Infliximab is Associated with an Increased Risk of Serious Infection in Patients with Psoriasis

Results from the British Association of Dermatologists Biologic Interventions Register (BADBIR)

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SUMMARY

Infliximab is associated with a higher risk of serious infection when compared to non-biologic systemic therapies in patients with psoriasis.

Patients with severe psoriasis who fulfill the criteria for the prescription of infliximab should be counselled for the associated risk of serious infection.

BACKGROUND

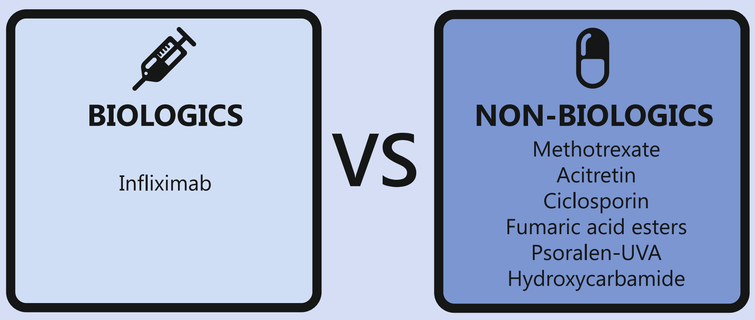
1. Adverse events (AE) can lead to discontinuation of biologics for the treatment of psoriasis[1]. Of these AEs, infection is the most common.
2. Randomised clinical trials are not powered to investigate AEs and have low external validity[2-3].
3. Risk of serious infection in patients with psoriasis on biologics is currently not well-understood.
4. Infliximab is prescribed to a select group of patients in the UK (PASI ≥ 20; DLQI > 18).

AIM

To determine whether infliximab is associated with a higher risk of serious infection as compared to non-biologic systemic therapies for psoriasis

METHODS

British Association of Dermatologists Biologic Interventions Register (BADBIR) - prospective safety registry of patients with psoriasis established in 2007 in the UK and the Republic of Ireland[4].



Compares a cohort on biologic therapies with a cohort on non-biologic systemic therapies with the same disease severity entry criteria: **Psoriasis Area and Severity Index (PASI)≥10 and Dermatology Life Quality Index (DLQI)>10**

Data collected 6 monthly for first 3 years, annually thereafter

Inclusion criteria

- Data lock October 2016
- Biologic-naive
- Chronic plaque psoriasis
- Follow-up data available

Serious infection defined by association with:

- Hospitalisation and/or;
- Intra-venous anti-microbial therapy and/or;
- Death

***A priori* chosen co-variates**

Demographics: age, gender, body mass index, waist circumference
Lifestyle factors and comorbidities: alcohol intake, smoking status, diabetes, chronic obstructive pulmonary disease (COPD), asthma, number of co-morbidities
Disease severity and treatment: PASI, presence of inflammatory arthritis, concomitant immuno-suppressants for psoriasis (e.g. methotrexate) adjusted for as a time-varying covariate

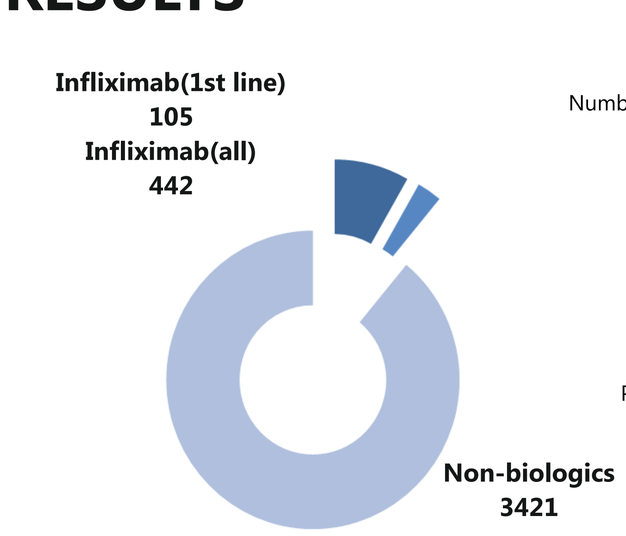
Crude incidence rates calculated for infliximab (1st line / all lines of therapy); non-biologic systemic cohort.

Potential confounding from co-variates controlled for using inverse probability treatment weighting (IPTW) by propensity score generated from a multi-nomial logistic regression model.

Balance between cohorts after weighting assessed using expected bias from a logistic regression model estimating effects of the co-variates on the outcome.

Cox proportional hazards model for hazard ratio (HR) to 1st serious infection; missing data treated with multiple imputation (20 cycles)

RESULTS



Median (IQR) follow-up duration
Non-biologic 1.5 (1.8) years; Infliximab (all) 1.5 (2.5) years
Infliximab (1st line) 1.8 (2.7) years

Figure 1: Number of patients and median follow-up in each cohort

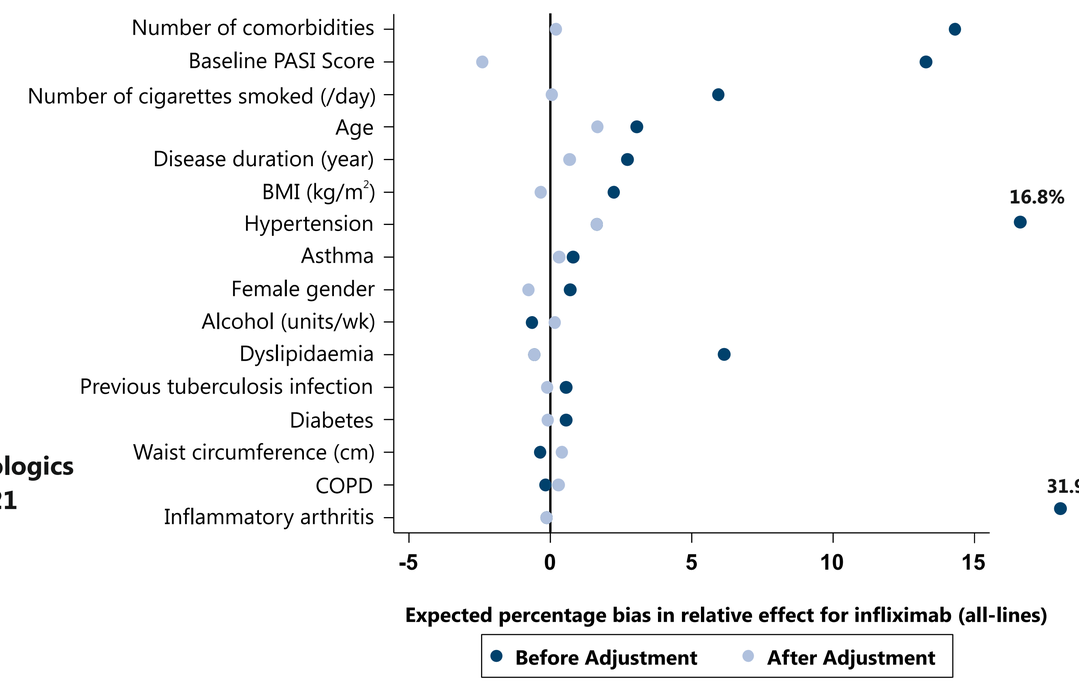


Figure 2: Forest plot showing the reduction in expected percentage bias for the individual co-variates after IPTW propensity score weighting

Treatment	Total Person-time	Infections (n=105)	Rate (/1000 person-years); 95% confidence interval (CI)
Non-biologics	6419.2	91	14.2 (11.5,17.4)
Infliximab (1st line)	238.9	14	58.6 (34.7,99.0)
Infliximab (all)	935.2	45	47.8 (35.7,64.0)

Table 1: Total person-time, number of infections, and crude incidence rate in each cohort

Treatment	Crude HR (95% CI)	Adjusted HR (95% CI)
Infliximab (1st line)	4.19 (2.42, 7.26)	1.37 (0.50, 3.74)
Infliximab (all)	3.41 (2.38, 4.90)	1.95 (1.01, 3.75)

Table 2: Crude and adjusted effect estimates for infliximab (1st and all-lines) against non-biologic therapies from the Cox regression models

DISCUSSION

1. Crude incidence rates of serious infections for infliximab are higher than reported figures.
2. Adjusted results similar to PSOLAR[5] (US based psoriasis registry) [HR 2.51 mixed prevalent/incident population; HR 1.78 incident population] when compared to acitretin/phototherapy; and BIOBADADERM[6] (Spanish psoriasis registry)[HR 2.52] when compared to methotrexate

Strengths and weaknesses of the study

✓ Real-world data
✓ Detailed data capture
✓ Involvement of 153 UK and ROI centres
✓ Fully industry independent data analysis

✘ Non-randomisation
✘ Residual confounding
✘ Small infliximab cohort
✘ Limited generalisability to non-UK populations

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1 Warren RB *et al.* (2015) *J Invest Dermatol* 135:2632-40. **2** Garcia-Doval *et al.* (2012) *Arch Dermatol* 148:463-70. **3** Yiu ZZ *et al.* (2016) *J Invest Dermatol* 136: 1584-91.
4 Burden AD *et al.* (2012) *Br J Dermatol* 166:545-54 **5** Kalb RE *et al.* (2015) *JAMA Dermatol* 151:961-9 **6** Davila-Seijo P *et al.* (2017) *J Invest Dermatol* 137:313-321

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