SERUM INTERFERON SCORE PREDICTS CLINICAL OUTCOME AT 12 MONTHS IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS AS MEASURED BY GLOBAL RANKED COMPOSITE SCORE (GRCS) AND COMPOSITE RESPONSE INDEX IN SSc (CRISS)

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Background: Systemic sclerosis (SSc) is a disease orphan of effective disease modifying agents. The diffuse cutaneous subset (dcSSc) is targeted in most clinical trials. Nevertheless, the high variability in clinical outcome at 12 months is limiting effective RCTs design and interpretation. The Global Ranked Composite Score (GRCS) and the Composite Response Index in SSc (CRISS) are the most recent attempts to capture overall response to treatment in dcSSc [1, 2]. Activation of interferon type 1 (IFN) pathway is associated with severe clinical manifestations in SSc. Several studies have indicated that the serum concentration of CCL2, CCL8, CCL19, CXCL9, CXCL10 and CXCL11 are the most relevant to disease progression [3,4].

Objectives: Here we aimed to determine whether IFN pathway activation measured by a serum test could be used to stratify patients with dcSSc for severe clinical outcome at 12 months as measured by GRCS and CRISS.

Methods: Serum concentration of CCL2, CCL8, CCL19, CXCL9, CXCL10, and CXCL11 was measured by Luminex xMAP technology (Myriad RBM) in 143 SSc patients and 35 healthy controls (HC). IFN score was calculated as the average of the natural logarithm of the above chemokines. IFN score mean + 2STDV in the HC sera was adopted as cut off for IFN LOW (IFN LO) patients.

Results: There was no difference associated with disease subset or duration. To simulate enrollment criteria in a RCT we analyzed the 12 month outcomes of the dcSSc patients with ≤6 years disease duration. Sixty-six 12-month outcome data were available. 37 were IFN HI and 29 IFN LO at baseline. The IFN HI group had a higher mRSS (median 9.5 vs 5, p=0.03), CRP (10.2 vs 5, p=0.003) and NT-proBNP (195 vs 50, p=0.001). We recorded 7 deaths for SSC and 5 lung failures (3 FVC drop, 2 DLCO drop) in the IFN HI group and 1 death and 1 lung failure (1 FVC drop, 1 DLCO drop) in the IFN LO group. In 15/58 (26%) patients with protein-IP AMA pattern we confirm the presence of AMAs in 13/15 (87%) patients with AMA protein-IP pattern but without clinical and histological evidence in 12/58 (21%) patients. We report a complete or partial protein-IP pattern of 75-50-40-34kD bands corresponding to the 4 proteins of the PDC complex recognized by AMA. In these sera we performed IIF and IP-WB to confirm the identity of these bands, by using established protocols. Clinical charts were used to analyze clinical and laboratory data for possible statistical correlation. Results: In 15/58 (26%) patients with protein-IP pattern we confirm a diagnosis of PBC, and all of them had a diagnosis of SSc without additional rheumatic disease. Their expression of the PDC subunits is variable by IP-WB (Figure panel A), but this variability is not associated with specific clinical and laboratory features. In the 42/58 (72%) cases of SSc patients with limited variant and serum anti-centromere antibodies (ACA). Indirect immunofluorescence (IIF) shows the cytoplasmic pattern that characterizes AMA positivity, but it is usually performed when a suspect of PBC is already present. Protein-immunoprecipitation (IP) and IP-Western Blot (WB) have the advantage of 1) identify AMA in an early screening phase, before the onset of PBC and liver function abnormalities; 2) detect the proteins that constitute the pyruvate dehydrogenase complex (PDC) complex (the subunits E1a, E1β, E2/E3, and E3βP) which seem to be associated to different risk of PBC onset.

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Fig 1
CONCLUSION: The expression of the PDC antigenic components is variable both in SSc patients withAMA positive PBC and in SSc patients AMA positive without PBC or altered liver function tests, but we could not identify a clinical significance of this variability. It may be necessary to maintain a strict follow-up of these patients and to perform longitudinal studies to determine the prognostic value of this variable expression of PDC components in the onset of PBC.

REFERENCES:

Disclosure of Interests: Angela Ceribelli: None declared, Natasa Isailovic: None declared, Carolina Gorilino: None declared, Elena Generali: None declared, Marta Caprioli: None declared, Piercarlo Sarzi-Puttini: None declared, Minoru Satoh: None declared, Carlo Selm Gran research support from: AbbVie, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, Alfa-Sigma, Biogen, Bristol-Myers Squibb, Celgene, Eli-Lilly, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genezyme, UCB, Speakers bureau: AbbVie, Alfa-Sigma, Biogen, Bristol-Myers Squibb, Celgene, Eli-Lilly, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genezyme, UCB


FRIO317

NOVEL CLASSIFICATION OF IDIOPATHIC INFLAMMATORY MYOPATHIES BASED ON DISTINCTIVE FEATURES AND AUTOANTIBODIES: ANALYSIS OF 67 KOREAN PATIENTS

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Background: Since Bohan and Peter first described their diagnostic criteria for idiopathic inflammatory myopathies (IMM) in 1975, new discoveries such as myositis-specific and myositis-associated autoantibodies (Abs) have been made.

Objectives: To investigate correlations between specific myositis Abs and clinical subsets of IMM using the sera of definite deramatomyositis (DM, n=36), definite polymyositis (PM, n=25), amyopathic DM (n=4), DM sine dermatitis (n=1), and immune mediated necrotizing myopathy (IMNM, n=1). Patients were classified based on three classifications: 1) novel clinicosorologic classification suggested by Troyanov et al. in 2017, 2) 2017 EULAR/ACR classification criteria, 3) 2004 European neuromuscular center (ENMC) criteria, Associations of myositis Abs and immune mediated necrotizing myopathy (IMNM, n=1). Patients were classified based on three classifications: 1) novel clinicosorologic classification suggested by Troyanov et al. in 2017, 2) 2017 EULAR/ACR classification criteria, 3) 2004 European neuromuscular center (ENMC) criteria.

Methods: We conducted a multicenter cohort study including 67adult patients (age>18 years) who have been diagnosed as IMM by ENMC criteria. Immunoblot assay with Euroline strip (EURALIMMUN, Germany) was performed using the sera of definite deramatomyositis (DM, n=36), definite polymyositis (PM, n=25), amyopathic DM (n=4), DM sine dermatitis (n=1), and immune mediated necrotizing myopathy (IMNM, n=1). Patients were classified based on three classifications: 1) novel clinicosorologic classification suggested by Troyanov et al. in 2017, 2) 2017 EULAR/ACR classification criteria, 3) 2004 European neuromuscular center (ENMC) criteria, Associations of myositis Abs and immune mediated necrotizing myopathy (IMNM, n=1). Patients were classified based on three classifications: 1) novel clinicosorologic classification suggested by Troyanov et al. in 2017, 2) 2017 EULAR/ACR classification criteria, 3) 2004 European neuromuscular center (ENMC) criteria.

Results: The distribution of the various IMM differed strikingly from those using the 3 classifications (Fig1). According to the 2004 ENMC classification and 2017 EULAR/ACR classification criteria, DM and PM was the most and the second frequent entities (DM: 55.2%, 56.7%; PM: 35.8%, 37.3%). But, using the new clinicosorologic classification, overlap myositis (OM) is the major type of IMM and the frequency of PM is significantly decreased. Anti-ARS Abs specificity included anti-Jo-1 (6.4%), -OJ (4.6%), -EJ (6.2%), -PL (7.3%), and -PL-12 (6.4%). Interstitial lung disease was closely associated with anti-MDA5 and anti-ARS Abs, while DM-specific skin lesion was frequently observed in patients with anti-TIF1γ and anti-ARS Abs. Seven patients with cancer-associated DM were identified. They were positive for anti-TIF1γ (5/7) and anti-SRP (3/7) (table 1).