

Risk for Lower Intestinal Perforations in RA Patients Treated with Tocilizumab in Comparison to Treatment with TNF Inhibitors, Rituximab, Abatacept or Conventional Synthetic Dmards

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SESSION INFORMATION

Date: Monday, November 9, 2015

Session Title: Rheumatoid Arthritis - Clinical Aspects II: Infection, Malignancy and Other Comorbidities in RA

Session Type: ACR Concurrent Abstract Session

Session Time: 2:30PM-4:00PM

Background/Purpose:

Interleukin-6 has a direct protective effect on intestinal cells. Although several cases of lower intestinal perforations (LIP) were reported in clinical trials of tocilizumab (TCZ), the incidence in daily care remains unclear. The event rate is low in patients with rheumatoid arthritis (RA), and several factors may contribute to the risk for LIP. We aimed to examine the incidence of LIP in RA patients treated with biologic or conventional synthetic DMARDs (bDMARDs, csDMARDs).

Methods:

We used data from the German biologics register RABBIT with 13,600 RA patients included since 2001 at start of a csDMARD or bDMARD after at least one csDMARD failure. All serious gastrointestinal adverse events reported until 30th April 2015 which were possibly associated with perforations (including haemorrhages) were filtered (n=137) and validated with medical records or specific queries, blinded for treatment exposure. Only events with a definite (non-traumatic and non-iatrogenic) perforation of the lower intestinal tract were selected for the analysis. Treatment exposure was defined as treatment given in the last 3-months before the event. Due to low numbers of events multi-variable adjustment was

not applied.

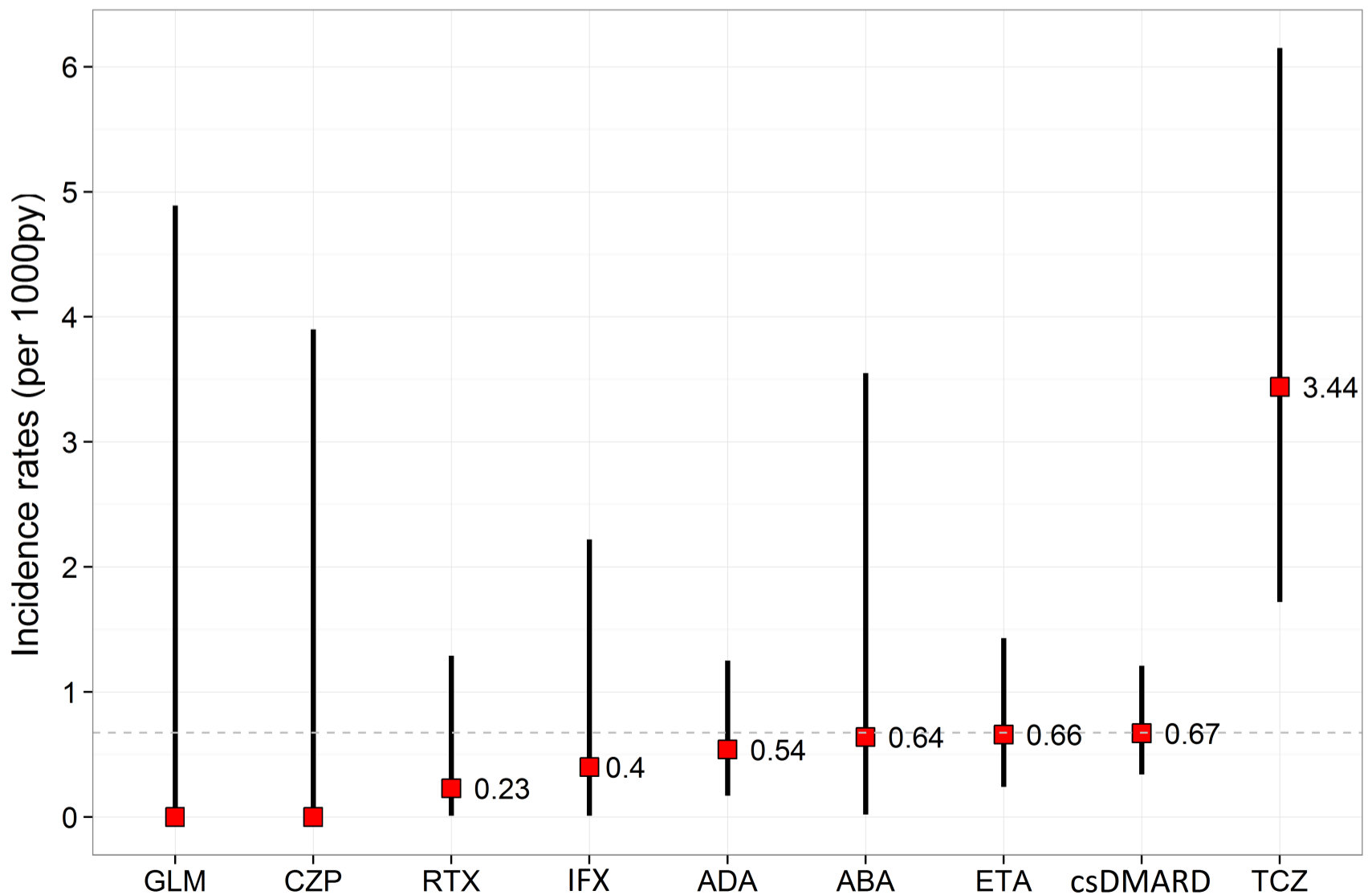
Results: In

total, 35 LIPs (colon/sigma: 30, appendix: 4, terminal ileum: 1) were observed in 48,102 patient years (PY) – 16 of the patients died. In total, 27 of 35 patients with LIP had concomitant GCs, with a daily dose of $\geq 7,5$ mg in 12 patients. In the univariate analysis, current use of glucocorticoids (GC) and age were significantly associated with a higher risk of LIP (hazard ratio (HR) 1.25 per 5mg increase in GC dose [95%CI=1.2, 1.4], and HR 1.5 [1.3, 1.9] per 5 years increase in age).

11 LIP were observed in 1,765 patients treated with TCZ, corresponding to a five times higher incidence rate than in patients receiving csDMARDs only (IRR 5.1 (2.2, 11.8)). The incidence rate was also higher compared to patients treated with other bDMARDs (figure). The increased risk could not be explained by GC use and age of the TCZ treated patients which were similar to patients treated with other bDMARDs.

None of the patients with LIP had a history of diverticulitis known to the treating rheumatologist. Most often, diverticulitis was diagnosed simultaneously with LIP.

The incidence rates in anti-TNF treated patients in RABBIT were similar to those reported by others¹.



Conclusion: This 1st comparison of all bDMARDs available for the treatment of RA showed a significant risk of LIPs in patients treated with TCZ and confirms the signal detected in clinical trials. In none of the patients with LIP a history of diverticulitis was known, which may therefore not constitute sufficient information to support treatment decisions. To avoid additive effects on the risk of LIP concomitant GCs, should be tapered with initiation of TCZ treatment.

(1) Myasoedova E, et al. (2012). *J Rheumatol* 39(7):1355-1362.

Disclosure: **A. Strangfeld**, AbbVie, Celltrion, Hospira, Bristol-Myers Squibb, MSD Sharp&Dohme, Pfizer, Roche, and UCB., 2,BMS, Merck-Sharp & Dohme, Pfizer, Roche, Sanofi-Aventis, 9; **A. Richter**, None; **P. Herzer**, Abbvie, 9,Pfizer Inc, 9; **K. Rockwitz**, None; **W. Demary**, None; **M. Aringer**, Pfizer Inc, 9; **A. Zink**, AbbVie, Celltrion, Hospira, Bristol-Myers Squibb, MSD Sharp&Dohme, Pfizer, Roche, and UCB., 2,BMS, Merck-Sharp & Dohme, Pfizer, Roche, UCB., 9; **J. Listing**, AbbVie, Celltrion, Hospira, Bristol-Myers Squibb, MSD Sharp&Dohme, Pfizer, Roche, and UCB., 2,Pfizer Inc, 5.

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