Abstract N°: 3171

Risk of herpes zoster in patients with rheumatoid arthritis under biological, targeted synthetic, and conventional synthetic DMARD treatment

Anja Strangfeld*[1], Imke Redeker[1], Jörn Kekow[2], Gerd Rüdiger Burmester[3], Juergen Braun[4], Angela Zink[1, 3]

[1]German Rheumatism Research Centre, Berlin, Germany, *[2]Scientific Advisory Board, Vogelsang-Gommern, Germany*, *[3]Charité University Medicine, Berlin, Germany*, *[4]Rheumatologist, Herne, Germany*

Background:

The risk of herpes zoster (HZ) is higher in patients with rheumatoid arthritis (RA) than in the general population. This risk is further increased with biologic disease-modifying anti-rheumatic drugs (bDMARDs) such as tumour necrosis factor inhibitors (TNFi) and targeted synthetic (ts)DMARDs such as Janus kinase inhibitors (JAKi) compared to patients taking conventional synthetic (cs)DMARDs such as methotrexate (MTX).

Objectives:

To compare incidence rates of HZ in RA patients under treatment with bDMARDs, tsDMARDs and csDMARDs with different modes of action and to find potential risk factors.

Methods:

Data of patients enrolled in the German biologics register RABBIT from 2007 onwards with the start of a bDMARD, tsDMARD or a change in csDMARD treatment were analysed. Patients were included when at least one follow-up documentation was available. All HZ events reported until 30 April 2019 were identified and assigned to treatments administered within the 3 month period prior to the HZ event. Crude incidence rates (IR) of HZ were calculated per 1,000 patient years (py). Cox regression was applied to investigate risk factors for the occurrence of HZ with and without inverse probability weights (IPW) to adjust for confounding by indication.

Results:

Data of 12,470 patients (53,218 py of observation) were included in the analysis. A total of 452 HZ cases in 433 patients were reported, of which 52 events were serious. The crude IRs per 1,000 py are illustrated by Figure. Adjusted for age, sex, and glucocorticoid use, a significantly increased risk was observed for treatment with monoclonal TNF antibodies (hazard ratio [HR], 1.55 [95% CI, 1.21-2.00]), B-cell targeted therapies (HR, 1.45 [95% CI, 1.07-1.97]), and tsDMARDs (HR, 3.55 [95% CI, 2.33-5.41]). Treatment with soluble TNF receptors, T-cell co-stimulation modulator, and IL-6 inhibitors were not significantly associated (Table). Adjustment with IPW amplified the effect and treatment with T-cell co-stimulation modulator and IL-6 inhibitors were also significantly associated with a higher risk compared to csDMARD treatment (Table).

Conclusion:

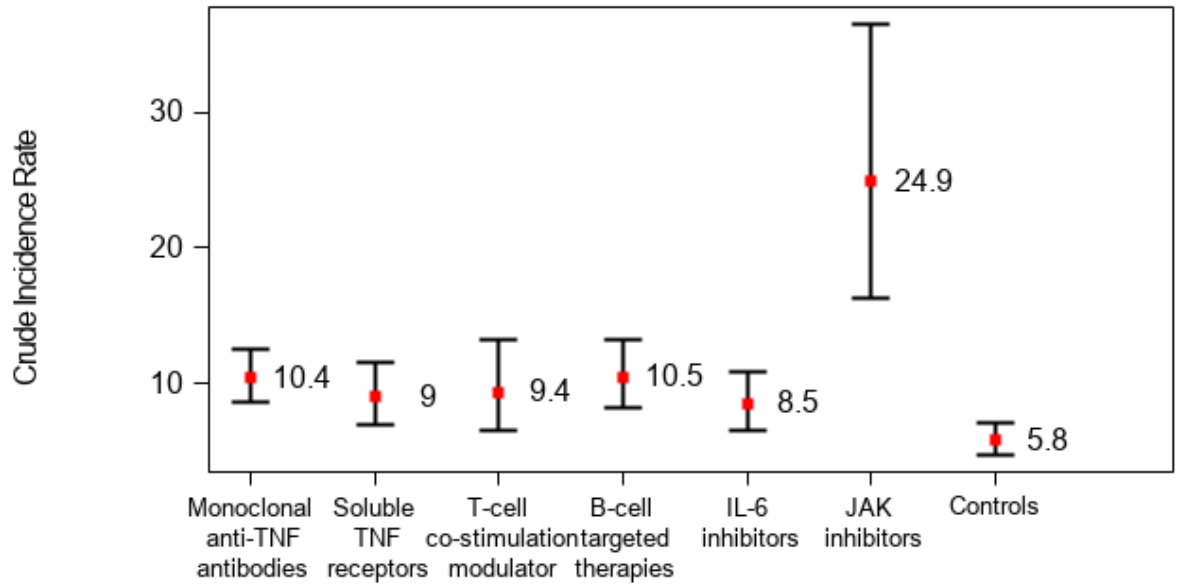
This is the first analysis in a European prospective cohort study comparing the incidence rates and risk of HZ in RA patients under treatment with six different modes of action within one cohort to csDMARD treatment. We found a significant association between HZ and treatment with JAKi. Our results also confirm a higher risk for monoclonal TNF antibodies and show a similar result for the T-cell co-stimulation modulator and B-cell targeted therapies. This study clearly supports systematic HZ vaccination of RA patients.

References:

Table Risk of herpes zoster: Results of adjusted regression analyses with and without inverse probability weights

	Multivariate Analysis without IPW		**Multivariate Analysis with IPW**	
	Adjusted HR (95% CI)	**P Value**	**Adjusted HR (95% CI)**	**P Value**
Female sex	1.42 (1.12-1.82)	**0.0042**	1.21 (0.96-1.53)	0.1095
Age per 10 years	1.23 (1.13-1.33)	**<.0001**	1.31 (1.2-1.43)	**<.0001**
Glucocorticoids, 5-10 vs 0 mg/d	1.16 (0.95-1.41)	0.1577	1.23 (1-1.52)	0.0501
Glucocorticoids, >10 vs 0 mg/d	1.58 (1.02-2.46)	**0.0417**	1.92 (1.27-2.92)	**0.0022**
csDMARD treatment	*Reference*		*Reference*	
Monoclonal TNFi antibodies	1.55 (1.20-2.00)	**0.0009**	1.63 (1.25-2.12)	**0.0003**
Soluble TNF receptors	1.32 (0.98-1.77)	0.0683	1.34 (0.98-1.83)	0.0631
T-cell co-stimulation modulator	1.41 (0.97-2.05)	0.0746	1.69 (1.17-2.45)	**0.0048**
B-cell targeted therapies	1.45 (1.07-1.97)	**0.0156**	1.66 (1.19-2.3)	**0.0026**
IL-6 inhibitors	1.31 (0.97-1.77)	0.0737	1.55 (1.15-2.09)	**0.0045**
JAK inhibitors	3.55 (2.33-5.41)	**<.0001**	5.01 (3.45-7.28)	**<.0001**

Figure Crude incidence rates of herpes zoster events per 1,000 patient-years



Patient-years	10818	7404	3506	6743	7375	1043	16178
No. events	113	67	33	71	63	26	94
of which serious	11	4	2	14	7	7	10

Acknowledgments: RABBIT is supported by a joint, unconditional grant from AbbVie, Amgen, BMS, Fresenius Kabi, Hexal, Lilly, MSD, Mylan, Pfizer, Roche, Samsung Bioepis, Sanofi-Aventis and UCB

Disclosure of interest: Anja Strangfeld Speakers bureau: AbbVie, BMS, Pfizer, Roche, Sanofi-Aventis, Imke Redeker: None declared, Jörn Kekow Speakers bureau: BMS, MSD, Pfizer, Roche, Gerd Rüdiger Burmester Consultant of: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Speakers bureau: AbbVie Inc, Eli Lilly, Gilead, Janssen, Merck, Roche, Pfizer, and UCB Pharma, Juergen Braun Grant/research support from: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Eli Lilly and Company, Medac, MSD (Schering Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi- Aventis, and UCB Pharma, Consultant of: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Eli Lilly and Company, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, and UCB Pharma, Speakers bureau: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Eli Lilly and Company, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, and UCB Pharma, Angela Zink Speakers bureau: AbbVie, Amgen, BMS, Gilead, Hexal, Janssen, Lilly, MSD, Pfizer, Roche, Sanofi Aventis, UCB