No increased risk of solid tumours in patients treated with biologics – a nested case-control study from the German biologics register RABBIT

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Conclusion

Based on a case-control design which is specifically appropriate in the case of rare events possibly biased by co-morbid conditions we found no difference in the incidence of solid malignancies in patients exposed or non-exposed to biologics.

Objective

To investigate the risk of developing solid tumours in patients with rheumatoid arthritis (RA) receiving biologics or conventional DMARDs.

Patients

- Data source: RABBIT (German biologics register)
- RA patients enrolled 05/2001 to 12/2006
- Excluded: Patients with prior malignancy

Methods

- Nested case-control study:
  For each patient who developed a solid tumour at follow-up (=case) one matched control patient was selected.
- Matching criteria:
  Sex, age, smoking status, selected chronic co-morbid conditions, follow-up time, and DAS28 at study entry.
- Patients who have ever been treated with anti-TNF agents or anakinra were classified as patients exposed to biologics.
- Analysis of time trends in hazard risk were conducted by means of Schönfeld residuals of Cox regression (based on the complete study population)

Results

From a total of 5,279 patients included in the register, data of 4,997 patients without prior malignancy and a follow-up time between 3 months and 6 years were available for the analysis (Tab.1).

Solid malignancies developed in 74 of these patients. Expected numbers, based on the rates found in the German population and observed frequency in the register differed for varying types of cancer (Fig. 1).

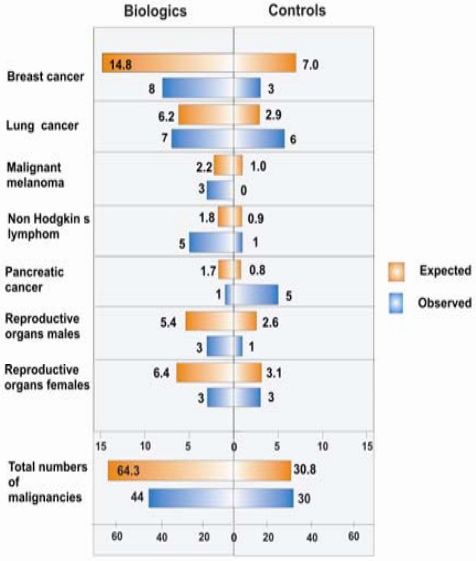

Figure 1. Expected and observed frequency of different malignancies.
In the total number of malignancies 7 non-melanoma skin cancer, 4 colorectal, 2 bladder, and 2 renal cancer, and 10 other neoplasms were included in addition.

	Biologics	Conventional DMARDs	p
N	3278	1719	
Females (%)	78.2	78.7	0.675
Age (mean ± SD)	53.6 (± 12.3)	55.9 (± 11.5)	<0.0001
Observation time (median (IQR))	2.4 (1.4 – 3.1)	2.5 (1.3 - 3.3)	0.081
RF+ (%)	80.2	71.3	<0.0001
DAS28 (mean ± SD)	5.8 (±1.3)	5.0 (±1.3)	<0.0001
Percent of full function (FFbH (mean ± SD))	57.0 (±23.0)	66.8 (±21.4)	<0.0001
CRP (median (IQR))	17.1 (7.9-38.0)	12.0 (5.0 – 26.7)	<0.0001
No. of co-morbidities (mean ± SD)	1.8 (± 2.0)	1.6 (± 1.7)	0.019

Table 1. Baseline characteristics of patients without prior malignancy

Matched pairs

	Cases (with incident malignancy)	Controls (without any malignancy)	p
N	74	74	
Females (%)	70.3	70.3	1.0
Age (mean ± SD)	61.3 (± 8.9)	60.9 (± 8.3)	0.45
Disease duration (median (IQR))	7 (3 – 13.5)	9 (5 – 17)	0.21
Observation time (median (IQR))	2.9 (1.8 – 4)	2.9 (1.8 – 3.9)	0.16
DAS28 (mean ± SD)	5.6 (± 1.0)	5.7 (± 0.99)	0.26
FFbH (mean ± SD)	57.1 (± 22.3)	63.3 (± 24.1)	0.087
Smoker (%)	25.7	25.7	1.0
Biologics before study entry (%)	14.9	13.5	1.0
Ever exposed to biologics (%)	59.5	62.2	0.72
only anti-TNF (%)	53	58	0.62
anakinra & anti-TNF (%)	4	5	1.0
only anakinra (%)	3	-	

Table 2. Baseline characteristics of cases and controls

Following co-morbid conditions were present in each of the matched pairs groups: COPD in 14.9%, other lung diseases in 2.7%, chronic kidney diseases in 5.4%, chronic gastro-intestinal diseases in 17.6% and psoriasis in 2.7% of the patients.

Incident cases did not differ from the matched controls regarding their exposition to anti-TNF agents, anakinra, or biologics in total (Tab. 2).

Is there a trend in the hazard ratio (HR) over time?

There was a non-significant increase in the hazard ratio of biologic treatment vs. conventional DMARD treatment over the time (Fig. 2). The lower risk for patients under biologic treatment at the beginning of the observation might be explained by thorough screening procedures before the start of biologic therapy.

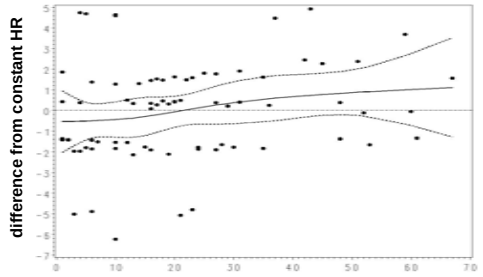

Figure 2. Time in months until occurrence of malignancy

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