The order of use of biologic agents after failing a TNF inhibitor is still a question for debate. Phase III trial data in TNF-IR patients show comparable efficacy results across biologic agents and limited head-to-head studies have been published. Prospective registries offer a unique opportunity to observe the effectiveness (combined evaluation of efficacy and safety profile over time) of these agents in a real world clinical setting, where patients with a specific diagnosis are treated according to the center’s preferences. We report here a sixth year follow-up analysis. Our objective is to evaluate if patients with rheumatoid arthritis (RA) treated with rituximab (RIT) after failing a first or a second anti-TNF agent (TNF-IR) have different six-year retention rate than patients similarly treated anti-TNF agents (pooled adalimumab, etanercept or infliximab) and compare the treatment strategies of using RIT as second or third biologic treatment.

METHODS

Data from TNF-IR RA patients prescribed adalimumab (ADA), etanercept (ETA), infliximab (INF) or rituximab (RIT) as second or third biologic agents on or after January 1st 2007 was extracted and subjects taking either ETA, ADA or INF were pooled to form the anti-TNF cohort. Baseline data included: age, disease duration, HAQ-DI, fatigue and pain visual analog scale (VAS), TJC, SJC, CRP and ESR, Methotrexate (MTX), other immunosuppressors, anti-cyclic citrullinated peptide (anti-CCP) or RF positivity. Treatment strategies were assessed using Kaplan-Meier survival estimates. Statistical analysis was performed using SAS version 9.4. RHUMADATA® is a clinical database and registry used in daily clinical practice at the IRM and CORQ. All patients with RA are followed over time irrespective of their treatment. The 6-year drug retention rates were estimated and compared using Kaplan-Meier survival estimates. Statistical analysis was performed using SAS version 9.4. Baseline characteristics were compared using chi-square test for categorical variables and independent sample t-test for continuous variables. Statistical significance was defined as p<0.05.

RESULTS

The data from 231 RA patients were extracted. 155 and 76 having respectively failed a first and a second anti-TNF agent. No clinically significant differences in baseline variables were observed between treatment groups in second and third intention. The principal reason for biologic cessation were treatment inefficacy, adverse events and other or unspecified reasons. The 6-year retention rates of second line RIT and anti-TNF use were 80.1% and 19.1%, respectively (overall retention difference log-rank p=0.0001, Figure 1). The overall retention after second anti-TNF treatment was not affected when considering RF+ or anti-CCP+ patients only. Figure 2. In patients having failed two anti-TNF, subsequent use of RIT and anti-TNF agents respectively demonstrated 6-year retention rates of 53.6% and 37.2% (overall retention difference log-rank p=0.0473). Second versus third line use was numerically (80.1% vs 53.6%) and statistically superior (overall retention difference log-rank p=0.0029).

CONCLUSIONS

As a second and third line agent, in TNF-IR RA patients, RIT demonstrate better 6-year retention rate than anti-TNF agents. Second line use show statistically superior retention rate over third line use. This suggests that using rituximab as a second line therapy after failing a first anti-TF agent is a better strategy than waiting to use it after different anti-TNF failures. Overall retention of second line biologic agents was not affected when considering RF+ or anti-CCP+ patients only.

Disclosure of interest: None declared


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**Figure 1. Retention probability of a second biologic agent. Comparing RIT to TNF among TNF-IR or RF positive patients.**

**Figure 2. Retention probability of a second biologic agent. Comparing RIT to TNF among RF or anti-CCP positive patients.**

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