To investigate the possible effects of nintedanib in contrasting the transition of SSc fibrocytes into myofibroblasts and their profibrotic activity, through the reduction of specific myofibroblast phenotype markers and ECM protein production. The results seem to suggest fibrocytes as further possible target of the anti-fibrotic action of nintedanib in SSc.

References:

Disclosure of Interests: Stefano Soldano: None declared, Giulia Martinelli: None declared, Samuele Tardito: None declared, Sabrina Paolino: None declared, Massimo Patanè: None declared, Emanuele Gotelli: None declared, Claudio Corallo: None declared, Carmen Pizzorni: None declared, Alberto Sulli Grant/research support from: from: The affiliated company received grants from Research Foundation - Flanders (FWO), Belgian Fund for Scientific Research in Rheumatic diseases (FWRWO), Boehringer Ingelheim Pharma GmbH & Co and Janssen-Cilag NV, Consultant of: Boehringer-Ingelheim Pharma GmbH & Co, Speakers bureau: Actelion Pharmaceuticals Ltd, Boehringer-Ingelheim Pharma GmbH & Co and UCB Biopharma Srl, Maurizio Cutolo Grant/research support from: Bristol-Myers Squibb, Actelion, Celgene, Consultant of: Bristol-Myers Squibb, Speakers bureau: Sigma-Aldrich.

AB0169
ENHANCED PLATELET ACTIVATION AMONG PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a chronic connective tissue disease characterized by microvascular alterations, dysregulated immune response and fibrosis [1,2]. Myofibroblasts are alpha-smooth muscle actin (alphaSMA) cells and play a crucial role in fibrosis, through the excessive synthesis and deposition of extracellular matrix (ECM) proteins, in particular fibronectin (FN) and type I collagen (COL1) [3]. Despite myofibroblasts primarily derive from resident fibroblasts transition and differentiation, another important source is represented by circulating fibrocytes [4]. Nintedanib is a tyrosine kinase inhibitor approved for the treatment of idiopathic pulmonary fibrosis that interferes with the signalling pathways involved in the pathogenesis of fibrosis [5].

Objectives: To compare the level of PLT activation in SSc and to correlate with physical findings.

Methods: Blood was sampled from 12 patients participating in the randomized, clinical trial LIGHT (ClinicalTrials.gov NCT040045743) evaluating the safety and efficacy of bermekimab in SSc. Patients had to meet the 2013 ACR/EULAR classification criteria and have a modified Rodnan skin severity index greater than 35.20. Sampling was done before allocation to treatment. Nil patient was on DMARDs. Ten healthy donors were used for comparison. Citrated whole blood was exposed to 0.1 mM adenosine diphosphate (ADP) to stimulate PLT. Total platelet populations were defined as CD42b-positive population; P-selectin (CD62p) served as an activation marker.

Results: Expression of 42b(+)/62p(+) PLT was greater among patients (Fig. 1). Mean fluorescence intensity (MFI) of 42b(+)/62p(+) PLTs was 0.16 +/- 0.08 in comparators and 0.51 +/- 0.07 in patients (p = 0.015). Negative correlation was found between the expression of 42b(+)/62p(+) on PLT and mRSS (r = -0.73, p = 0.028). Patients with grade 2 findings at capillaroscopy had greater expression of 42b(+)/62p(+) than patients with grade 3 findings (45.9 +/- 7.2% vs 27.2 +/- 6.7%: p = 0.041).

References: