Efficacy and Safety of Rituximab in Rheumatoid Arthritis Patients with Concomitant Interstitial Lung Disease: 10-Year Experience at Single Centre

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Background: Interstitial lung disease (ILD) is a common extra-articular manifestation in RA and is associated with increased mortality. Worsening of ILD has been reported in patients receiving TNF inhibitors, therefore rituximab is commonly used instead. However evidence of efficacy and safety of rituximab in RA-ILD from cohort studies/registries is scarce as these patients are often excluded from clinical trials. Our aims were to evaluate whether rituximab therapy led to worsening of lung function in patients with previously stable ILD and to evaluate serious adverse events (SAEs) and serious infection. Methods: We conducted an observational study of consecutive RA patients with ILD (detected by high-resolution CT prior to rituximab) in a single centre between January 2004 and July 2014. Each cycle consisted of 2 × 1000 mg infusions, repeated on clinical relapse. Pulmonary function test parameters (forced vital capacity (FVC) and carbon monoxide diffusing capacity (DLCO)) were recorded at baseline, 6–12 months post-rituximab and latest time point. SAEs were defined as those resulting in hospitalization for more than 24h, flares requiring i.v. therapy, malignancies, life-threatening events or death. Results: 53 patients with ILD were identified from a cohort of 576. 19 were male and 34 female; median age 63.4 years (interquartile range (IQR) 58–72); median RA duration 9.3 years (IQR 8–12); median ILD duration 5 years (IQR 3–7) at baseline. Total follow up was 171 patient-years. There was no substantive or significant reduction in FVC and DLCO over time; all p > 0.1. 9 patients received CYC (CYC) prior to rituximab: 6 had stable ILD during rituximab treatment while 3 required further CYC due to ILD progression. 2 patients who had not previously received prior CYC required CYC treatment due to worsening ILD after rituximab. Only three patients (0.5%) were diagnosed with new ILD after rituximab. 78 SAEs were recorded in 33 patients: 72 were hospitalization (median duration 8.5 days), 2 malignancies and 15 serious infections (8.8 per 100 patient-years); mostly due to chest infection. Of the 12 deaths, 9 were due to progressive ILD with median DLCO of 41% (range 35–64%) prior to rituximab. Other deaths were: 1 lung cancer, 1 colon cancer and 1 infection post-surgery. Median time from last rituximab infusion to death was 11.5 months (range 6–72). Conclusion: Mortality rates and SAEs, although notable, are as might be expected for this advanced RA cohort with multiple comorbidities. Most patients with stable ILD before rituximab remained stable over prolonged follow up. Due to the time elapsed since last rituximab, and since the patients who died or deteriorated had the most severe ILD before rituximab, these observations suggest the drug may not be necessarily causative. Analysis of detailed respiratory investigations is in progress and will help to identify patients whose ILD improved after treatment. Disclosure statement: Md.Y.Md.Y. has received funding from the NIHR. S.D. has received honoraria from Roche and GSK. E.M.V. has received honoraria and research grants from Roche and GSK; and has received funding from the NIHR. P.E. has received consultant fees from BMS Abbott, Pfizer, MSD, Novartis, Roche and UCB; and has received research grants from Abbott, BMS, Pfizer, MSD and Roche. All other authors have declared no conflicts of interest.