INTENSIFIED B-CELL DEPLETION THERAPY IN DISEASE-SPECIFIC AUTOANTIBODIES ASSOCIATE WITH REMARKABLY DIFFERENT RISK OF DEVELOPMENT OF SIGNIFICANT LUNG FIBROSIS IN SYSTEMIC SCLEROSIS

A. Sari, S.I. Nihyanyova, A. Gill, V.H. Ong, C.P. Denton. Rheumatology, Royal Free Hospital, University College London, London, UK

Background: Pulmonary fibrosis (PF) is an important complication of systemic sclerosis (SSc), being a leading cause of disease related death. Some studies suggest that the timing of PF development differs between patients with different autoantibodies. Objectives: We set out to assess a large single-centre SSc cohort, focusing on the timing of clinically significant PF (csPF), and to compare this within subgroups with different disease-specific autoantibodies, in particular anti-centromere antibody (ACA), anti-topoisomerase I antibody (ATA) and anti-RNA polymerase antibody (ARA).

Methods: Patients with confirmed SSc and information on autoantibodies were included. PF was confirmed on high-resolution CT and defined as clinically significant based on at least one of the following: FVC <70%; a drop in FVC >15%; DLCO<70% with no pulmonary hypertension (PH) present; or a drop in DLCO>15% with no PH. Only subjects who had first available lung function test result within the first 3 years from onset were included. Kaplan-Meier (1 KM) estimation was used to calculate cumulative incidence of csPF. To assess the timing of highest rates of csPF development, hazard rates were calculated within intervals of 12 months over the follow-up.

Results: A total of 450 subjects, 75 (16.7%) male, mean age of onset 47.4 years, were included in the study. Of those 225 (50%) had diffuse cutaneous SSc, 105 (23.3%) carried ACA, 113 (25.1%) ATA and 72 (16%) ARA. Mean follow-up was 12 years, interquartile range 8–16 years. Over the entire follow-up period, 196 (43.6%) of the subjects developed csPF.

Using 1 KM estimation, for the whole cohort, over the first 20 years of disease, 32.9% of the patients developed csPF. Three quarters of the patients who developed csPF had reached this endpoint by 5 years (38.2%) with much lower incidence thereafter (at year 10, 15 and 20% respectively). Analysis within subgroups showed that, ACA+ patients were associated with a very low risk of csPF development (cumulative incidence of 5.9%, 8.1%, 9.8% at 5, 10 and 15 years from SSc onset). On the other hand, ATA+ patients had a remarkably high risk of csPF development, which ultimately occurred in the majority of cases, with cumulative incidence of 77.6% at 5 years, 82.7% at 10 years and 87.1% at 15 years. Rates of csPF development among ARA+ patients were higher than those in ACA+, but still much lower than ATA+ and even after 20 years of follow-up, the cumulative incidence of csPF among them was less than a half of that among ATA+ patients (23.7%, 33% and 41% at years 5, 10 and 15, figure 1). The hazard of csPF among ACA+ patients was highest in the second year from SSc onset (3%) and in the subsequent years varied between 0% and 1.8%. On the other hand, among ATA+ patients hazard of csPF was 28.3% in year 1, 44.9% in year 2, peaked at 52.5% in year 3 and went down sharply thereafter. Although hazard was much lower among ARA+ patients, this still peaked at year 3 (2.8%, 6.1% and 12.1% at year 1, 2 and 3 respectively) and declined after.