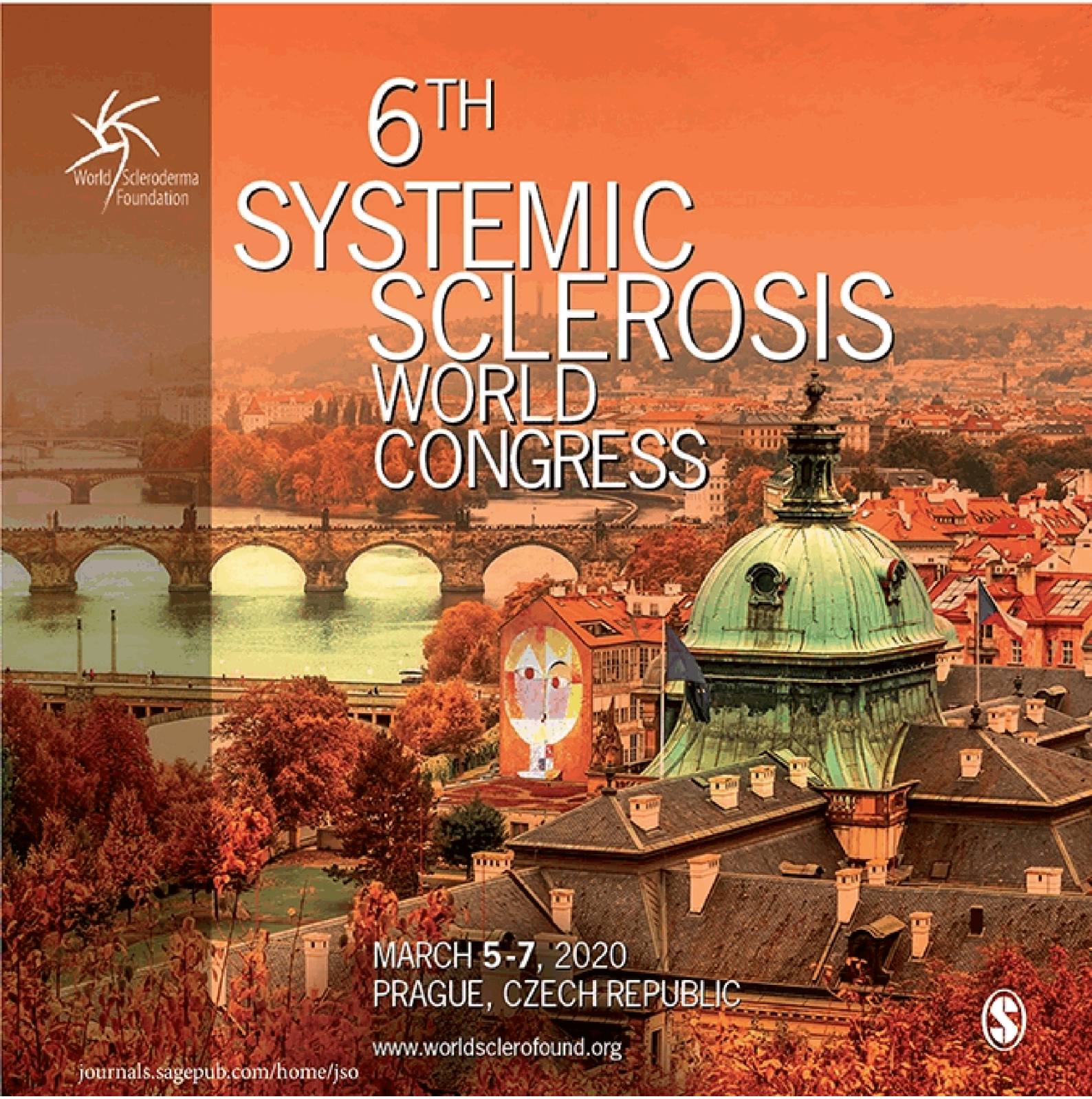
JSRD
Journal of Scleroderma and Related Disorders



p=0.08). There was highly significant difference in the sTIM-3 levels between healthy controls (mean 4721.9 ng/ml) and dcSSc patients (8728.0 ng/ml, p<0.0001). There was a trend for association between anti-Scl70 (ATA) positivity and sTIM-3 levels (p=0.0944). Hb levels showed significant association with sTIM-3, with higher Hb levels associated with lower sTIM-3 levels (p=0.02).

Conclusions: Soluble co-inhibitors are differentially expressed in early dcSSc and correlate with key clinical features. Our experiments show that the Co-IRs are selectively affected by certain immunosuppressive therapies, which may reflect pathway dysregulation and act as biomarkers for evaluation of disease severity and activity.

P.058

FEATURES OF THE DEBUT OF SYSTEMIC SCLERODERMA ARE ABLE TO DETERMINE THE DISEASE PATTERN

A. Aleksandrov[1,2], L. Shilova[1], V. Aleksandrov[1,2]

[1]Volgograd State Medical University, Department of Hospital Therapy, Volgograd, Russia, [2]Research Institute for clinical and experimental rheumatology named after A.B. Zborovsky, Volgograd, Russia

Introduction: The importance of early detection of systemic scleroderma (SSc) is due to the complexity of the diagnosis at the early stages of the disease.

Objective: to study the effect of various options for the onset of SSc on the dynamics of the clinical picture of the disease, taking into account the clinical, laboratory and instrumental features of the early SSc.

Material and Methods: The study included 83 patients with a reliable diagnosis of SSc (97.6% of women, mean age 50.3±11.9), 30 patients with localized scleroderma, 30 patients with primary Raynaud's syndrome (PRS). A complete clinical, laboratory and instrumental examination was carried out, including capillaroscopy of the vessels of the nail bed. A limited form of the disease was determined in 67.5% of patients with SSc, a diffuse form in 32.5%, and in 11 cases an overlap syndrome was noted. Early scleroderma was diagnosed in 33.7% of patients.

Results: The study of the SSc debut showed that in 34.9% of cases the disease started with skin syndrome, in 48.2% with Raynaud's syndrome, in 16.9% with articular syndrome. The average diagnosis term for SSc was 3.1±1.01 years; later diagnosis was observed in patients with Raynaud's syndrome and plaque form of skin manifestations.

The number of capillaries of the nail bed in the group of patients with early SSc averaged 6.5±2.0, avascular zones - 2.0±1.17, bush-shaped capillaries - 1.53±1.23, dilated capillaries - 1.9±1.54, extravasates - 0.12±0.33. When comparing these indicators with early SSc, differences were obtained with patients with localized scleroderma (p<0.001 for all indicators); with patients with PRS, significant differences were revealed in the number of capillaries (M-W U-test=35.5, p=0.0003), the presence of avascular zones (M-W U-test=35.0, p=0.0003) and bush-shaped deformity (MW U-test=49.5, p=0.001).

Changes in laboratory parameters (increase in ESR in 57.1% of cases, CRP - in 21.4%, decrease in hemoglobin - in 25%) in patients with early SSc indicated the inflammatory processes in the early stages of the disease. Immunological changes were characterized by an increase in the titer of antinuclear antibodies in 89.3% of patients; these changes were detected in the first 3 years of the disease in 90% of cases.

Conclusions: The early form of SSc has its own clinical, laboratory and instrumental features that can determine different dynamics of the clinical picture of the disease. Careful attention is required to all patients with Raynaud's syndrome and localized forms of skin manifestations, as well as screening for the presence of antinuclear antibodies.

P.059

A NOVEL HUMANIZED MOUSE MODEL OF SKIN FIBROSIS

G. Moroncini[1], C. Paolini[1], F. Orlando[2], A. Grieco[1], S. Agarbati[1], C. Tonnini[1], S. Svegliati Baroni[1], T. Spadoni[1], A. Funaro[3], E. Avvedimento[4], M. Provinciali[2], A. Gabrielli[1]

[1]Università Politecnica delle Marche, Dipartimento di Scienze Cliniche e Molecolari, Ancona, Italy, [2]IRCCS - INRCA, Servizio di Allevamento e Sperimentazione Animale, Polo Scientifico Tecnologico, Ancona, Italy, [3]Università di Torino, Dipartimento di Scienze Mediche, Torino, Italy, [4]Università Federico II, Dipartimento di Medicina Molecolare e Biotecnologie Mediche, Napoli, Italy

Introduction: Platelet Derived Growth Factor (PDGF) Receptor alpha (PDGFR alpha) is a target of the autoimmune response in scleroderma (SSc). Both total serum IgG (SSc-IgG) and anti-PDGFR alpha antibodies cloned from memory B cells of SSc patients (SSc-Mabs) demonstrated the ability to increase collagen gene transcription in healthy donor skin fibroblasts and to induce fibrosis ex vivo, in skin grafts in SCID mice. In order to replicate these findings in vivo, we generated human PDGFR alpha-transgenic mice.

Material and Methods: Full length human PDGFR alpha cDNA was knocked-in into the ubiquitously expressed Rosa26 locus on mouse chromosome 6. Correctly targeted C57BL/6 ES cell clones were selected for blastocyst microinjection, followed by chimera production. F2 heterozygous C57BL/6-hPDGFR alpha transgenic mice were used to establish the colony. Twelve weeks-old male mice were injected into the back skin at days 0, 3, 6 and 9, either with 0.02 mg/ml of SSc-Mabs (VHPAM-VK16F4 or