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.
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FRI0409 OSTEONECROSIS OF THE LUNATE BONE ASSOCIATED TO SYSTEMIC SCLEROSIS

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

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

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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/m^2 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 ($AUC_{0\text{-}tz}$) of nintedanib. The secondary endpoint was the AUC from time 0 extrapolated to infinity ($AUC_{0-\infty}$) for nintedanib.
Results: Thirteen subjects (12 White; mean [SD] age 35.0 [9.8] years and BMI 24.5 [2.5] kg/m^2) were treated. All subjects completed the planned observation period. Based on C_{max}, $AUC_{0\text{-}tz}$ and $AUC_{0-\infty}$, 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)
$AUC_{0\text{-}tz}$ (ng·h/mL)	194.9	192.6	98.9 (91.3, 107.0)
$AUC_{0-\infty}$ (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.