Methods: Patients recruited to both the British Society for Rheumatology Biologics Register-RA (safety data) and the Biologics in RA Genetics and Genomics Syndicate (serological samples) were included. Both are large national prospective RA cohorts. Biologic drug levels were measured at 3/6/12 months after biologic initiation and stratified as low/normal or high drug levels (HL) as per thresholds defined using concentration-effect curves for each drug. The risk of first and total infections within the first year was analysed. Events occurring on drug or within 90 days of last dose were included. The risk of an event was compared between low/normal vs HL groups using Cox proportional-hazard models. Factors affecting both drug levels and infection risk were adjusted for in the models.

Results: 703 patients (286 etanercept, 179 adalimumab, 120 certolizumab, 104 tocilizumab and 14 infliximab) had clinical data and serological samples. 74% were women, mean (SD) age 58¹² years, on a first biologic (89%). The crude rate/1000 pyrs was 314 and 464 for AI; 54 and 76 for SI in the low/normal and HL groups respectively. The adjusted hazard ratio for AI within the first year differed significantly between the two groups with the HL group having 50 percent higher risk of AI (HR: 1.51; 95% CI: 1.14, 2.01) (table 1). The most common types of AI in the HL group were lower (34%) and upper (16%) respiratory tract infections, urinary tract infections (15%), skin infections including shingles (8%).

Abstract OP0229 – Table 1

	Low/normal drug level (n=241)	High drug levels (n=462)
All events with follow up censored at 1 year (95% CI)		
All infections (n)	63	232
Crude rate (/1000 pyrs)	314 (245–401)	464 (408, 528)
Unadjusted HR	Ref	1.44 (1.09, 1.91)*
Adjusted HR †	Ref	1.51 (1.14, 2.01)*
Serious infections (n)	11	38
Crude rate (/1000 pyrs)	54 (30–98)	76 (55–104)
Unadjusted HR	Ref	1.36 (0.70–2.67)
Adjusted HR†	Ref	1.17 (0.58–2.30)
First event within 1 st year (95% CI)		
All infections (n)	46	150
Crude rate (1000 pyrs)	229 (172–256)	300 (256–352)
Unadjusted HR	Ref	1.24 (0.89–1.73)
Adjusted HR †	Ref	1.26 (0.91–1.78)
Serious infections (n)	6	22
Crude rate (/1000 pyrs)	29 (13–67)	44 (28–67)
Unadjusted HR	Ref	1.39 (0.56–3.44)
Adjusted HR†	Ref	1.26 (0.50–3.16)

*p<0.05 † Adjusted for age, gender, DAS score, methotrexate use

Abstract OP0229 – Figure 1 All infection Nelson-Aalen cumulative hazard estimates

Conclusions: RA patients with high biologic drug levels have a higher risk of infection. Monitoring drug levels may be helpful in prediction of infection. In disease remission patients with HL, biologic dose tapering may lower infection risk.

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OP0230

PREDICTORS OF HYPOGAMMAGLOBULINEMIA DURING RITUXIMAB MAINTENANCE THERAPY IN RHEUMATOID ARTHRITIS: A 12-YEAR LONGITUDINAL MULTI-CENTRE STUDY

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Background: Rituximab (RTX) is an anti-CD20 monoclonal antibody that selectively depletes B-cell population. One of the drawbacks of a prolonged peripheral B-cell depletion is the suppression of protective antibodies and an increased risk for infectious events. However, few long-term data are available on predictors for the development of low levels of serum immunoglobulins in patients receiving repeated courses of RTX.

Objectives: We aimed at the identification of predictors for hypogammaglobulinemia occurrence in RA patients long-term treated with RTX in a 'real-life' setting.

Methods: Multicenter longitudinal observational usual care study including RA patients according to ACR 1987 and/or ACR/EULAR 2010 classification criteria followed and treated with RTX. A previous study assessing the safety profile of RTX in patients with RA reported a median follow-up of 30 months.¹ Therefore, we decided to include RA patients on RTX maintenance therapy, after a minimal exposition of 30 months. Serum protein electrophoresis was performed before each RTX infusion. Hypogammaglobulinemia and severe hypogammaglobulinemia were defined as total gammaglobulin <6 g/L and <4 g/L, respectively. Safety monitoring included the collection of all adverse events (AE) in particular severe infections.

Results: 134 patients met inclusion criteria: 113 female subjects (84.3%); mean age 52.1±11.4 years. Mean follow-up was 79.5±24.6 months and analysis was based on 854.9 patient-years (pt-yrs). Mean RTX cumulative dose was 12.0 ±4.9 g. Hypogammaglobulinemia (<6 g/L) occurred during the follow-up period in 23 patients (2.7 events per 100 pt-yrs), leading to an incidence of 17.1%. The mean time to development of hypogammaglobulinemia was 64±23 months. A total of 9.7% of patients had severe infections (1.5 events per 100 pt-yrs). Patients who developed hypogammaglobulinemia were more likely to experience severe infections (26.1% vs 6.3%, p=0.033). Univariate Cox analysis identified age over 65 years (HR 4.28 [95% CI: 0.92 to 19.97], p<0.001), low gammaglobulin levels prior the first RTX infusion (<8 g/L) (HR 7.35 [95% CI: 1.82 to 29.68], p<0.001) as predictors of protective factor (HR 0.26 [95% CI: 0.08 to 0.87], p=0.03).

Conclusions: Our results show that gammaglobulin levels of less than 8 g/L at baseline is a strong independent risk factor for developing subsequent hypogammaglobulinemia, whereas concomitant MTX therapy seems to be a protective factor in RA patients treated long-term with RTX. Identifying such predictors will raise clinicians' awareness and allow more tailored monitoring of RA patients long-term treated with RTX.

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OP0231

GASTRO-INTESTINAL PERFORATIONS AMONG RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BIOLOGIC DMARDS: A NATIONWIDE SWEDISH COHORT STUDY

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Background: Use of glucocorticosteroids and NSAIDs for the treatment of RA has been associated with an increased risk of gastrointestinal (GI) perforations. The introduction of disease modifying agents, such as methotrexate or tumour necrosis factor inhibitors (TNFi) provided a seemingly safer treatment option, but the safety of other types of biologics relative to TNFi remains unclear.

Objectives: To estimate the incidence of gastro-intestinal perforations among Swedish RA patients treated with TNFi and non-TNFi biologics, and compare it with the incidence among bionative patients with RA and a matched general population comparator group.

Methods: We performed a register-based cohort study, including all Swedish RA patients, with follow-up between 2010 and 2015. For these, all treatment initiations with biologic disease modifying anti-rheumatic drugs were identified through the Swedish Rheumatology register (SRQ), and grouped by class into TNFi and non-TNFi drugs (10 857 and 5823 treatment starts). Biologics naïve patients with RA were identified by recorded diagnosis in the Swedish National Patient Register (NPR), since 2001 (n=54,732). Five general population controls were matched to