Rates and risk factors of new-onset psoriasis under different biologic agents and conventional synthetic DMARD treatment

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Background & Objectives

Psoriatic skin disease is a burdensome dermatologic condition which was reported to occur as an adverse event during TNF inhibitor (TNFi) treatment of rheumatoid arthritis (RA). Single case reports revealed the occurrence of psoriasis also during treatment with non-TNFi, but the magnitude under those agents remains unclear. Our aim was to

- compare the incidence of psoriasis in RA under differing biologic (b) and conventional synthetic (cs)DMARD treatments and to
- investigate additional risk factors.

Patients & Methods

We used data of **13,321 patients** (with 57,422 patient years (py) of follow-up) enrolled with the start of a b/csDMARD in the German biologics register RABBIT, a prospective longitudinal cohort study. For this analysis, patients were required to have no psoriasis at baseline and at least one follow-up. All psoriatic events reported until 31st of October 2016 were selected and assigned to treatments administered within 3 months prior to the event. We calculated crude incidence rates (IR) per 1,000 py and hazard ratios using Cox regression analyses with inverse probability weights (IPW).

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Results

First events of psoriasis were reported 101 times. Only 5 of those were categorized as being serious. 19 (19%) were palmoplantar manifestations and 10 were reported as pustular type. In patients with incident psoriasis the median time between enrollment in the cohort and onset of psoriasis was 22 months (IQR: 11-47 months).

Table 1: Baseline characteristics of patients enrolled under different treatments.

	csDMARD	TNFi	RTX	ABA	TOC
N	4691	6433	885	403	909
Age in years	57.6 (12.3)	55.1 (12.7)	58.6 (11.9)	58.2 (13.2)	56.6 (13)
Female patients, n (%)	3567 (76)	4879 (75.8)	682 (77.1)	307 (76.2)	705 (77.6)
Rheumatoid factor positive, n (%)	2985 (63.8)	4766 (74.9)	733 (83.5)	290 (73.8)	637 (73)
Disease duration in years	7.4 (8.1)	10.5 (9.1)	13.7 (9.9)	11.9 (9.3)	10.8 (9.1)
CRP	14.6 (22.4)	20.5 (27.9)	17.6 (23.9)	18.7 (26.6)	17.4 (24.9)
DAS28-ESR	4.7 (1.3)	5.3 (1.3)	5.4 (1.3)	5.3 (1.3)	5.2 (1.3)
Erosions, n (%)	1962 (44.3)	4069 (66.1)	565 (73.1)	244 (64)	530 (61)
% of full physical function	68.9 (22)	62 (23.3)	56.2 (23.4)	59.1 (23.7)	62.8 (24)
Glucocorticoids in mg/d	3.8 (4.5)	5.8 (6.7)	5.8 (6.6)	5.2 (6.1)	4.8 (5.2)

Values are means (SD) unless otherwise specified. csDMARD: synthetic DMARD, TNFi: TNF inhibitor, RTX: rituximab, ABA: abatacept, TOC: tocilizumab.

Crude incidence rates

Compared to csDMARD treatment, crude IRs found under TNFi and abatacept were significantly higher. This was not the case in patients treated with rituximab or tocilizumab (table 2). No significant difference was found across TNFi. The individual IRs (95% confidence intervall) were: etanercept 2.3 (1.5;3.7), adalimumab 3.4 (2.4;4.7), infliximab 2.8 (1.1;5.8), certolizumab pegol 6.1 (2.9;11.2), and golimumab 4.3 (1.4;10.0).

Table 2: Frequency of psoriasis and crude incidence rates per 1,000 py with 95% confidence intervals under different DMARDs.

	csDMARD	TNFi	Abatacept	Rituximab	Tocilizumab
Number of events	9	74	9	9	3
Patient years	19,526	25,430	2,279	5,329	4,860
crude IR (95 % CI)	0.46 (0.2;0.9)	2.91 (2.3;3.7)*	3.95 (1.8;7.5)*	1.69 (0.8;3.2)	0.62 (0.1;1.8)

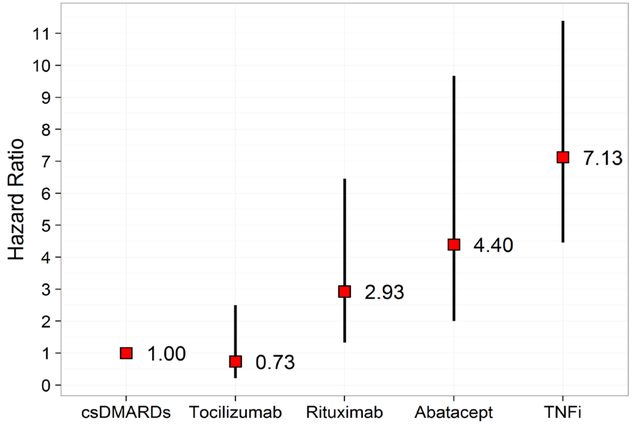
* significantly increased compared to csDMARD treatment

Adjusted Hazard Ratios (aHR)

Adjusted regression analysis (IPW) showed higher risk for incident psoriasis with TNFi, abatacept and rituximab (figure).

Additional significant risk factors were **female sex** (aHR 2.2 (1.3;3.6)), **current smoking** (aHR 2.1 (1.4;3.1)), **glucocorticoids** per 5 mg/d increase (aHR 1.1 (1.0;1.2)), and **skin infections** within the last 6 months (aHR 3.1 (1.0;9.0)).

Figure: Hazard Ratios for new onset psoriasis adjusted for sex, glucocorticoid dosage per 5 mg/d, smoking and prior skin infections.



Conclusions

This is the first analysis comparing the incidence of new onset psoriasis under biologics with different modes of action within one cohort. Our results confirmed a higher risk for TNFi and showed a similar result for abatacept. A lower but still significant increased risk was found for rituximab, whereas there was no difference for tocilizumab compared to csDMARDs. New onset psoriasis is a rare and most often non-serious event. The number needed to harm is 344 patients treated with TNFi for one year to observe one psoriatic event.

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