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Supplementary material

Table 1. Key findings on overall and solid organ cancer risk in biologic-exposed patients with RA

Study	Register(s)	Number of patients (n) biologic exposed/non-exposed (and/or other comparator group)	Main findings
Mercer et al., 2015[1]	BSRBR-RA	11767/3249	Adding TNFi to sDMARD does not alter the risk of cancer in RA patients. No difference in the relative risk of cancer for any of the individual TNFi drugs.
Dreyer et al., 2013[2]	DANBIO	3347/3812	No overall excess of cancer in TNFi exposed, although observed excess of colon and ovarian cancer. When comparing TNFi exposed RA patients with the general population, there was a significantly increased risk for all cancers.
Raaschou et al.,2013[3]	ARTIS, Swedish outpatient register, Swedish cancer register linkage	10878/42198 (non-biologic cohort); 162743(general population)	No increased overall risk of cancer in TNFi-exposed RA patients
Strangfeld et al., 2010[4]	RABBIT	3346/1774	No significant difference in risk of those exposed to TNFi or anakinra vs those non-exposed; no significant difference in the risk of recurrent malignancies between the two groups.
Pallavicini et al., 2010[5]	LORHEN	1114/general population of 2 large towns in North Italy	Overall cancer risk in RA exposed to TNFi similar to that in general population in the same geographical area. Male gender, age >65 years, steroid dose of >5mg/day were associated with a significantly higher risk of malignancies, whereas combination biological agent and methotrexate therapy seemed to have a protective effect.
Dixon et al., 2010[6]	BSRBR-RA	177/117*	No increased rate of incident malignancy in patients with RA and prior malignancy selected to receive TNF therapy after an average of 3 years follow-up.
Askling et al., 2009[7]	ARTIS, Swedish RA registers, Swedish Cancer Register	6366/61160 (national biologics-naïve RA cohort); 5989(RA cohort newly starting methotrexate); 1838 (RA cohort newly starting DMARD combination therapy; general population of Sweden	No increased cancer risk during the first 6 years after TNFi start in routine care & no increase with follow-up time or cumulative active TNFi treatment duration.
Du Pan et al., 2009[8]	SCQM-RA	2364/NA	In total, 15 cases of malignancies led to TNFi treatment-discontinuation (most common: breast cancer, lymphomas and urogenital). No significant differences detected between the TNFi agents used. (no non-biologic comparator group in the study)

**All patients had prior malignancy. Studies listed in chronological order*

Table **2.** Key findings on haematological cancer* risk in biologic-exposed patients with RA

Authors	Register(s)	Number of patients (n) biologic exposed/non-exposed	Main findings
Mercer et al., 2016[9]	BSRBR-RA	11931/3367	No difference in risk of lymphoma between the TNFi versus the biologic-naive group and no risk differences observed for individual TNFi.
Dreyer et al., 2013[2]	DANBIO	3347/3812	Although increased risk of lymphoma relative to the general population, no increased risk among TNFi-exposed patients.
Pallavicini et al., 2010[5]	LORHEN	1114/ general population of 2 large towns in North Italy	Haematological cancer risk significantly greater in TNFi-exposed.
Mariette et al., 2010[10]	RATIO	Case-control study; 38 validated cases of lymphoma	Some lymphomas associated with immunosuppression may occur in patients receiving TNFi drugs. Exposure to adalimumab or infliximab versus etanercept was an independent risk factor for lymphoma.
Askling et al., 2009[7]	ARTIS, Swedish RA registers, Swedish Cancer Register, pre-existing RA cohorts & cross-linkage with other national health and census registers	6604/471024(general population comparator)	Statistically significant increased risk of lymphoma in RA patients treated with TNFi compared to the general population. Slight and non-significant increased risk in TNFi-treated RA patients compared to non-TNFi-treated RA patients. Stratified analyses suggested that these increases were accounted for by those patients who were first to receive TNFi therapy with no increase observed in RA patients starting TNFi in 2002 or later. No increase in lymphoma risk shortly after TNFi start, nor any increase in lymphoma risk with increasing time since treatment start, accumulated time on active TNFi therapy, or by any particular TNFi.
Geborek et al., 2005[11]	SSATG	757/800	Possible additional risk of lymphoma associated with TNFi use
Askling et al., 2005[12]	ARTIS, Swedish Cancer Register and RA cohorts one prevalent & one incident cohort)	4160/53067 (prevalent RA cohort), 3703 (incident RA cohort), Swedish cancer register linkage	Patients with RA have an equally raised risk for lymphoma and leukaemias, but TNFi-exposed RA patients did not have higher lymphoma risks than other RA patients.

**Predominantly lymphoma.*

Table 3. Key findings on skin cancer risk in biologic-exposed patients with RA.

Study	Register(s)	Number of patients (n) biologic exposed/non-exposed	Main findings
Raaschou et al., 2013[3]	ARTIS, Swedish outpatient register, Swedish cancer register linkage	10878/42198(RA patients on non-biologics), 162743 (general population)	TNFi-exposure in RA patients has been associated with a 50% increased relative risk of invasive melanoma, but no increased risk of in situ melanomas.
Dreyer et al., 2013[2]	DANBIO	3347/3812	Although increased risk of non-melanoma skin cancer relative to the general population, no increased risk among TNFi-exposed patients.
Mercer et al., 2012[13]	BSRBR-RA	11881/3629	Risk of skin cancer increased in both TNFi-exposed and non-biological DMARD exposed RA patients compared with the general population. No evidence was found that TNFi-exposure exacerbates the risk of BCC or SCC.
Dixon et al., 2010[6]	BSRBR-RA	177/117*	Three patients with prior melanoma and TNFi-exposure developed an incident malignancy compared to none in the non-biologic DMARD cohort.

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