SHOULD ANTI-CCP/ACPA POSITIVITY BECOME A CLASSIFICATION CRITERION FOR RA?

The meeting ended with a comprehensive discussion, led by David Pisetsky (Durham, USA), Josef Smolen (Vienna, Austria), and Peter Lipsky (Bethesda, USA), on the question of whether anti-CCP/ACPA positivity should become a classification criterion for RA. There was general agreement that because the anti-CCP/ACPA antibody system is more specific than, and at least as equally sensitive as, the rheumatoid factor, it could and probably should replace rheumatoid factor or be added to the existing classification criteria. However, because so many other new tools of possible relevance for the classification and diagnosis of RA (for instance in the field of imaging and genetics) have become available recently, the majority favoured that such additions should be part of a comprehensive revision of the 1987 ACR criteria. The ACR and EULAR are already discussing this topic.

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E R Vossenaar,
Department of Biochemistry, Radboud University Nijmegen, Nijmegen, The Netherlands

W H Robinson,
Division of Immunolgy and Rheumatology, Stanford University School of Medicine, Stanford, USA; Palo Alto Veterans Affairs Health Care System, Palo Alto, California, USA

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Autologous Stem cell Transplantation International Scleroderma (ASTIS) trial: hope on the horizon for patients with severe systemic sclerosis

The ASTIS (Autologous Stem cell Transplantation International Scleroderma) trial was launched in 2001 under the auspices of the European League Against Rheumatism (EULAR) and the European Group for Blood and Bone Marrow Transplantation (EBMT) to compare safety and efficacy of high dose immunosuppressive treatment (HDIT) and autologous haematopoietic stem cell transplantation (HSCT) with 12×monthly treatments with intravenous pulse cyclophosphamide (750 mg/m^2). The trial builds upon the results from previous pilot studies conducted in various European centres, which demonstrated the feasibility and potential long term benefits of HDIT + HSCT in patients with severe rheumatic autoimmune diseases, including progressive systemic sclerosis. To combine safety and efficacy, a medium intensity regimen was chosen to achieve immunoablation in the ASTIS protocol, consisting of high dose cyclophosphamide (2×2 g/m^2) + Filgrastim (granulocyte-colony stimulating factor; 10 μg/kg) for mobilisation of haematopoietic stem cells, leukapheresis, and CD34 selection of the apheresis product, conditioning with high dose cyclophosphamide (200 mg/kg, rabbit ATG 7.5 mg/kg), followed by HSCT.

The ASTIS trial targets patients with early diffuse systemic sclerosis at risk of early mortality. These include patients with disease duration of $\leqslant$4 years, a modified Rodnan skin score (mRSS) of at least 15 (out of a maximum of 51), evidence of heart, lung, or kidney disease; and patients with a maximum disease duration of 2 years, an mRSS of 20 or more plus laboratory signs of acute phase reaction. Exclusion criteria are end stage organ failure, extensive pretreatment with cyclophosphamide (over 5 g intravenously or 3 months' oral treatment), and common reasons that preclude participation in a trial.

The primary end point is event-free survival, defined as the time in days since randomisation until death or the development of irreversible end stage organ failure. The major secondary end points are progression-free survival, treatment related mortality, and toxicity according to WHO criteria. It is postulated that HDIT + HSCT is a better treatment than pulse therapy because of its more profound perturbation of the immune system, although other mechanisms may also be involved.

Interim safety analyses are conducted after groups of 20 patients have been enrolled, and the results from the first analysis were presented at the 2004 EULAR meeting in Berlin. At the time of writing (July 2005), 55 patients have been randomised in 20 European centres, 25 to the investigational arm and 30 to the control arm. No treatment related mortality or unexpected toxicity has been seen in either treatment arm (median follow up 24 months, range 1–51).

EBMT registered transplant centres with expertise in the treatment of severe scleroderma are highly encouraged to participate in this unique joint effort, which will remain open until 2008. Information on the trial is regularly updated on the trial's website: http://www.astistrial.com (accessed 15 August 2005). It is hoped that the ASTIS trial, and its North American counterpart (the SCOT trial) will result in more effective treatment of patients with severe systemic sclerosis, with the aim of inducing a durable remission in the majority of patients treated.

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J M van Laar,
Leiden University Medical Centre, Leiden, The Netherlands

D Farge,
Hopital St Louis, Paris, France

A Tyndall,
Felix-Platter Spital, Basel, Switzerland
Correspondence to: Dr J M van Laar, Department of Rheumatology, Leiden University Medical Centre, Albinusdreef 2, 2333 ZA Leiden, The Netherlands; j.m.van_laar@lumc.nl