Actelion, Bayer, BMS, Boehringer, Roche, Sanofi, Margarida Alves Employee of: Employee of Boehringer Ingelheim, Nicole Graf Grant/research support from: Received consulting fees or other remuneration from Astellas and Biotronik, Paolo Airò: None declared, Lidia P. Ananyeva: None declared, László Cziráj: None declared, Serena Guiducci: None declared, Eric Hachulla Consultant for: Received consulting fees or other remuneration from Actelion, GSK, Pfizer, and Bayer, Mengtao Li: None declared, Carina Mihai Consultant for: Received consulting fees or other remuneration from Actelion, Geneva, Roche, and Rofarm, Consultant for: F. Hoffmann-La Roche, Actelion, Geneva Romfarm, Gabriela Riemekasten Consultant for: Chugai, F. Hoffmann-La Roche, Speakers bureau: Chugai, F. Hoffmann-La Roche, Petros Sfrikakis: None declared, Gabriele Valentini Grant/research support from: Received research funding and other remuneration from AbbVie, BMS, Lilly, Pfizer, and Sanofi, Consultant for: Received consulting fees and other remuneration from AbbVie, BMS, Lilly, Pfizer, and Sanofi, Otylia Kowal-Bielecka Consultant for: Received consulting fees or other remuneration from Bayer, Boehringer Ingelheim, Inventiva, Medac, Novartis, and Roche, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inventiva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclis, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/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

DOI: 10.1136/annrheumdis-2019-eular.2586

OP0240

ASSESSMENT OF PULSE WAVE VELOCITY IN SYSTEMIC SCLEROSIS: POTENTIAL BENEFICIAL EFFECTS OF BOSENTAN ON FOREARM ARTERIAL STIFFNESS? AN EXPLORATORY STUDY

Anniek van Roon¹, Amaal Eman Abdulle¹, Saskia van de Zande¹, Arie Van Roon¹, Dan Zhang², Reinhard Bos², Hendrika Bootsma³, Andries Smit¹, Douwe J Mulder¹.
¹University of Groningen, University Medical Center Groningen, Internal Medicine, division Vascular Medicine, Groningen, Netherlands; ²Medical Center Leeuwarden, Rheumatology, Leeuwarden, Netherlands; ³University of Groningen, University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands

Background: Systemic sclerosis (SSc)-related vasculopathy is generally thought to occur on a microvascular level. However, some observations also suggest involvement of arterial vessels. Macrovascular involvement (e.g., aorta or upper extremity) can be non-invasively assessed by measuring pulse wave velocity (PWV). Although, several studies have assessed aortic and upper extremity PWV in SSc, studies have not reached a consensus regarding this matter. Furthermore, we hypothesized that the endothelin antagonist bosentan may improve arterial stiffness by its direct endothelial and potential anti-fibrotic effects.

Objectives: The aim of this exploratory study was two-fold. First, we aimed to compare arterial stiffness in patients with SSc and age and sex-matched healthy controls (HC). Secondly, we will investigate the effect of bosentan on both short-term (three month) and long-term (one year) PWV.

Methods: Baseline differences between HC and SSc patients were studied in a case-control design. The follow-up of SSc patients was a randomized, prospective, 2-arm parallel group, open-label, (usual care with bosentan versus usual care only), blinded endpoint, intervention study. PWV (Sphygmocor) in meters/second, was measured to assess arterial stiffness in the aorta (carotid-femoral PWV), upper arm (carotid-brachial PWV), and forearm (brachial-radial PWV), adjusted for mean arterial pressure.

Results: Baseline characteristics are shown in table 1. No significant differences were observed in PWV (at all sites) between HC and SSc patients. No effect of bosentan on aortic, and upper arm PWV was found. The change in forearm PWV was different between the groups, with a decrease (e.g. lowering arterial stiffness) in the bosentan group (figure 1).

Table 1. Baseline characteristics

	Healthy controls (n=19)	Systemic sclerosis patients (n=19)	Bosentan group (n=9)	Usual care group (n=7)
Female, n (%)	13 (69)	13 (69)	5 (56)	6 (86)
Age in years, median (IQR)	53 (47–63)	50 (44–54)	52 (49–66)	44 (43–54)
Pack years, median (IQR)	0 (0–7.5)*	2.5 (0–30.6)*	17.3 (0.7–34.1)	0.8 (0–2.75)

Body mass index in kg/m ² , median (IQR)	25 (23–27)	25 (21–29)	25 (22–27)	26 (20–37)
Systolic blood pressure in mm Hg, median (IQR)	130 (121–137)	127 (123–134)	126 (117–142)	127 (123–132)
Diastolic blood pressure in mm Hg, median (IQR)	81 (72–88)	85 (79–89)	84 (76–87)	83 (79–85)
Raynaud's phenomenon duration in years, median (IQR)	N/A	8.0 (4.0–13.0)	1.0 (1.0–7.0)	13.0 (6.0–16.0)
Systemic sclerosis disease duration since first non-Raynaud symptom in years, median (IQR)	N/A	2.0 (1.0–7.0)	1.0 (1.0–7.5)	5.0 (2.0–14.0)

*difference between groups with a p<0.05

Figure 1. The median (IQR) of the brachial-radial pulse wave velocity over time of the bosentan and usual care group

Conclusion: This small study shows that aortic, upper arm, and forearm arterial stiffness does not appear to be increased in patients with SSc, as compared to age- and sex-matched healthy controls. To the best of our knowledge, this is the first study to investigate the concept of potential effects of an endothelin receptor antagonist on macrovascular involvement in SSc. Although the results demonstrate no effects on aorta and upper arm arterial stiffness, they may indicate a beneficial effect on the stiffness of the smaller arteries of the forearm. Future studies are needed to further investigate the potential effect of bosentan on these smaller arteries.

Acknowledgement: Actelion for co-funding the study

Disclosure of Interests: Anniek van Roon: None declared, Amaal Eman Abdulle: None declared, Saskia van de Zande: None declared, Arie Van Roon: None declared, Dan Zhang: None declared, Reinhard Bos Grant/research support from: SUN Pharma, Hendrika Bootsma Grant/research support from: Unrestricted grants from Bristol-Myers Squibb and Roche, Consultant for: Roche, Bristol-Myers Squibb, Novartis, Medimmune, Union Chimique Belge, Speakers bureau: Bristol-Myers Squibb, Novartis, Andries Smit Shareholder of: Has been co-founder, and is still shareholder of Diagnostica Technologies, the company which developed the AGE reader., Douwe J Mulder Grant/research support from: My University has received research grants for my research from: Boehringer Ingelheim and Actelion, Speakers bureau: My University has received speakers fee from: Sanofi

DOI: 10.1136/annrheumdis-2019-eular.6756

OP0241

SAFETY AND EFFICACY OF LENABASUM IN AN OPEN-LABEL EXTENSION OF A PHASE 2 STUDY OF LENABASUM IN REFRACTORY SKIN-PREDOMINANT DERMATOMYOSITIS (DM) SUBJECTS

Victoria Werth^{1,2}, David Pearson^{1,2}, Joyce Owaka^{1,2}, Rui Feng², Josef Simon Concha^{1,2}, Basil Patel^{1,2}, Emily Hejazi^{1,2}, Caitlin Cornwal³, Scott Constantine³, Nancy Dgetluck³, Barbara White³. ¹Philadelphia Veterans Affairs Medical Center, Philadelphia, United States of America; ²University of Pennsylvania, Philadelphia, United States of America; ³Corbus Pharmaceuticals, Inc., Norwood, United States of America

Background: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses. Lenabasum had acceptable safety and tolerability and improved efficacy outcomes in the initial 16-week double-blind, randomized, placebo-controlled Part A of Phase 2 trial JBT101-DM-001 (NCT02466243) in dermatomyositis (DM) subjects with refractory, skin-predominant involvement.

Objectives: To provide long-term safety and efficacy data in DM subjects in this study.

Methods: Subjects who completed Part A were eligible to receive oral lenabasum 20 mg BID in an open-label extension (OLE) that assessed safety and efficacy at 4 weeks, then every 8 weeks.

Results: 20/22 (90.9%) eligible subjects received open-label lenabasum, following a mean interval of 31 weeks from end of Part A, during which when they received only standard-of care, to start of OLE during which lenabasum 20 mg BID was added. 17/20 (85.0%) subjects were on stable baseline

immunosuppressive drugs. At the time of data cut-off, all subjects who entered OLE completed 12 months of dosing. Nineteen/20 (95%) of subjects experienced at least 1 AE, with 59 AEs occurring among the subjects during the OLE to date. The majority of AEs were mild ($n = 16$, 80%), with 1 severe AE (fatigue) considered unrelated to lenabasum reported. AEs occurring in ≥ 2 subjects were: dermatomyositis worsening, dizziness, fatigue, herpes zoster, nasopharyngitis, nausea, upper respiratory tract infection, and urinary tract infection. No serious AEs related to lenabasum have been reported. Improvement was seen in multiple physician- and patient-reported efficacy outcomes; selected outcomes are presented in Figure 1. Mean (SE) changes from study start at Week 52 in the OLE were: CDASI activity score = -17.6 (SD), Patient Skin Activity VAS = -2.6 (SD); Skindex-29 Symptoms Domain = -21.6 (SD); Patient Itch VAS = -2.8 (SD); Physician Overall Disease VAS = -3.0 (SD); and Patient Pain VAS = -2.3 (SD). Improvements were seen in other efficacy outcomes. 12 subjects had no changes in immunosuppressive drugs during the OLE, 3 reduced chronic steroids, 2 reduced mycophenolate, 3 were switched from methotrexate to mycophenolate, 1 started methotrexate, and 1 had a burst and taper of steroids.

Figure 1. Change from Baseline in Selected Efficacy Outcomes in OLE of Phase 2 Trial JBT101-DM-001

Conclusion: Lenabasum continues to have a favorable safety and tolerability profile in the OLE of the Phase 2 trial JBT101-DM-001 with no serious AEs or study discontinuations related to lenabasum. The CDASI activity score and multiple other physician and patient-reported outcomes improved, although limitations of attributing efficacy to lenabasum in the setting of open-label dosing is acknowledged. These data support further testing of lenabasum for the treatment of DM, and a Phase 3 study of lenabasum in DM has started.

Disclosure of Interests: Victoria Werth: None declared, David Pearson: None declared, Joyce Owaka: None declared, Rui Feng: None declared, Josef Simon Concha: None declared, Basil Patel: None declared, Emily Hejazi: None declared, Caitlin Cornwall Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc., Scott Constantine Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc., Nancy Dgetluck Employee of: Corbus Pharmaceuticals, Inc., Barbara White Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc.

DOI: 10.1136/annrheumdis-2019-eular.3397

OP0242

SAFETY PROFILE OF NINTEDANIB IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE AND IDIOPATHIC PULMONARY FIBROSIS

Kristin Highland¹, Oliver Distler², Martina Gahlemann³, Arata Azuma⁴, Aryeh Fischer⁵, Maureen Mayes⁶, Ganesh Raghu⁷, Wiebke Sauter⁸, Mannaig Girard⁹, Veronika Kohlbrenner¹⁰, Emmanuelle Clerisme-Beaty¹¹, Susanne Stowasser¹¹, Masataka Kuwana¹², Toby M Maher¹³, SENSICIS trial investigators. ¹Respiratory Institute, Cleveland Clinic, Cleveland, Ohio, United States of America; ²Dept of Rheumatology, University Hospital Zurich, Zurich, Switzerland; ³Boehringer Ingelheim (Schweiz) GmbH, Basel, Switzerland; ⁴Dept of Pulmonary Medicine and Oncology, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan; ⁵University of Colorado School of Medicine, Denver, Colorado, United States of America; ⁶Division of Rheumatology and Clinical Immunogenetics, University of Texas McGovern Medical School, Houston, Texas, United States of America; ⁷University of Washington, Seattle, United States of America; ⁸Boehringer Ingelheim Pharma GmbH and Co. KG, Biberach an der Riss, Germany; ⁹Boehringer Ingelheim France S.A.S., Reims, France; ¹⁰Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, Connecticut, United States of America; ¹¹Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; ¹²Dept of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan; ¹³National Heart and Lung Institute, Imperial College London, UK, and National Institute for Health Research Clinical Research Facility, Royal Brompton Hospital, London, United Kingdom

Background: Nintedanib has been investigated in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) in the SENSICIS trial and idiopathic pulmonary fibrosis (IPF) in the INPULSIS trials. These patient populations differ in age, sex, disease characteristics and comorbidities.

Objectives: To compare the safety and tolerability of nintedanib in patients with SSc-ILD and IPF.

Methods: Adverse events that occurred over 52 weeks of treatment in the SENSICIS and INPULSIS trials were assessed descriptively in subjects who received ≥ 1 dose of trial drug.

Results: A total of 576 subjects were treated in the SENSICIS trial (288 nintedanib; 288 placebo) and 1061 in the INPULSIS trials (638 nintedanib; 423 placebo). At baseline, mean (SD) age was 54.0 (12.2) and 66.8 (8.0) years in SENSICIS and INPULSIS, respectively. The proportion of males was 24.8% and 79.3%, respectively. Over 52 weeks, 19.4% and 10.8% of patients treated with nintedanib and placebo discontinued treatment in SENSICIS, compared with 24.5% and 18.9% of patients treated with nintedanib and placebo in INPULSIS. Gastrointestinal adverse events were the most frequently reported adverse events with nintedanib and, as expected based on the underlying disease, were more frequent in patients with SSc-ILD than IPF in both treatment groups (Table). Diarrhoea adverse events were reported in 75.7% and 31.6% of patients treated with nintedanib and placebo in SENSICIS, and 62.4% and 18.4% of patients treated with nintedanib and placebo in INPULSIS, respectively.

	SENSICIS	INPULSIS
	Nintedanib (n=288)	Placebo (n=288)
Diarrhoea	218 (75.7)	91 (31.6)
Nausea	91 (31.6)	38 (13.2)
Vomiting	71 (24.7)	30 (10.4)
Nasopharyngitis	34 (11.8)	49 (17.0)
Cough	34 (11.8)	85 (29.7)
Upper respiratory tract infection	27 (9.4)	42 (14.6)
Decreased appetite	27 (9.4)	42 (14.6)
Upper respiratory tract infection	27 (9.4)	42 (14.6)
Abdominal pain	27 (9.4)	42 (14.6)
Pharyngitis	27 (9.4)	42 (14.6)
Congestive	27 (9.4)	42 (14.6)
Progression of IPF*	27 (9.4)	42 (14.6)
Death due to	27 (9.4)	42 (14.6)

*Data shown are n (%) of patients with ≥ 1 such event. Table shows adverse events reported in $\geq 10\%$ of patients in any of the treatment groups shown. Adverse events are listed by preferred term in the Medical Dictionary for Regulatory Activities (MedDRA). *Corresponds to MedDRA term "IPF" which included disease worsening and acute exacerbations.

Conclusion: The safety and tolerability profile of nintedanib in patients with SSc-ILD is similar to that observed in patients with IPF.

Disclosure of Interests: DOI: 10.1136/annrheumdis-2019-eular.3237

OP0243

EFFICACY OF PIRFENIDONE IN SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE – A RANDOMISED CONTROLLED TRIAL

Nupoor Acharya¹, Debasish Mishra¹, Sahajal Dhoria², Varun Dhir¹, Sanjay Jain¹, Shifali Khanna Sharma¹. ¹Post Graduate Institute of Medical Education and Research, Chandigarh, Internal medicine, Division of Rheumatology, Chandigarh, India; ²Post Graduate Institute of Medical Education and Research, Chandigarh, Pulmonary Medicine, Chandigarh, India

Background: Interstitial lung disease (ILD) is a major cause of morbidity and mortality in systemic sclerosis (SSc). (1) Lung fibrosis in systemic sclerosis shares