of neopterin was well correlated with the level of ferritin ($r=0.95$), IL-18 ($r=0.77$) and soluble IL-2 receptor ($r=0.75$).

Conclusions: Anti-MDA5 antibody titer is useful if the patients could reach and maintain the remission or not. Serum neopterin level is useful to predict the clinical status at present for therapeutic indication.

References:

[1] Matsushita, et al. Br J Dermatol. 2016 Jul 25. doi: 10.1111/bjd.14882.
[2] Xu Y, et al. Clin Rheumatol. 2016; 35: 113–6.
[3] Enomoto Y et al. Arthritis Res Ther. 2017;19:9. doi:10.1186/s13075-016-1214-8.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4880

FRI0409 OSTONECROSIS OF THE LUNATE BONE ASSOCIATED TO SYSTEMIC SCLEROSIS

M. Llop Vilaltella, S. Zegarra Mondragón, W.A.A. Sifuentes Giraldo, C. de la Puente Bujidos, M. Vázquez Díaz. *Rheumatology, Ramon y Cajal University Hospital, Madrid, Spain*

Background: Osteonecrosis of the lunate bone (OLB), also known as Kienböck's disease, is a rare disorder that has been recently reported in several patients with systemic sclerosis (SSc)¹, but still it is not clear if this is only a coincidence of 2 rare disorders or whether OLB is a potentially under-recognized manifestation of SSc.

Objectives: To describe the clinical features of patients with SSc seen in a Spanish tertiary care center, who develop OLB.

Methods: We performed a retrospective observational study that included patients followed in our center between January 2010 and December 2015. Demographic data, clinical and laboratory features, risk factors for osteonecrosis, imaging, treatment and outcome were collected.

Results: A total of 115 SSc patients were identified and 4 of them (3.47%) developed OLB. Mean age of these patients was 59.5 (range: 52–73), being all women. 2 cases were limited cutaneous SSc (lcSSc) and 2 cutaneous diffuse SSc. 3 cases showed anticentromere antibodies and 1 anti-topoisomerase I antibodies, but none presented anticardiolipin antibodies nor had previous thrombotic events. Mean disease duration was 13.5 years (range: 7–17). One patient was ex-smoker, but none had alcohol consumption, and one case was hypertensive. All patients had vascular manifestations (severe Raynaud phenomenon, digital ulcers in treatment with endothelin antagonists and perfusion of iv prostaglandins, and one case had critical digital ischemia); all the patients showed calcinosis in the upper limbs, and they also had joint involvement (50%), gastrointestinal (100%), and pulmonary (50%) manifestations. History of prolonged corticosteroid therapy at low doses (prednisone 5–10 mg/day) was present in all cases and was discontinued one year before the onset of osteonecrosis in one case. OLB was unilateral right in 3 cases and bilateral in one case. The patients presented with clinical pain and/or swelling in the affected wrist in the months prior to diagnosis of OLB, which was evidenced by simple radiography, MRI and bone scintigraphy. One of the cases also showed extensive synovitis in the affected wrist and another one developed collapse of the lunate bone with displaced fragment and edema. Treatment was surgical in 25% of the cases (proximal carpectomy), and conservative in the rest. Among the total SSc population studied there was another case of lcSSc presenting osteonecrosis of the left tarsal scaphoid bone.

Conclusions: A total of 15 cases of OLB associated to SSc have been reported to date, so it could be an underestimated disease-associated feature of SSc. It has been suggested that its etiology is linked to SSc-related vasculopathy and all our cases had evidence of severe vasculopathy. The location and vascularization of the lunate bone should be taken into account, since no case developed osteonecrosis in other common locations despite corticotherapy, and complete occlusion of the distal ulnar artery has been reported in 3 cases of the literature. The presence of pain, with or without wrist inflammation in SSc patients should make us consider OLB, which is probably more frequent than expected, especially when there is evidence of severe SSc-related vasculopathy.

References:

[1] Frerix M, et al. Is osteonecrosis of the lunate bone an underestimated feature of systemic sclerosis? A case series of nine patients and review of literature. *Semin Arthritis Rheum.* 2016;45:446–54.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5965

FRI0410 PREDICTORS OF MORBIDITY AND MORTALITY IN PATIENTS WITH EARLY SYSTEMIC SCLEROSIS: LONG-TERM FOLLOW-UP FROM A SINGLE CENTRE INCEPTION COHORT STUDY

S. Panopoulos, V.-K. Bournia, G. Konstantonis, K. Fragiadiaki, P.P. Sfikakis, M.G. Tektonidou. *First Department of Propedeutic and Internal Medicine and Joint Academic Rheumatology Program, National and Kapodistrian University, Medical School, Athens, Greece*

Background: Several studies have investigated the predictors of morbidity and mortality in Systemic sclerosis (SSc). However long-term follow-up data from inception cohorts of early SSc patients are limited.

Objectives: To identify predictors of morbidity and mortality in a single centre inception cohort of early SSc patients at long-term follow-up.

Methods: Our inception cohort comprised SSc patients who fulfilled the American College of Rheumatology criteria, were recruited within 12 months of disease onset and followed prospectively for at least 3 years. Clinical manifestations, laboratory and lung function tests were recorded for each patient at baseline and at 3rd and 6th years of follow up. Multivariate regression analysis and Cox proportional hazard models were used to identify predictors (clinical manifestations, laboratory and lung function tests at baseline) of morbidity and mortality in SSc, respectively.

Results: A total of 114 patients (96 female, mean age at diagnosis 48.1±13.5 years, 53 diffuse SSc subtype) were included in the study, from January 1997 to December 2012. All patients were followed for at least 3 years and 84 patients for at least 6 years. Twenty (17.5%) of 114 patients died during a mean follow up of 101.8±48.5 months. In multivariate regression analysis predictors for major SSc outcomes at 6 years were: diffuse subtype (OR: 6.2, $p=0.015$), anti-scl-70 positivity (OR: 3.9, $p=0.05$), esophageal involvement (OR: 6.5, $p=0.017$) and digital ulcers (OR: 8.6, $p=0.003$) at baseline for the development of pulmonary fibrosis (PF). The presence of digital ulcers at baseline was a predictor for the development of arrhythmias (OR: 3.7, $p=0.05$) and the presence of arrhythmias at baseline for the development of pulmonary hypertension (PH) (OR: 5.4, $p=0.039$). Cox proportional hazard models multivariate analysis revealed that independent predictors of mortality were: male gender (HR: 3.3, $p=0.023$), diffuse type (HR: 8.7, $p=0.004$), PF at baseline (HR: 2.7, $p=0.05$), PH based on echocardiography at baseline (HR: 12.7, $p=0.001$) FVC <80% (HR: 2.74, $p=0.042$) and DLCO <60% of predicted value at baseline (HR: 2.97, $p=0.019$).

Conclusions:

Results from long-term follow-up data from a single centre inception cohort indicate that diffuse SSc subtype, anti-Scl-70 positivity, esophageal involvement and digital ulcers at baseline are independent predictors for the development of PF. Male gender, diffuse subtype, PF, PH and decreased FVC and DLCO at baseline are prognostic factors of mortality.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6656

FRI0411 COADMINISTRATION OF BOSENTAN HAS NO EFFECT ON THE PHARMACOKINETICS OF NINTEDANIB

S. Wind¹, G. Simons¹, J. Bertulis¹, C. Coeck². ¹Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany; ²SCS Boehringer Ingelheim Comm. V., Brussels, Belgium

Background: Nintedanib is a potent intracellular inhibitor of tyrosine kinases that has been approved for the treatment of idiopathic pulmonary fibrosis and is being investigated as a treatment for interstitial lung disease associated with systemic sclerosis (SSc-ILD). Bosentan is a dual endothelin receptor antagonist used in the treatment of pulmonary arterial hypertension, which is a common comorbidity of SSc-ILD.

Objectives: To ascertain the effect of bosentan on the pharmacokinetics of nintedanib.

Methods: In an open-label, single-centre study, healthy male subjects aged ≥18 and ≤55 years with a body mass index (BMI) ≥18.5 and ≤29.9 kg/m² received a single dose of nintedanib 150 mg alone (period 1) followed by bosentan 125 mg twice daily (bid) for 8 days (bosentan loading dose phase on days 1–6) with a single dose of nintedanib 150 mg on day 7 (period 2). The primary endpoints were the maximum plasma concentration (C_{max}) of nintedanib and the area under the plasma concentration-time curve from time 0 to the last quantifiable concentration (AUC_{0-tz}) of nintedanib. The secondary endpoint was the AUC from time 0 extrapolated to infinity ($AUC_{0-∞}$) for nintedanib.

Results: Thirteen subjects (12 White; mean [SD] age 35.0 [9.8] years and BMI 24.5 [2.5] kg/m²) were treated. All subjects completed the planned observation period. Based on C_{max} , AUC_{0-tz} and $AUC_{0-∞}$, exposure to nintedanib was similar after a single dose of nintedanib given alone or in combination with multiple doses of bosentan 125 mg bid (Table). Adverse events were reported in 4 subjects (30.8%) on nintedanib alone (period 1), 4 subjects (30.8%) on bosentan 125 mg bid (days 1–6 of period 2) and 2 subjects (15.4%) after administration of bosentan with nintedanib (days 7 and 8 of period 2). All adverse events were mild in intensity.

	Nintedanib 150 mg alone	Nintedanib 150 mg coadministered with multiple doses of bosentan 125 mg bid	Adjusted geometric mean ratio (90% CI)
C_{max} (ng/mL)	21.9	22.7	103.4 (86.1, 124.0)
AUC_{0-tz} (ng·h/mL)	194.9	192.6	98.9 (91.3, 107.0)
$AUC_{0-∞}$ (ng·h/mL)	204.3	208.3	102.0 (94.9, 109.6)

Conclusions: Coadministration of bosentan 125 mg bid had no effect on the pharmacokinetics of a single dose of nintedanib 150 mg.

Disclosure of Interest: S. Wind Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG, G. Simons Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG, J. Bertulis Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG, C. Coeck Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG
DOI: 10.1136/annrheumdis-2017-eular.5849

FRI0412 THE POSITIVE EFFECT OF RITUXIMAB IN PULMONARY FIBROSIS OF SYSTEMIC SCLEROSIS

P. Kirytopoulos¹, T. Michailidis¹, E. Papchianou¹, M. Charalampidis², P. Dimitriadis³, A. Agorastos⁴. ¹Department of Internal Medicine, General Hospital of Veria, Veria; ²Gastroenterology Department, Theageneio Hospital of Thessaloniki, Thessaloniki; ³Health Center of Alexandria, Alexandria, Greece; ⁴Oncology Department, St. Thomas Hospital, London, United Kingdom

Background: Pulmonary fibrosis is one of the gravest manifestations of Systemic Sclerosis (SSc) and conventional DMARDs therapy has not shown any particular positive effect.

Objectives: Our goal was to see whether the elimination of B-lymphocytes through use of anti-CD20 Mab, Rituximab (RTX) would offer to the improvement of the pulmonary function of SSc patients.

Methods: We studied 23 SSc patients with pulmonary fibrosis, who received treatment with RTX (n=12) or DMARDs treatment (n=11) for 1 to 3 years (1,9 years). Conventional therapy included azathioprine (n=4), mycophenolate (n=6) and methotrexate (n=2). RTX-treated patients were recorded with FVC improvement in the first year of treatment (FVC 81,3 +/- 12,6 vs FVC 87,4 +/- 11,3 out on the onset of the study and at the first year respectively, p=0,02) when on the other hand DMARDs treated patients didn't show any FVC improvement at all.

Results: All RTX-treated patients did not present any lung HRCT deterioration imaging, in contrast to DMARDs-treated patients who were also submitted to lung HRCT each year of the study, all showing signs of CT imaging deterioration. Similar findings, as far as FVC was concerned, were recorded at the 3rd year of the study (RTX patients, n=6 and DMARDs patients, n=11). 3rd year RTX FVC was 92,6 +/- 13,2 vs 80,7 +/- 11,8 at the onset of the study, p=0,04 when DMARDs treated patients were all presented with worst 3rd year FVC compared to their primary FVC, p<0,01.

Conclusions: Our small cohort of SSc patients with pulmonary fibrosis shows that it is possible that rituximab may be proven helpful to at least prevent the deterioration of the interstitial pulmonary fibrosis of Systemic Sclerosis. The pathophysiology of this particular fibrosis and the possible molecular role of B-lymphocytes in the inversion of this procedure need yet to be further explored.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6398

FRI0413 ACUTE EFFECT OF ILOPROST ON PERIPHERAL CIRCULATION AS ASSESSED BY VIDEOCAPILLAROSCOPY AND 22-MHZ POWER DOPPLER ULTRASONOGRAPHY

T. Schioppo^{1,2}, A. Orenti^{1,3}, P. Boracchi^{1,3}, O. De Lucia², A. Murgo², P.L. Meroni^{1,2}, F. Ingegnoli^{1,2} on behalf of OPERA study group. ¹Università degli Studi di Milano; ²ASST Pini-CTO; ³Lab of Medical Statistics, Epidemiology and Biometry GA Maccacaro, Milan, Italy

Background: Vascular involvement is a hallmark of systemic sclerosis (SSc) and it is responsible for some of the most common complications of the disease such as Raynaud's phenomenon (Rp), digital ulcers (DUs) and pulmonary arterial hypertension. I.V. iloprost (ILO), a prostacyclin analogue, has been shown to be effective in reducing Rp severity, DUs healing and preventing [1].

Objectives: To assess the acute effect of ILO on acral circulation as assessed by nailfold videocapillaroscopy (NVC) and 22-MHz Power Doppler ultrasound (PDUS).

Methods: 44 SSc consecutive patients fulfilling the 2013 EULAR classification criteria were enrolled. Each patient was evaluated before and immediately after I.V. ILO administration (0.5–2.0 ng/Kg/min for 6 consecutive hours). PDUS was performed at the 3rd and 4th finger of the dominant hand after exclusion of ulnar artery occlusion (UAO). In case of UAO non-dominant hand was examined. Ultrasound investigation was performed with Esaote MyLab 70 XVG by means of linear array transducer (10–22 MHz). Power Doppler settings were standardized (Doppler frequency 14.3 MHz, Gain 55%, PRF 750 Hz). PDUS measurements included sagittal scan of nailbed and fingertip qualitatively graded from 1 (no signal) to 4 (marked hyperemia) [2], and resistivity index (RI) of ulnar and radial proper digital arteries. Capillary width (sum of capillary width/mm) was calculated by NVC with magnification 200X performed on two images of the same digits examined by PDUS.

Results: The study population included 44 SSc patients, 40 (90.9%) women, 35 (79.5%) limited cutaneous SSc, median age 60.2 years old and median disease duration 8 years. 19 (43.2%) had history of DUs, among them 15 had experienced more than one DUs and 1 had active DU at the moment of evaluation. Semiquantitative perfusion score of sagittal scan of nailbed and fingertip pre- and post-therapy are shown in Table 1.

Changes in RI and capillary width pre- and post-infusion are reported in Table 2.

Conclusions: A statistically significant post-infusion rise in RI, fingertip and

Table 1

	Pre-infusion		Post-infusion		OR (95% CI)
	%	Cumulate %	%	Cumulate %	
Fingertip PDUS					4.21 (2.12–8.35) p-value<0.001
Grade 1	29.55	29.55	14.77	14.77	
Grade 2	22.73	52.28	15.91	30.68	
Grade 3	12.50	64.78	12.50	43.18	
Grade 4	35.23	100	56.82	100	
Nailbed PDUS					8.96 (4.15–19.32) p-value<0.001
Grade 1	17.05	17.05	6.82	6.82	
Grade 2	34.09	51.14	13.64	20.46	
Grade 3	18.18	69.32	14.77	35.23	
Grade 4	30.68	100	64.77	100	

Table 2

	Pre-infusion	Post-infusion	Mean difference (95% CI)
Resistivity index	0.773	0.794	0.021 (0.005, 0.037) p-value=0.0122
Capillary width	247.5	257.9	12.321 (-2.528, 27.171) p-value=0.1077

nailbed PDUS grade were found. Capillary width was also increased, but it was not statistically significant. As such, these novel results indicate that ILO, alongside its clinical effect, is able to enhance vascularization even at the most peripheral levels.

References:

[1] Pope J et al. Cochrane Database Syst Rev. 2000;(2):CD000953.

[2] Newman JS et al. Radiology. 1996;198:582–584.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3849

FRI0414 CAN ECHOCARDIOGRAPHY REPLACE FOLLOW-UP CARDIAC CATHETERIZATION IN RE-EVALUATION OF PULMONARY ARTERIAL HYPERTENSION? A LONGITUDINAL SINGLE-CENTER STUDY OF 30 CONNECTIVE TISSUE DISEASE PATIENTS

V.-K. Bourنيا¹, I. Tsangaris², L. Rallidis², D. Konstantonis², A. Anthi², S. Orfanos², S. Panopoulos¹, P.P. Sfikakis¹. ¹First Department of Propedeutic Internal Medicine and Joint Rheumatology Program; ²Pulmonary Hypertension Clinic, Attikon University General Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Background: Transthoracic echocardiography (TTE) is well validated for initial assessment of connective tissue disease patients with suspected pulmonary arterial hypertension (PAH). However, in patients with PAH confirmed by the gold-standard method of right heart catheterization (RHC) the role of TTE in their follow-up is less known.

Objectives: To test the hypothesis that TTE can replace follow-up RHC in connective tissue disease-associated PAH.

Methods: This retrospective study included 30 consecutive patients with systemic sclerosis (n=24) and mixed connective tissue disease (n=6) (mean age±SD: 60±12 years, 87% women), in whom PAH was suggested by TTE and further confirmed by a baseline RHC [pulmonary artery systolic pressure (PASP): 56.8±19.1, range 25–90mmHg; pulmonary vascular resistance (PVR): 5.9±3.8, range 0.7–14.5 Wood units; cardiac output: 4.4±1.3, range 2–7.8 L/min]. All 30 patients underwent a second RHC and TTE at follow-up, after 11±6 (range 4–29) months. Ten patients had a 3rd follow-up RHC and TTE 22±7 (range 15–37) months from baseline, thus producing in all 50 pairs of baseline and follow-up measurements. By considering follow-up RHC as the gold-standard, we examined whether clinically meaningful hemodynamic changes (i.e. >15% change from baseline) in either RHC-derived PASP or PVR could be predicted by the corresponding changes from baseline in follow-up TTE. RHC and TTE were always performed, each, by the same examiner.

Results: In 68% of comparisons between baseline and follow-up, the latter TTE measurements could safely replace RHC in terms of PASP estimation. Using McNemar's test we confirmed that the two methods did not differ significantly (Table 1). When in addition to changes in PASP, PVR changes were also considered, follow-up TTE could again safely replace the second RHC in 70% patient retests (Table 2). Of note, baseline hemodynamic values or TTE measurements did not differ between patients in whom TTE could replace RHC and those in whom the results of the two methods at follow-up were divergent.

Table 1. McNemar's test comparing PASP estimated by repeat TTE to that measured by repeat RHC shows no difference between the two methods

Repeat TTE	Repeat RHC	
	Stable or improved PASP	Deteriorated PASP (>15%)
Stable or improved PASP	25	9
Deteriorated PASP (>15%)	7	9

P=NS (0.8).

Conclusions: In a study where operator-dependent methodological errors are limited we found that the majority of connective tissue disease patients with PAH