Risk of Cancer Recurrence or new tumors in RA Patients with Prior Malignancies treated with various Biologic Agents

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Background: If patients with rheumatoid arthritis (RA) have a history of malignancy, the choice of treatment is an important clinical question. The aim is to control disease activity with a minimum of risk for recurrence. During the past years we have observed in our register that rheumatologists tend to prefer rituximab over other biologic agents for the treatment of patients with prior malignancies. Our aim was to analyse the risk for recurrence or new tumors under different treatment regimens.

Methods:
We used data from the German biologics register RABBIT which observes patients with RA from start of treatment with any approved biologic agent or with a nonbiologic (nb) DMARD. Only patients with a history of malignancy were included in our analysis. All data until 30st of October 2012 were used. Because of a possibly different risk for recurrences patients with prior lymphoma and skin cancer were looked at separately from patients with other malignancies.

Results: At time of the analysis 10,168 patients comprising 36,595 patient years of observation (PY) were included in the register. 367 patients (3.6%) had a history of cancer at time of enrollment. A remarkably high proportion of patients with prior malignancies (28%) were treated with rituximab. The mean time of observation in the register was 3 years for patients with prior lymphomas and 2.6 years for those with prior solid malignancies. The rates for recurrences or new incident tumors are shown in the table.

	Start of treatment with			
	nonbiologic DMARDs	Rituximab	antiTNF agents*	Other biologics§
Total number of patients	3399	770	5231	768
PY observed	12,190	2236	20,446	1722
Patients with **prior lymphomas**, n (%)	10 (0.3)	24 (3.1)	6 (0.1)	2 (0.3)
Median years between lymphoma and start of treatment	7.6	4.0	1.3	3.6
Recurrence rate / 100 PY# (n events)	0	**3.4** (2)	**4.5** (1)	0
CI		0.4-12.3	0.1-25.3	
Patients with **prior solid malignancies**, n (%)	112 (3.3)	77 (10)	109 (2.1)	32 (4.2)
Median years between malignancy and start of treatment	5.9	3.3	6.8	5.2
Recurrence rate / 100 PY# (n events)	**3.6** (13)	**3.9** (7)	**5.7** (21)	**4.0** (3)
CI	1.9-6.1	1.6-8.0	3.5-8.8	0.8-11.7
Patients with **prior skin cancer**				

Prior melanoma, n	6	4	7	1
Prior basal cell carcinoma, n	3	1	7	5
Prior squamous cell carcinoma, n	-	3	1	2
Total of patients with prior skin cancer	**9**	**8**	**15**	**10**
Recurrences, n events	0	0	3	1

*antiTNF agents: adalimumab, etanercept, infliximab, certolizumab pegol, golimumab

§ other biologics: abatacept, anakinra, tocilizumab

[#] PY= patient years between enrollment (start of treatment) and new or recurrent malignancy or end of observation, whichever came first

Conclusion: Our data suggest that patients with a history of lymphomas, solid malignancies or skin cancer do not have higher recurrence rates when treated with rituximab in comparison to treatment with nbDMARDs. This finding is strengthened by the fact that the median time between prior solid malignancy and start of treatment was remarkably shorter in patients receiving rituximab than in all other treatments.

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