Infection-related rheumatic diseases

**POS178** PRESCRIBING RITUXIMAB IN PATIENTS WITH AUTO-IMMUNE DISEASES AND ACQUIRED HYPOGAMMAGLOBULINEMIA: DESCRIPTION OF THE RISK OF SEVERE INFECTION IN 121 PATIENTS BEFORE THE SARS-COV2 ERA

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**Background:** Rituximab (RTX) induces rapid, usually complete and prolonged depletion of circulating B cells, and also hypogammaglobulinemia in some patients. There are limited data regarding the risk of severe infection events (SIE) when initiating or continuing rituximab in patients with acquired hypogammaglobulinemia, especially in patients suffering from autoimmune diseases (ADs) other than rheumatoid arthritis (RA) (1).

**Objectives:** To describe the risk of severe infectious events (SIE) following initiation (rituximab-naive patients [RNP]) or continuation of RTX therapy (rituximab-continuing patients [RCP]) in patients suffering from severe ADs other than RA and acquired hypogammaglobulinemia.

**Methods:** We conducted a single-center retrospective cohort study at the University Hospital of Toulouse (France) between 2010 and 2018. Patients were included if they had received at least one dose of RTX in the year following the evidence of hypogammaglobulinemia (defined as gammaglobulins [GG]<6g/L on serum protein electrophoresis) in the setting of ADs other than RA. The primary outcome was the occurrence of a SIE within 2 years after the date of first RTX infusion (T0) prescribed after the evidence of hypogammaglobulinemia. SIE were infections either fatal or requiring hospitalization.

**Results:** We included 121 patients (37 RNP and 84 RCP): 48 had ANCA-associated vasculitis (AAV), 48 multiple sclerosis (MS, n=41) or neuromyelitis optica (NMO, n=7), and 21 another severe AD. RTX was prescribed as induction therapy in 39 patients and as maintenance therapy in 82; 112/121 patients were followed for 2 years. Mean GG level were 5.5g/L (IQ 25-75 4.6-5.7) at T0, 5.5g/L (IQ 25-75 5.4-6.4) at one year, 5.7g/L (IQ 25-75 4.8-6.1) at two years and 8 patients had a decrease of their GG level below 4g/L. Ten patients received immunoglobulin replacement therapy (IGRT) mostly after infection (n=6). Twenty-six patients (23.2%) had at least one SIE during follow-up: 12.8% in the MS/NMO group with a 2-year incidence of 6.9 (3.1-15.5) per 100 person-years, 29.5% in the AAV group with a 2-year incidence to 18.3 (9.3-20.1) per 100 person-years, 33.3% in the ‘other ADs’ group with a 2-year incidence at 33.3% (9.3-59.9) and 21 another severe AD. RTX was prescribed as induction therapy in 39 patients and as maintenance therapy in 82; 112/121 patients were followed for 2 years. Mean GG level were 5.5g/L (IQ 25-75 4.6-5.7) at T0, 5.5g/L (IQ 25-75 5.4-6.4) at one year, 5.7g/L (IQ 25-75 4.8-6.1) at two years and 8 patients had a decrease of their GG level below 4g/L. Ten patients received immunoglobulin replacement therapy (IGRT) mostly after infection (n=6). Twenty-six patients (23.2%) had at least one SIE during follow-up: 12.8% in the MS/NMO group with a 2-year incidence of 6.9 (3.1-15.5) per 100 person-years, 29.5% in the AAV group with a 2-year incidence to 18.3 (9.3-20.1) per 100 person-years, 33.3% in the ‘other ADs’ group with a 2-year incidence at 33.3% (9.3-59.9) and 21 another severe AD. RTX was prescribed as induction therapy in 39 patients and as maintenance therapy in 82; 112/121 patients were followed for 2 years. Mean GG level were 5.5g/L (IQ 25-75 4.6-5.7) at T0, 5.5g/L (IQ 25-75 5.4-6.4) at one year, 5.7g/L (IQ 25-75 4.8-6.1) at two years and 8 patients had a decrease of their GG level below 4g/L. Ten patients received immunoglobulin replacement therapy (IGRT) mostly after infection (n=6). Twenty-six patients (23.2%) had at least one SIE during follow-up: 12.8% in the MS/NMO group with a 2-year incidence of 6.9 (3.1-15.5) per 100 person-years, 29.5% in the AAV group with a 2-year incidence to 18.3 (9.3-20.1) per 100 person-years, 33.3% in the ‘other ADs’ group with a 2-year incidence at 22.2 (10.6-46.6) per 100 person-years. Infection was opportunistic in 8 patients (33.3%) and 4 died from SIE. Risk factors of SIE at T0 were male gender (61.5% vs. 39.5% p<0.05), lung disease (65.4% vs. 37.2% p=0.01), renal failure (59.1% vs. 26.8% p=0.01), a higher Charlson comorbidity index (CIM>0.001), a previous treatment by cyclophosphamide (53.8% vs. 30.2% p<0.03), ≥ 5mg/d prednisone (69.2% vs. 33.7% p=0.003), lack of pneumococcal vaccination (61.5% vs. 31.4% p=0.01), GG level was 5.3g/L [4.1-5.6] in the ‘SIE’ group vs 5.6g/L [4.8-5.8] in the ‘no SIE’ group (p=0.04). Incidence of SIE was 46% and 20.2% among patients with GG< 4 g/L or GG≥ 4 g/L, respectively (p=0.07). No multivariable analysis provided reliable results.

**Conclusion:** Our study provides useful information for clinicians considering initiating or continuing rituximab therapy in patients with acquired hypogammaglobulinemia before Sars-Cov2 era. Prospective studies are necessary to improve the knowledge on outcome of patients treated by rituximab despite low immunoglobulins levels. Prophylactic IGRT may be appropriate in higher risk patients, especially if the GG level is below 4 g/L.

**REFERENCES:**