New incident or recurrent malignancies in patients with rheumatoid arthritis and a history of malignancy in routine care

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INTRODUCTION

Rheumatoid arthritis (RA) is associated with an increased risk for malignancies differing between cancer types. Dealing with both a chronic inflammatory disease and cancer is challenging for patients and physicians. Based on available data, the risk of new malignancies is not increased in RA patients with a history of malignancy treated with biological (b) disease-modifying anti-rheumatic drugs (DMARDs) compared to conventional synthetic (cs) DMARDs. There is some evidence for tumour necrosis factor inhibitors (TNFi) to have a lower malignancy risk than csDMARDs. However, for some of the DMARD therapies, e.g. Interleukin-6 inhibition (IL6i) or Janus Kinase inhibition (JAKi) there is no data on cancer development after a previous cancer.

AIM

To estimate and compare the effects of JAKi, TNFi, abatacept (ABA), rituximab (RTX), IL6i and csDMARDs on the risk of new incident or recurrent malignancies in RA patients with prior malignancy in routine care.

PATIENTS AND METHODS

Data source: German RA registry RABBIT, a nationwide, multicentre, longitudinal cohort study, initiated in 2001 to investigate disease and therapy courses of RA patients in routine care.

Selection criteria: Data from patients with a history of malignancies (other than non-melanoma skin cancer, NMSC) enrolled in RABBIT 11/06 –12/21 with the start of a DMARD therapy were analysed.

Data analysis: Incidence rates (IR) of new incident or recurrent malignancies (without NMSC) per 1,000 patient-years (PY) with 95% confidence intervals (CI) were calculated. Relative risk was estimated as hazard ratios (HR) by Cox regression, adjusted by stabilized and winsorized inverse probability weights based on relevant covariates (see table 1). A 6-month latency period after treatment start and multiple imputation of missing data were applied. Events were assigned to therapies by the "once exposed, always at risk" rule.

RESULTS

Baseline characteristics:

- 118 JAKi, 278 TNFi, 87 ABA, 202 RTX, 104 IL6i and 413 csDMARD treatment episodes were documented from a total of 706 patients (see table).
- JAKi patients were older on average and more frequently smokers than others.
- Patients receiving ABA, RTX and IL6i on average had a longer disease duration and were more frequently seropositive than other patients.
- Patients under RTX on average had a higher disease activity and received more frequently glucocorticoids than others.
- Patients under TNFi were slightly more often male and had received considerably less prior DMARD therapies, particularly less TNFi and IL6i.

***Table**: Characteristics of patients with prior malignancies at treatment start*

	JAK N=118	TNFi N=278	ABA N=87	RTX N=202	IL6i N=104	csDMARDs N=413
Age, years	69.9 ± 16.9	66.1 ± 15.0	64.5 ± 16.7	65.1 ± 13.0	64.1 ± 15.0	66.1 ± 14.5
Male sex	26 (22.0)	90 (32.4)	22 (25.3)	56 (27.7)	29 (27.9)	110 (26.6)
Ever smoker	69 (58.5)	44 (51.8)	44 (50.6)	112 (55.4)	51 (49.0)	210 (50.8)
Any cancer-relevant comorbidity	62 (52.5)	152 (54.7)	37 (42.5)	108 (53.5)	47 (45.2)	209 (50.6)
Disease duration, years	9.1 ± 12.3	8.1 ± 11.0	11.1 ± 12.5	12.5 ± 15.0	11.6 ± 13.3	8.5 ± 12.0
Rheumatoid factor / ACPA positive	86 (74.8)	187 (71.9)	72 (85.7)	173 (89.6)	81 (86.2)	304 (77.2)
DAS28-ESR	4.3 ± 2.3	5.2 ± 2.0	4.5 ± 2.2	5.4 ± 2.1	5.0 ± 1.8	4.5 ± 1.9
No prior b/tsDMARDs	34 (28.8)	214 (77.0)	24 (27.6)	74 (36.6)	28 (26.9)	186 (45.0)
# prior TNFi/IL6i, mean ± SD	1.1 ± 1.1	0.2 ± 0.6	1.1 ± 1.0	0.8 ± 0.9	1.0 ± 0.9	0.6 ± 0.8
# prior other b/tsDMARDs, mean ± SD	0.4 ± 0.7	0.2 ± 0.5	0.4 ± 0.5	0.3 ± 0.5	0.5 ± 0.7	0.4 ± 0.6
Concomitant csDMARDs	39 (33.1)	170 (61.2)	62 (71.3)	138 (68.3)	41 (39.4)	NA
No glucocorticoids	50 (42.7)	116 (42.2)	37 (43.0)	64 (32.5)	38 (38.0)	186 (45.9)
Glucocorticoids ≤ 5 mg/d	45 (38.5)	92 (33.5)	28 (32.6)	52 (26.4)	36 (36.0)	130 (32.1)
Glucocorticoids > 5 and ≤ 10 mg/d	17 (14.5)	48 (17.5)	15 (17.4)	68 (34.5)	19 (19.0)	73 (18.0)
Glucocorticoids > 10 mg/d	5 (4.3)	19 (6.9)	6 (7.0)	13 (6.6)	7 (7.0)	16 (4.0)

Results are based on treatment episodes without missing values for each variable and given as median ± interquartile range for continuous variables and number (percentage) for categorical variables unless defined otherwise. Abbreviations: DAS28-ESR, Disease Activity Score based on erythrocyte sedimentation rate and 28 joints; NA, not available; SD, standard deviation.

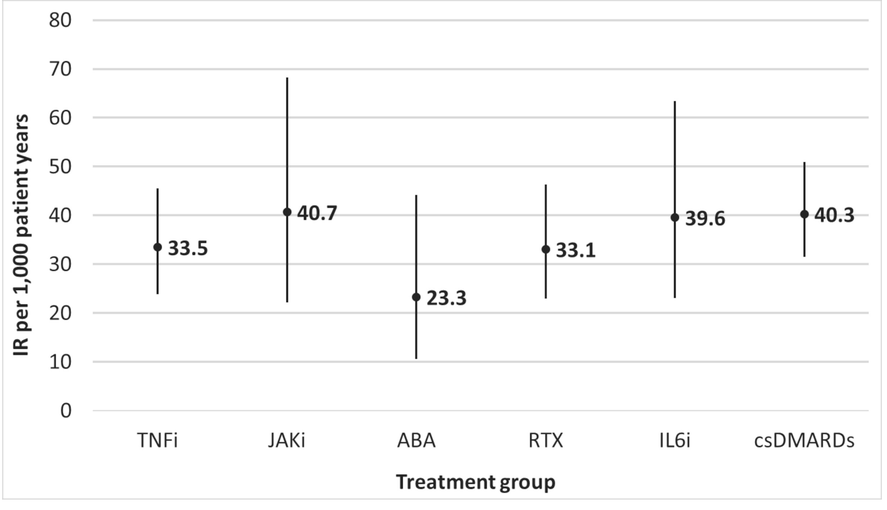
Incidence rates:

- 127 malignancies were reported, with 14, 40, 9, 34, 17 and 70 occurring under JAKi, TNFi, ABA, RTX, IL6i and csDMARDs, respectively.
- IRs ranged from 23 under ABA to about 40 under csDMARDs and JAKi (see figure).

Adjusted Cox regression analyses:

- The adjusted hazard ratios comparing the different treatment groups to TNFi regarding their associated risk of new incident or recurrent malignancy were 0.85 (95% CI: 0.38; 1.88) for JAKi, 0.49 (0.20; 1.21) for ABA, 1.12 (0.69; 1.81) for RTX, 1.07 (0.52; 2.18) for IL6i and 1.20 (0.77; 1.85) for csDMARDs.

***Figure**: Raw incidence rates for new incident or recurrent malignancies*



CONCLUSIONS

- **In this analysis, no statistical evidence was found of an increased risk of new incident or recurrent malignancies for any DMARD mode of action compared to TNFi in RA patients with a history of malignancies.**
- **The numbers of cancer events under some modes of action were limited and further analyses are needed.**

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