Initiation of a Janus kinase inhibitor before and after the safety warnings: Changes in characteristics of patients with rheumatoid arthritis

Doreen Huschek[1], Peter Herzer[2], Angela Zink[3], Martin Feuchtenberger[4], Anja Strangfeld[1,5]

[1]German Rheumatism Research Centre Berlin (DRFZ), Epidemiology and Health Services Research, Berlin; [2]Rheumatologist, Munich; [3]Scientific Advisory Board RABBIT, Berlin; [4]Rheumatologist, Innklinikum, Burghausen Altötting, [5]Department of Rheumatology and Clinical Immunology, Charité University Medicine Berlin, all Germany

German Rheumatism Research Centre Berlin, Epidemiology and Health Services Research

EULAR 2023 POS1085

Conclusion

The analyses show that after the launch of JAKi treatment in 2017, comorbidities increased the likelihood to receive JAKis as a new treatment option. In 2021, rheumatologists tend to prescribe JAKis to patients with a high disease burden and with many other previous therapies but not to those with comorbidities. This trend shows that German rheumatologists transferred safety recommendations from warnings immediately and strictly into their daily practice.

Background

In 2019, 2020 and 2021, the European and US-American regulatory agencies issued warnings about venous thromboembolism, major cardiovascular events and malignancy risks associated with the Janus kinase inhibitor (JAKi) tofacitinib and required changes in labelling.

Objectives

To investigate whether characteristics of patients with rheumatoid arthritis receiving a JAKi versus biologic therapy differed before and after the safety warnings.

Methods

RA patients observed in the German biologics register RABBIT between 01/2017 and 04/2022 when starting treatment with any JAKi or biologics. Logistic regression analyses were used to examine differences in patient characteristics at treatment start in three time periods: **2017** the year first JAKis became available in Germany, **2019** before the EMA safety warnings and **2021**. In each year, only the first treatment episodes of each JAKi, TNF inhibitor, interleukin-6 inhibitor or B/T-cell targeted therapy were considered.

Results

Table 1: Patient characteristics at treatment start of a JAKi compared to a bDMARD in 2017, 2019, 2021

	2017		2019		2021	
	JAKi	bDMARD	JAKi	bDMARD	JAKi	bDMARD
n	549	2404	707	2107	700	1250
Age higher than 65 years (%)	30.6	34.1	34.9	35.4	37.1	35.3
Females (%)	76.1	73.8	79.1	72.9	73.9	73.3
Relevant comorbidities*(%)	63.8	56.2	62.0	58.1	57.9	57.0
Hypertension (%)	54.4	44.7	49.5	47.6	47.9	45.7
Seropositivity (%)	75.2	78.3	74.5	77.8	76.6	75.7
Disease duration [years]	13.4	12.5	11.9	12.7	12.4	11.5
# previous b/tsDMARDs	2.6	1.6	1.8	1.8	3.5	2.7
Physician global health (0-10)	4.9	4.4	4.5	3.8	4.2	4.0
Patient global health (0-10)	5.4	5.1	5.4	4.8	5.0	5.0
% of full physical function	60.4	65.8	64.0	68.0	66.5	68.3
mg/d glucocorticoids	5.7	4.7	4.7	4.0	3.7	4.0

Values are numbers, percent or means.

**≥ 1 comorbidity (hypertension, coronary heart disease, diabetes, hyperlipoproteinaemia, thrombosis, malignancy, lymphoma)*

Results of the logistic regression (table 2) showed that characteristics or patients starting a JAKi have changed over time:

In 2017: compared to patients receiving a biologic, patients starting a JAKi had more prior therapies, had a worse physician reported health assessment and were more likely to have comorbidities such as hypertension, coronary heart disease, diabetes, hyperlipoprotein-aemia, thrombosis, malignancy or lymphoma.

In 2019: compared to patients starting a biologic, those initiating a JAKi therapy were less likely to be women, had a worse physician reported health and were more likely to receive low dose glucocorticoids than no glucocorticoids.

In 2021: after the safety warnings, compared to patients receiving a biologic, those who started a JAKi were older, had a worse physician reported health, had received a higher number of previous therapies, had poorer self-reported health and were less likely to receive a high dose of glucocorticoids. Although not significant, patients with comorbidities were less likely to receive a JAKi.

Table 2: Odds Ratios of the logistic regressions for treatment start of a JAKi compared to a bDMARD in 2017, 2019, 2021

	2017	2019	2021
Ref: age <50 years			
50-65 years	1.00 (0.77-1.31)	1.27 (0.99-1.64)	**1.50 (1.14-1.97)**
65+ years	0.81 (0.60-1.10)	1.15 (0.86-1.53)	**1.51 (1.11-2.05)**
sex (male versus female)	0.96 (0.76-1.20)	**0.74 (0.60-0.91)**	1.03 (0.83-1.26)
Relevant comorbidities*	**1.37 (1.10-1.70)**	1.16 (0.96-1.40)	0.86 (0.70-1.06)
Seropositivity	0.95 (0.76-1.19)	0.98 (0.13-1.20)	1.16 (0.93-1.45)
disease duration	0.99 (0.98-1.00)	0.99 (0.98-1.00)	1.00 (0.99-1.01)
# previous b/tsDMARDs	**1.37 (1.30-1.44)**	1.02 (0.98-1.07)	**1.18 (1.12-1.25)**
physician global health (0-10)	**1.16 (1.10-1.22)**	**1.09 (1.04-1.14)**	**1.08 (1.03-1.13)**
patient global health (0-10)	0.95 (0.89-1.01)	1.02 (0.97-1.08)	0.95 (0.90-1.00)
% of full physical function	1.00 (0.99-1.00)	1.00 (0.99-1.00)	1.00 (0.99-1.00)
Ref: 0 mg/d glucocorticoids			
>0 - < 10 mg/d glucocorticoids	0.89 (0.70-1.12)	**1.27 (1.05-1.54)**	1.01 (0.83-1.24)
>= 10 mg/d glucocorticoids	0.75 (0.54-1.03)	1.01 (0.75-1.37)	**0.70 (0.50-0.98)**

Funding

RABBIT is currently supported by a joint, unconditional grant from AbbVie, Amgen, BMS, Celltrion, Fresenius-Kabi, Galapagos, Hexal, Lilly, MSD, Pfizer, Samsung Bioepis, Sanofi-Aventis, VIATRIS SANTE and UCB, and previously by Roche.

doreen.huschek@drfz.de