

No increased risk of solid tumors in patients treated with biologics

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Conclusion

No differences in the incidence of solid malignancies in patients exposed or non-exposed to biologics were found. The same applied to the risk of recurrent malignancies.

However, patients with prior malignancies had a slightly lower probability of receiving biologics.

Objective

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

Patients

- RA patients of the German biologics register RABBIT.
- Enrollment from May 2001 to December 2006 with
 - a new prescription of etanercept, adalimumab, infliximab or anakinra (biologics group, n= 3,445) or
 - start of a new DMARD treatment or combination after failure of at least one DMARD (control group, n=1,836).

Risk of recurrences in patients with prior malignancies

In 122 of the included patients a prior malignancy was reported. Those patients did not differ from the other patients regarding the activity of the disease at baseline. Nonetheless they were older, had a significantly lower functional capacity, and had less often been treated with biologics before they were enrolled in the register (Tab. 1).

Time since onset of the prior malignancy did not influence the decision for a biologic treatment: median time until the start of a biologic treatment was 6 (IQR: 3 – 9.5) years, for the start of a conventional DMARD treatment 5 (IQR: 3 – 11) years.

	Patients with prior malignancy	Patients without prior malignancy	p
n	122	4998	
Mean age (SD)	63.7 (8.4)	54.4 (12.1)	<0,0001
Females (%)	70.5	78.4	0.047
DAS28 (mean SD)	5.6 (1.2)	5.5 (1.3)	0.282
FFbH (mean ± SD)	55.7 (22.5)	60.4 (22.9)	0.025
Smoker (%)	31.7	27.0	0.259
Ever treated with biologics (%)	7.6	14.0	0.048
Included in RABBIT with (%)			
Etanercept	22.9	24.4	0.835
Infliximab	4.9	11.7	0.019
Adalimumab	19.7	28.0	0.032
Anakinra	7.4	1.5	<0.0001
conv. DMARD	45.1	34.4	0.018

Table 1. Baseline characteristics of patients with or without prior malignancy

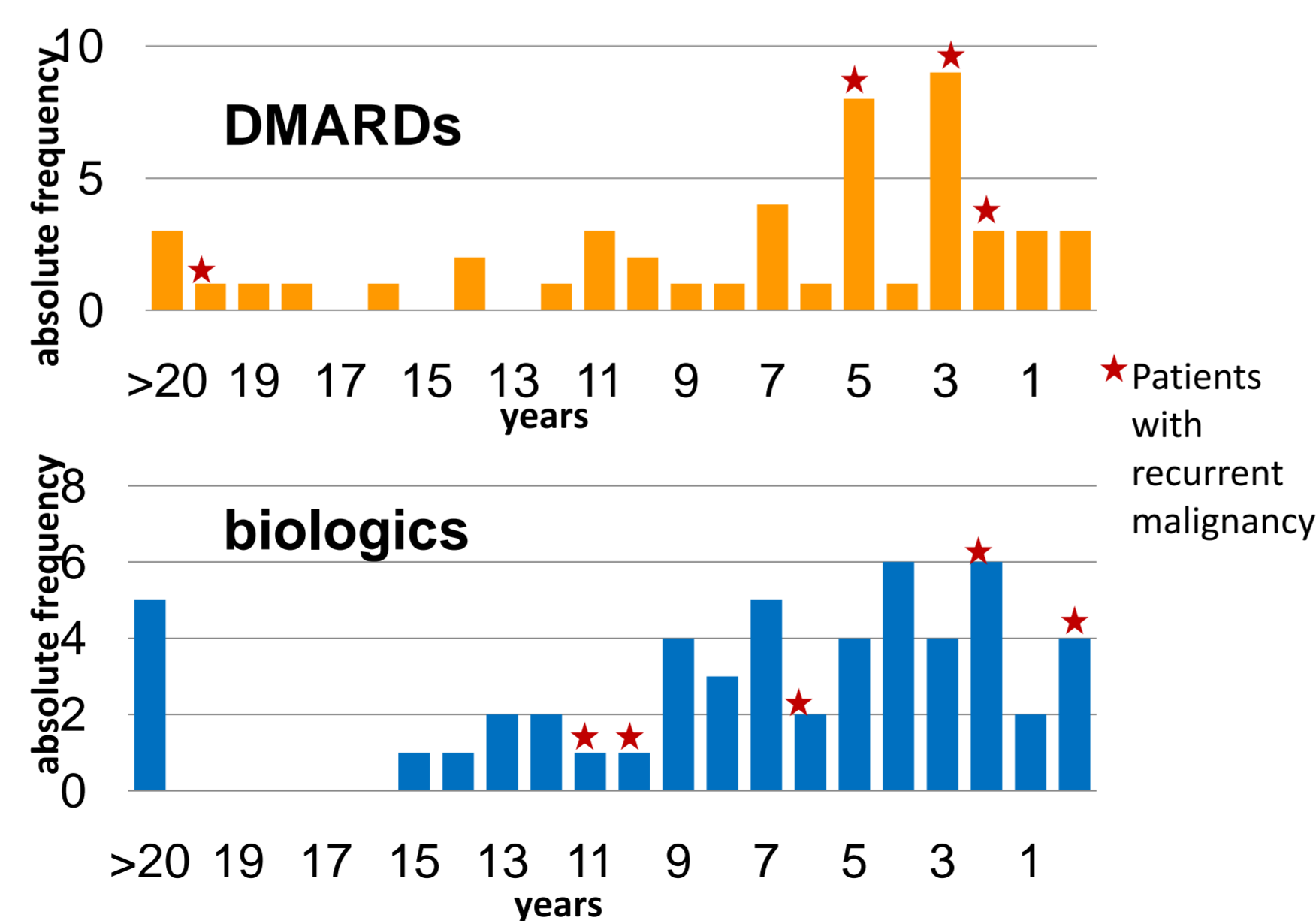


Figure 1. Duration from 1st malignancy to study entry

Ten recurrent malignancies were observed in 9 patients (5 female) after a median of 8 years (IQR: 5 -12). Recurrent malignancies were breast cancer (3), bladder cancer (2) and liposarcoma, signet-ring carcinoma, lung cancer, prostate cancer and metastatic manifestations of an unknown primary cancer (20 years after treatment of a metastatic testicular cancer).

Risk for incident malignancies in patients without prior malignancy – a nested case-control study

Solid malignancies occurred in 74 patients corresponding to an incidence rate of 5.8/1000 patient years.

Patients who developed a malignancy were on average 7 years older than the remaining patients.

The spectrum of malignancies (adjusted for age and sex) was comparable with that found in the German population (Fig.2).

A higher incidence was found for lymphomas. The standardized incidence rate (SIR) for lymphomas in patients treated with biologics was 2.8 (p>0.05).

The SIR of the total number of malignancies was lower in patients treated with biologics 44/64.3=0.68.

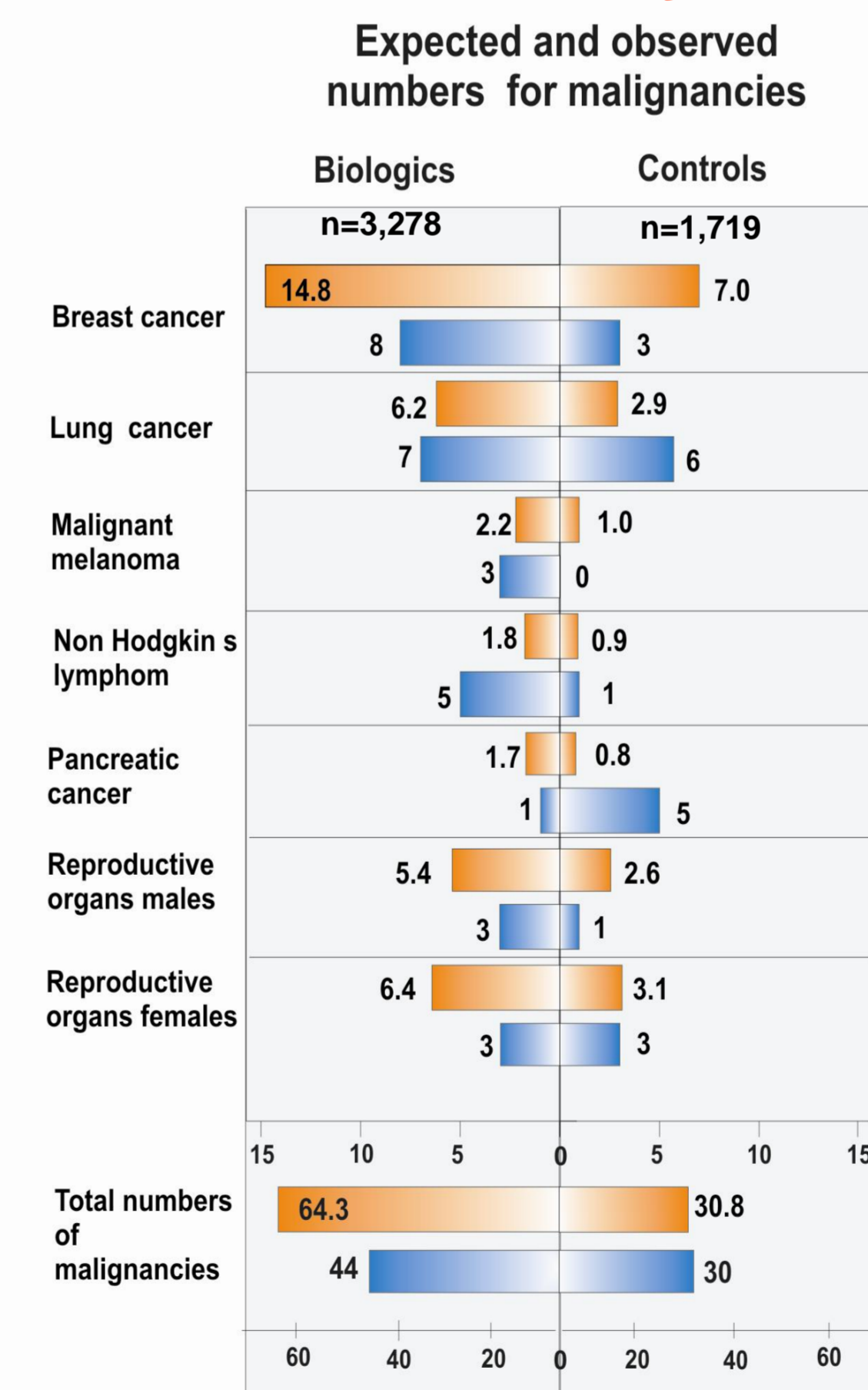


Figure 2. Expected (German population) and observed frequency of malignancies standardized by age and sex.

For each patient who developed a solid tumor at follow-up (=case) one matched control patient was selected. Matching criteria were sex, age, smoking status, selected chronic comorbid conditions, follow-up time, and DAS28 at study entry. The following co-morbid conditions were present in each of the matched 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.

	Cases (with incident malignancy)	Controls (without any malignancy)	p
n	74	74	
Mean age (SD)	61.3 (8.9)	61.4 (8.5)	0.97
Female (%)	70.3	70.3	na
Disease duration (Median(IQR))	7 (3 – 14)	9 (5 – 16)	0.22
Follow-up (years) (Median (IQR))	2.9 (1.8 – 4)	2.9 (1.6 – 3.9)	0.25
DAS28 at baseline (Mean (SD))	5.6 (1.0)	5.7 (1.0)	0.26
FFbH at baseline (Mean (SD))	57.1 (22.3)	63.2 (22.6)	0.09
Smoker (%)	25.7	25.7	na
Biologics before RABBIT (%)	14.9	13.5	1.0
Ever exposed to biologics (%)	59.5	60.8	1.0

Table 2. Characteristics of cases and controls

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