 (0.88 to 2.99) and 1.28 (0.82 to 1.90), respectively. The number of observed and expected cancers and the SIRs of any and selected site-specific cancers are listed in **table 1**.

Table 1. Standardized incidence ratios (SIR) of TNFi-treated patients from 4 Nordic countries compared with the general population.

	Observed cancers	Expected cancers	SIR (95% confidence interval)
All cancers	282	281.6	1.00 (0.89 to 1.13)
Colorectal	32	26.5	1.21 (0.85 to 1.71)
Hodgkin's and non-Hodgkin's lymphoma	21	11.4	1.84 (1.20 to 2.82)
Lung	20	25.4	0.79 (0.51 to 1.22)
Malignant melanoma	20	18.6	1.07 (0.69 to 1.66)
Pancreas	8	6.6	1.21 (0.60 to 2.41)
Brain	7	7.4	0.95 (0.45 to 1.99)
Female breast	58	48.4	1.20 (0.93 to 1.55)
Corpus uteri	6	9.0	0.67 (0.30 to 1.49)
Prostate	34	48.8	0.70 (0.50 to 0.98)

Only included sites with >5 cancer outcomes.

Conclusion: Our results suggest that the overall cancer risk for TNFi-treated PsA patients is not increased compared to the general population. Further analysis of the risk of malignant lymphomas will inform on whether the increased risk we observed is attributed to the PsA disease or treatment with TNFi.

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OP0006

IMPROVEMENT OF ENDOTHELIAL DYSFUNCTION AND INFLAMMATION IN PSORIATIC ARTHRITIS: IMPROVE – PSA STUDY

Ashit Syngle^{1,2}, Nidhi Garg³, Pawan Krishan³, Innovators. ¹Healing Touch City Clinic, Cardio-rheuma, Chandigarh 160015, India; ²Fortis Hospital, Mohali, Sahibzada Ajit Singh Nagar, India; ³Punjabi University patiala, Department of Pharmaceutical Sciences and Drug Research, Patiala, India

Background: Cardiovascular (CV) disease is leading cause of death in Psoriatic Arthritis (PsA)¹. Chronic inflammation in PsA is associated with vascular

endothelial dysfunction and enhanced CV risk. However, the therapeutic options to treat this enhanced CV risk are limited.

Objectives: To investigate the impact of Olmesartan and Rosuvastatin on endothelial dysfunction and inflammation in PsA.

Methods: 54 PsA patients randomized to receive 24 weeks of treatment with Olmesartan (OLME) (10mg/day, n=18), Rosuvastatin (Rvs) (10mg/day, n=18), and placebo (PL) (n=18) as an adjunct to existing stable antirheumatic drugs. FMD assessed by AngioDefender. EPCs estimated by flow cytometry. Serum nitrite, TBARS, ICAM-1, VCAM-1 and lipids levels estimated at baseline and after treatment. Inflammatory measures included DAS28, DAPSA, ESR and CRP, pro-inflammatory cytokines. Quality of life and CV 10-year risk (SCORE high risk charts) were estimated using standard tools.

Results: Baseline levels of FMD and EPC population were impaired indicating endothelial dysfunction. Basal concentrations of inflammatory markers, pro-inflammatory cytokines and markers of endothelial dysfunction were elevated among three groups. After 24 weeks treatment, FMD improved significantly in rosuvastatin and olmesartan group as compared to placebo. {OLME vs. PL (p<0.01), Rvs vs. PL (p<0.01), Rvs vs. OLME (p=0.10)} (Fig.1A). EPCs and nitrite (Fig.1B) levels improved significantly in both rosuvastatin and olmesartan groups. Significant reduction found in ICAM-1 after rosuvastatin treatment (p<0.01) where as olmesartan significantly decreased VCAM-1 (p=0.04) and TBAR levels (p≤0.05). Both rosuvastatin and olmesartan resulted in significant reductions of DAS28, DAPSA, ESR, CRP, IL-6 (Fig.1C) and TNF-α (Fig.1D) as compared to placebo. There was a significant reduction in SCORE, HAQ-DI and SF-36 (PH) score after treatment with rosuvastatin and olmesartan.

Figure 1A Effect of treatment on FMD in PsA. (OLME vs. PL (p<0.01), Rvs vs. PL (p<0.01), Rvs vs. OLME (p=0.10)) after 24 weeks.

Figure 1B Effect of treatment on Nitrite in PsA. (OLME vs. PL (p<0.01), Rvs vs. PL (p<0.01), Rvs vs. OLME (p=0.04)) after 24 weeks.

Figure 1C Effect of treatment on IL-6 in PsA. (OLME vs. PL (p=0.02), Rvs vs. PL (p<0.01), Rvs vs. OLME (p=0.40)) after 24 weeks.

Figure 1D Effect of treatment on TNF-α in PsA. (OLME vs. PL (p=0.02), Rvs vs. PL (p<0.01), Rvs vs. OLME (p=0.37)) after 24 weeks.

Conclusion: Olmesartan and rosuvastatin improve endothelial dysfunction, inflammation, CV risk and quality of life in PsA patients. Olmesartan and Rosuvastatin lower the proinflammatory cytokines, especially TNF-α, that down regulates production of CRP, adhesion molecules and nitric oxide which in turn improves endothelial dysfunction. Both drugs also decrease nitrite concentration and improve the EPC population in PsA patients. The augmentation of EPCs by olmesartan and rosuvastatin represents a fascinating new approach for the management of PsA. However, Rosuvastatin in addition also favourably impacted ICAM-1 and lipid abnormalities. In contrast, olmesartan has beneficial effect on blood pressure. Thus, both rosuvastatin and olmesartan demonstrate immunomodulatory, vasculoprotective and cardioprotective potential in PsA mediated through anti-proinflammatory cytokine action.

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