O32 SERIOUS INFECTION WITH TOCILIZUMAB COMPARED TO TNF-INHIBITORS AND OTHER BDMARDS IN RHEUMATOID ARTHRITIS PATIENTS: DOES LINE OF THERAPY MATTER?

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Background/Aims
In the real-world, tocilizumb is prescribed to a population of patients different from those prescribed TNF-inhibitors, often older with longer disease duration, worse functional status and more previous b- or tsDMARDS. The aim of this study was to evaluate if and how the risk of serious infection on tocilizumab and other bDMARDs differs when stratifying by line of therapy in a real-world population of rheumatoid arthritis patients.

Methods
We included patients registered in the BSRBR-RA treated with tocilizumab, etanercept, adalimumab, infliximab, certolizumab, abatacept or rituximab, including biosimilars. Primary outcome was the occurrence of a serious infection (defined as infection requiring hospitalisation, intravenous antibiotics or resulting in death). Primary covariate of interest was line of therapy (from first to fifth line of therapy). Every change to another b- or tsDMARD was considered a new line of therapy, but not a change between a bio-original and a biosimilar. Hazard ratios (HR) of serious infections were estimated using an inverse probability weighted Cox regression, based on a propensity score including baseline patient and disease characteristics, and adjusting for time in study (see table). The reference group was etanercept, which included the highest number of patients. Treatment exposure was analysed without and with stratification by line of therapy.

Results
A total of 33,916 treatment courses were included (Table) contributing to 62,532 years of follow-up. Compared to etanercept, participants starting abatacept, tocilizumab and rituximab were older, had more previous bDMARDs, longer disease duration and more comorbidities. The crude HR of serious infections were higher with infliximab and adalimumab, lower with certolizumab and rituximab, and not significantly different for abatacept and tocilizumab compared to etanercept. After adjustment, HR of serious infections were higher with tocilizumab, adalimumab and infliximab. However, when stratified by line of therapy, HR were no longer significantly different compared
to etanercept for tocilizumab, adalimumab and infliximab for most lines of therapy.

Conclusion
Whilst initially there appears to be a difference in rates of serious infections between biologic therapies, line of therapy may be a confounding factor when comparing the risk of serious infections between bDMARDs.

Disclosure
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Table 1:

|            | N  | ETN | TCZ | ADA | IFX | CERT | RTX | ABA |
|------------|----|-----|-----|-----|-----|------|-----|-----|
| N          | 33,916 | 10,655 | 2,632 | 7,839 | 4,430 | 1,816 | 5,556 | 1,188 |
| Patient-years | 19,129 | 4,312 | 4,342 | 14,504 | 8,135 | 2,726 | 12,009 | 1,686 |
| Incidences per 100 patient-years (95% CI) | 4.2 (3.9-4.5) | 4.4 (3.8-5.1) | 4.6 (4.1-5.1) | 5.9 (5.4-6.5) | 2.7 (2.2-3.4) | 3.6 (3.3-4.1) | 4.0 (3.2-5.1) |
| Unadjusted HR (95% CI) | Ref. | 1.0 (0.9-1.2) | 1.1 (1.0-1.2) | 1.4 (1.2-1.5) | 0.5 (0.6-0.8) | 0.9 (0.8-1.0) | 0.9 (0.7-1.2) |

Adjusted on inverse probability weighting (with age, gender, concomitant steroids, concomitant DMARDs, comorbidities, seropositivity, smoking, disease duration, HAQ and DAS28 at baseline in the model) and time since study entry (categorised from 0 to 4, 0 starting just before or at the moment of entering study, 1 starting during the first year, 2 starting during the second year until 4 for the fourth year and more). ABA, abatacept; ADA, adalimumab; CERT, certolizumab; ETN, etanercept; HR, hazard ratio; IFX, infliximab; RTX, rituximab; TCZ, tocilizumab.