**Scleroderma, myositis and related syndromes**

**FR0300**  
**IMPACT OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS IN A COMPLETE, NATIONWIDE COHORT**

Anna-Maria Hoffmann-Vold1, Håvard Fretheim1, Anna-Kristine H Halse2, Mark Seip3, Helle Bitter1, Marianne Wal lenius1, Anne Salberg4, Torhild Garen4, May Brit Lund1, Trond M Aaløkken5, Øyvind Midttvedt6, Øyvind Molberg6, Nils Dibbelt6, Robert Jergen7, going, Southern Norway, Kristiansand, Norway

**Background:**Interstitial lung disease (ILD) represents a clinical challenge in systemic sclerosis (SSc) and associates with high mortality. The presence of severe lung fibrosis is a strong predictor for early mortality. There is substantial progress in SSc-ILD research, but precise, population-based data on cumulative incidence, range of severity and predictive value of clinical risk factors are lacking. Such data are vital for clinical decision making, and highly warranted as background information for appropriate development of screening and management strategies for SSc-ILD.

**Objectives:**To assess cumulative incidence of ILD, range of ILD severity and mortality risk predicted by baseline pulmonary function tests (PFT) and ILD extent by CT in a complete, nationwide SSc cohort.

**Methods:**The Norwegian SSc cohort study (Nor-SSc) includes all the 630 incident cases diagnosed from 2000-2012 (the 630 incident cases) were included and compared with 15 age- and gender matched controls per patient drawn from the national population registry. Vital status was available for all patients. Descriptive statistics from the national population registry. Vital status was available for all patients and controls at study end (January 2018). Descriptive statistics and standardized mortality ratios (SMR) were estimated.

**Results:**Of the 815 patients in the total Nor-SSc cohort, 682 (84%) were female and 629 (77%) had limited cutaneous SSc. Mean age at baseline was 94% of expected value, and nearly half of the patients (42%) had an FVC<100% (Figure 1B). Proportionate distribution of FVC values in patients with no lung fibrosis, <10% lung fibrosis of total lung volume and >10% lung fibrosis is shown in Figure 1C. During the mean 8.6 yrs observation period of this study, 148 of the 630 SSc patients died, corresponding to an overall SMR of 2.4. Separate analyses of the 650 patients with baseline HRCT data showed that the SMR correlated with presence and extent of lung fibrosis, from SMR 2.2 in patients with no fibrosis to SMR 8 in patients with >25% lung fibrosis (Figure 1D). Correspondingly, we found that the SMR changed across patient groups stratified by baseline FVC%, with increased mortality evidence already in the FVC 90-100% group (Figure 1E).

**Conclusion:**The results from this population based SSc cohort study provide new, unbiased data regarding the impact of ILD. Our results indicate a dose-response relationship between lung fibrosis extent and SMR; and between FVC% and SMR. Importantly, this relationship was evident even in groups with limited lung fibrosis and groups with normal range FVC%, strongly suggesting that all SSc patients should be screened with PFT and HRCT at baseline, to diagnose ILD early and tailor further management.

**Disclosure of Interests:**Anna-Maria Hoffmann-Vold Grant/research support from: Received research funding or other remuneration from Boehringer Ingelheim, GSK, and Actelion, Consultant for: Received consulting fees or other remuneration from Boehringer Ingelheim, GSK, and Actelion, Speakers bureau: Actelion and Boehringer Ingelheim. Håvard Fretheim Consultant for: Received consulting fees or other remuneration from GSK, and Actelion, Anna-Kristine H Halse: None declared, Mark Seip: None declared, Helle Bitter: None declared, Marianne Wallenius: None declared, Anne Salberg: None declared, Torhild Garen: None declared, May Brit Lund: None declared, Trond M Aaløkken: None declared, Øyvind Midttvedt: None declared, Øyvind Molberg: None declared.

**DOI:**10.1136/annrheumdis-2019-eular.6743

---

**FR0301**  
**GASTROINTESTINAL ADVERSE EVENTS IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) TREATED WITH NITENDIVAB: DATA FROM THE SENSICIS TRIAL**

Toby Maher1, Kristin Hindland2, Martina Gahlenmann3, Arata Azuma4, Ayeh Fischer5, Maarja Ingri5, Marit Kaira5, Harri Lyyra5, Mannaig Girard5, Margarida Alves10, Emmanuelle Clerisme-Beatty10, Veronika Kohlbrenner11, Masataka Kuwana12, Oliver Distler13, SENSICIS trial investigators.1National Heart and Lung Institute, Imperial College London, United Kingdom, and National Institute for Health Research Clinical Research Facility, Royal Brompton Hospital, London, United Kingdom; Cleveland Clinic, Cleveland, Ohio, United States of America; 2Boehringer Ingelheim (Schweiz) GmbH, Basel, Switzerland; 3Department of Pulmonary Medicine and Oncology, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan; 4University of Colorado School of Medicine, Denver, Colorado, United States of America; 5Division of Rheumatology and Clinical Immunogenetics, University of Texas McGovern Medical School, Houston, Texas, United States of America; 6University of Washington, Seattle, United States of America; 7Boehringer Ingelheim Pharma GmbH and Co. KG, Biberach an der Riss, Germany; 8Boehringer Ingelheim France S.A.S., Reims, France; 9Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; 10Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, Connecticut, United States of America; 11Department of Allergy and Immunology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan; 12Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland

**Background:**In patients with idiopathic pulmonary fibrosis (IPF), nintedanib has a manageable adverse event (AE) profile characterised predominantly by gastrointestinal (GI) events. The efficacy and safety of
Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom ≤7 years were randomised to receive nintedanib 150 mg bid or placebo double-blind. Dose reductions to 100 mg bid and treatment interruptions were allowed to manage adverse events. AE’s were reported over 52 weeks of treatment were coded using preferred terms in the Medical Dictionary for Regulatory Activities and analysed descriptively. A questionnaire was used to collect additional information on diarrhea AEs.

Results: A total of 576 patients (288 per group) received ≥1 dose of nintedanib or placebo. Over 52 weeks, 13.9% and 7.3% of patients treated with nintedanib and placebo discontinued study treatment due to AE. The most frequent AE’s in patients treated with nintedanib were diarrhea (75.7% vs 31.6%), nausea (31.6% vs 13.5%) and vomiting (24.7% vs 10.4%). Serious diarrhea AEs were reported in 2 patients (0.7%) in each group, and serious vomiting AEs were reported in 2 patients (0.7%) in the placebo group and none in the nintedanib group. Of the 216 nintedanib-treated patients who experienced a diarrhea AE, most experienced events that were at worst of mild (49.5%) or moderate (45.0%) intensity, most (70.2%) experienced 1 or 2 events, and the duration of diarrhea AEs was ≤9 days for 50% of the events reported over 52 weeks. Among nintedanib-treated patients who experienced >1 diarrhea AE, 26.1% had a permanent dose reduction and 9.2% discontinued study drug due to the AE. Among the 91 patients in the placebo group who experienced >1 diarrhea AE, the duration of diarrhea AEs was ≤3 days for 50% of the events reported over 52 weeks, 2.2% had a permanent dose reduction and 1.1% discontinued study drug due to the AE.

Conclusion: In patients with SSc-ILD, the gastrointestinal AE’s associated with nintedanib were manageable for most patients and consistent with its known safety and tolerability profile in patients with IPF.

Disclosure of Interests: Toby Maher Grant/research support from: Received funds from BI advisory board participation and conference travel. Received research funding and/or consulting fees or other remuneration from: GSK, UCB, AstraZeneca, Roche, Bayer, Biogen Idec, Cipla, Prometic, and Sanumed. Toby Maher has, via his institution, received industry-academic funding from GlaxoSmithKline R&D and UCB. Consultant for: Toby Maher has received consultancy or speakers fees from Apeiler, AstraZeneca, Bayer, Biogen Idec, Boehringer Ingelheim, Galapagos, GlaxoSmithKline R&D, Indalo, Pliant, ProMetic, Roche, Samumed and UCB; and has received consultancy fees from Galeco., Kristin Highland Grant/research support from: Kristin Highland is a site PI for the SENSCIS trial (Dr Highland’s institution has the contract for the study) which is funded by Boehringer Ingelheim., Consultant for: Kristin Highland is a paid consultant for Boehringer Ingelheim through her role sitting on the steering committee., Speakers bureau: Kristin Highland is on the speakers’ bureau for Boehringer Ingelheim., Martina Gahlemann Employee of: of Employee of Boehringer Ingelheim, Arata Azuma Consultant for: Arata Azuma has received personal fees from Boehringer Ingelheim (B I), Biocartis Co., Ltd, Taiho Pharmaceutical Co., Ltd, and Asahikasei Pharma Co., Arayeh Fischer Grant/research support from: Arayeh Fischer has received a grant from Boehringer Ingelheim (Consultant/steering committee member/ principal investigator on clinical trials), Genentech-Roche (Consultant/steering committee member/principal investigator on clinical trials), Pfizer (Consultant) and Genentech (Consultant), Maureen Mayes Grant/research support from: Maureen Mayes is a clinical trial investigator for Boehringer-Ingelheim; Galapagos, Reata, Sanofi, Merck-Serono, Consultant for: Maureen Mayes is a member of scientific advisory boards for Galapagos NV (Pharma), Boehringer-Ingelheim, Mitsubishi-Tanabe, Astellas; Grant Review Board for Actelion., Speakers bureau: Maureen Mayes received personal fees for being a conference speaker on the use of autoantibodies in connective tissue diseases for Medtellin, Genahes Raghu Grant/research support from: Genahes Raghu is the principal investigator for IPF net studies and is a steering committee member/IPF net studies for the NIH. Consultant for: the principal investigator for IPF net studies is a consultant for Boehringer Ingelheim, Biellerophan, Biogen, BMS, Fibrogen, Gilead, Netto, Revistan, Promodori, Sanofi, Veracode and Roche-Genentech; and a consultant and chair of the DSMB for Avalyan., Wiebke Sauter Employee of: Wiebke Sauter is an employee of Boehringer Ingelheim, Mannina Girard Employee of: Mannina Girard is an employee of Boehringer Ingelheim, Margarida Alvies Employee of: Employee of Boehringer Ingelheim, Emmanuelle Clerisme-Beaty Employee of: Emmanuelle Clerisme-Beaty is an employee of Boehringer Ingelheim, Veronika Kopeckova Employee of: Veronika Kopeckova is an employee of Boehringer Ingelheim, Masataka Kuwana Grant/research support from: Actelion., Consultant for: Chugai, Reata, GlaxoSmithKline, Bayer, Boehringer-Ingelheim, Corus, CSL-Berling, Mochida, Speakers bureau: Actelion, Pfizer, Bayer, Nippon Shinyaku, Chugai, Oliver Distler Grant/research support from: Prof. Distler has a consultancy relationship within the last 3 years with Actelion, AnelMar, Bayer, Boehringer Ingelheim, ChemomedAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmaceuticals, Novartis, Pfizer, Sanofi, Sero-dapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he has had consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders.

Disclosure of Interests:

Background: recent data support the use of rituximab (RTX) in Systemic Sclerosis (SSc). RTX biosimilars (RTX-B) offers a more affordable option but its efficacy and safety have not yet been evaluated.

Objectives: To assess the safety and efficacy of RTX-B in SSc.

Methods: Data about SSc patients treated with RTX-B (1gr repeated after 2 weeks) and with a follow-up >6 months were retrospectively collected from 5 Italian centres. Both SSc patients naïve to RTX (RTX-Bn) or already treated with >1 course of RTX originator (RTX-O) and switched to RTX-B(RTX-Bs) were considered. A comprehensive assessment of disease features and organ involvement was available at baseline and at final follow-up for all patients. Non parametric tests were used.

Results: Data of 21 SSc patients (20 female, mean age 50.5±11.8 years) were collected; mean disease duration at RTX-B therapy was 6.8±4.8 yrs. Eleven patients (52%) had diffuse cutaneous SSc (dcSSc), 12 (57%) were anti-topoisomerase I+, 5 anti-RAA-polymeraseII+ and 4 anti-centromere+. Twelve patients (57%) were RTX-Bn and 9 RTX-Bs (43%). In RTX-B patients, the median number of previous RTX-O courses was 3(range 1 – 8). RTX was decided because of skin progression in 11(52%), interstitial lung disease[ID](worsening in 9(43%), arthritis in 6(29%), myositis and mycologistic in 1 patient each. All patients had been previously treated with immunosuppressants: mycophenolate mofetil(MMF) 14(67%), methotrexate(MTX) 7(33%), cyclophosphamide 6(29%), azathioprine 4(19%), toclizumab and etanercept 1(5%) patient each. At RTX-B introduction, 14(67%) patients were on concomitant immunosuppressant (10(48%) MMF and 4(19%) MTX); 15 patients(71%) were also on steroids(mean dose:3.1±1.1mg/day). At 6 months after RTX-B treatment, a significant reduction of the modified Rodnan skin score(mRSS), DAS28 and erythrocyte sedimentation rate(ESR) was observed in the entire cohort (p<0.001,p<0.028, p<0.003, respectively); mRSS was significantly reduced also in RTX-Bn (p<0.011) and RTX-Bs patients (p<0.048) (Table 1). No significant changes were observed for lung function tests. Only 1 RTX-Bs patient experienced a transient neutropenia 3 months after the 2nd RTX-B infusion whilst also on MTX.

Conclusion: in agreement with previous data published on RTX-O, also RTX-B seem efficient in improving skin and joint involvement and in stabilizing lung function, either in RTX-Bn and in RTX-Bs SSc patients.

REFERENCES: