After four perfusions (weeks 0, 2, 6, 10) clinical improvement (healing of skin necrosis, reduced dyspepsia and dyspnoea, increased general feeling, reduced VAS from 80 to 20, increased opening of the mouth, increased movement of the hands and fingers) permitted a slow reduction of the daily steroid dose.

Objectives ./.

Methods ./.

Results ./.

Conclusion This is a case with positive therapeutic onset of infliximab (remicade) in a case with systemic sclerosis.

FRI0184 ANGIOTENSIN-CONVERTING ENZYME AND ANTI-ANGIOTENSIN-CONVERTING ENZYME ANTIBODIES IN SYSTEMIC SCLEROSIS

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Background

Objectives To investigate the levels of angiotensin-converting enzyme (ACE) and anti-angiotensin-converting enzyme antibodies (ACEab) in patients with systemic sclerosis (SSc).

Methods Thirty five patients with systemic sclerosis, age $50,0 \pm 11,7$ (mean $\pm$ SD), range 27–71 years, were included in the study. Duration of disease ranged from 1 to 20 years, means $7,0 \pm 5,2$. Thirteen pts had diffuse systemic sclerosis (dSSc), twenty two had limited systemic sclerosis (lSSc). Ten healthy subjects were selected as controls. Spectrofluorimetry for detection of ACE and ELISA for ACEab were used.

Results We revealed the two-fold lower levels of ACE in SSc pts compared with controls ($0,022 \pm 0,021$ vs $0,044 \pm 0,028$; $\delta = 0,012$). There were no differences in ACE values observed between the dSSc and lSSc groups ($0,019 \pm 0,017$ and $0,024 \pm 0,024$ respectively). The lowest levels of ACE were found in SSc pts treated with inhibitors of ACE ($0,013 \pm 0,010$), but was not statistically different from those of untreated SSc pts. In SSc pts, a positive correlation was detected between the levels of ACE and erythrocyte sedimentation rate ($r = 0,505$; $p = 0,019$), fibrinogen ($r = 0,578$; $p = 0,015$), titers of antinuclear antibodies ($r = 0,529$; $p = 0,029$).

The levels of ACEab in SSc pts were similar to those of the control group ($0,180 \pm 0,190$ and $0,208 \pm 0,057$, respectively). However, the ACEab levels in pts with dSSc were significantly higher than those in lSSc pts ($0,29 \pm 0,24$ vs $0,14 \pm 0,16$; $p = 0,041$). Comparable to lSSc group impaired results were also seen in pts treated with ACE inhibitors ($0,1642 \pm 0,1093$). The ACEab levels positively correlated with ANA titers only in dSSc pts ($r = 0,835$; $p = 0,019$). There was no relation between the ACE and ACEab levels neither in SSc pts nor in controls.

Conclusion ACEab can be involved in pathogenesis of SSc and further investigation is needed.

FRI0185 AUTOLOGOUS STEM CELL TRANSPLANTATION INTERNATIONAL SCLERODERMA TRIAL

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Background Autologous hemopoietic stem cell transplantation (HSCT) is emerging as a potential therapy for severe rheumatic autoimmune diseases, including systemic sclerosis. Phase I/II studies involving 65 patients with progressive SSC and organ involvement proved the feasibility of HSCT and demonstrated significant longterm effects on skin score, but with considerable toxicity including a treatment-related mortality of 12%. These results must be viewed against current data on morbidity and mortality (5-yr survival 50%) for this patient category. At the recent EBMT/EULAR consensus meeting, the concept for a randomised, controlled trial was approved to investigate whether the longterm benefits of HSCT outweigh the risks. As a result the ? ASTIS Trial? (Autologous Stem cell Transplantation International Scleroderma Trial) has now been launched.

Objectives To compare efficacy and safety of HSCT versus monthly intravenous pulse-therapy cyclophosphamide in patients with diffuse systemic sclerosis and heart, lung or kidney involvement at risk for premature mortality. The goal of both treatments is to prolong survival by arresting or retarding the disease process. It is postulated that HSCT has superior efficacy, which needs to be balanced against potentially higher toxicity.

Methods The ASTIS Trial is an international, multicenter, prospective, controlled, randomised, phase III study in selected patients with early diffuse SSC and major organ involvement. The ASTIS Trial is conducted under the auspices of EBMT/EULAR (Basel, Switzerland). The investigational treatment arm (HSCT) comprises the following consecutive steps: mobilisation of hematopoietic stem cells with i.v. cyclophosphamide (2×2 gr/m²) and filgrastim (10 ug/kg/day), leukapheresis and selection of CD34⁺ stem cells, conditioning with i.v. cyclophosphamide (200 mg/kg) and rbATG (7.5 mg/kg), followed by reinfusion of autologous stem cells. The control treatment arm consists of 12 monthly i.v. pulses cyclophosphamide (750 mg/m²).

The primary endpoint is event-free survival during the study period of 2 years, events defined as the development of persistent major organ failure (heart, lung, kidney) and death. Secondary endpoints include treatment-related mortality, toxicity, skin score, SHAQ, and quality-of-life. Side studies include evaluation of immune reconstitution in blood and fibrotic activity in skin. It is intended to enrol 200 patients in 3 years.

Results

Conclusion The ASTIS Trial is the first randomised study to evaluate the potential clinical benefits of HSCT versus conventional therapy in severe rheumatic autoimmune disease. The study will address whether a short period of intense immune suppression differs from chronically given, more moderate immune suppression, both qualitatively and quantitatively. Given the low incidence of severe forms of systemic sclerosis, and the efforts needed to conduct the study, international collaboration is mandatory.

FRI0186 CIRCADIAN PROFILE OF SERUM MELATONIN IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background Melatonin (MT) is secreted by the pineal gland and a circadian rhythm of MT secretion is related to light-darkness exposure. MT has been found to influence immune and endocrine functions and is a free radical scavenger. Immune