

Foreword: Seminars in Research 2014 Joint Experiences in Rheumatology and Dermatology

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It is a pleasure for us to present this special issue of *The Journal of International Medical Research*, which brings together a series of brief communications focusing on the use of biological therapy in rheumatology and dermatology based on recent research into the pathogenic mechanisms of immune-mediated inflammatory diseases of the skin and joints. The articles were written by members of the faculty of a Seminar held on 4–5 December 2014 in Sarteano, Italy and facilitated by an unrestricted grant from Pfizer Italia. The contributors are rheumatologists and dermatologists with substantial experience in the treatment of chronic inflammatory rheumatic and dermatological conditions such as rheumatoid arthritis, psoriasis, psoriatic arthritis, and spondyloarthropathies.

Although the pathogenic mechanisms of immune-mediated inflammatory diseases are not fully understood, these apparently unrelated conditions actually share an immune aetiology that is mediated by cytokines and immune cells. Advances in the understanding of the inflammatory pathways has allowed the development of a number of effective biological agents targeting specific disease mechanisms, particularly agents that inhibit proinflammatory cytokines such as tumour necrosis factor (TNF)

and interleukins. These drugs have demonstrated their ability to control disease activity and to delay the progression of tissue damage. However, although targeted therapies provide excellent anti-inflammatory activity in rheumatological and dermatological conditions, some concerns remain about their cardiovascular safety and potential metabolic effects. To ensure the full therapeutic potential of any biological therapy, clinicians should be aware of these issues in order to use biological agents safely and effectively.

This supplement covers six interesting topics: (i) gene/molecular research on immune-mediated diseases; (ii) immune-mediated diseases and treatment immunogenicity; (iii) immune-mediated diseases and treatment comorbidities; (iv) immune-mediated diseases and obesity; (v) immune-mediated diseases and cardiovascular risk; and (vi) real-life experiences.

The first section contains papers on recent advances in genetic and molecular research on immune-mediated diseases.

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Among articles presented, Campanati et al. report that the TNF- α inhibitor, etanercept, reduces the production of the proangiogenic cytokine vascular endothelial growth factor (VEGF) in the mesenchymal stem cells that are implicated in the 'psoriatic march' – the hypothesized cascade of events linking psoriasis and cardiovascular comorbidities. In a series of articles, Chimenti et al. investigate the action of proteins involved in inflammatory pathways and their role in modulating the immune response and inflammation. Cacciapaglia et al. describe the effect of TNF- α inhibition on disease activity and levels of circulating reactive oxygen species in patients with rheumatoid arthritis, suggesting a cardioprotective role of early treatment with TNF- α inhibitors. Ganzetti et al. provide evidence that the expression of interleukin 1- β in the salivary secretions of patients with psoriasis is significantly reduced in response to TNF- α inhibitors, suggesting that salivary interleukin 1- β could play a role as a noninvasive oral inflammatory biomarker for monitoring inflammation in psoriasis.

In the second section, Vultaggio et al. explore the mechanisms of tolerance and adaptive immune responses to biological agents, pointing towards new assays that may provide useful tools for monitoring immunogenicity and preventing adverse events. A paper by Potenza et al. evaluates heart rate variability analysis as a clinical tool to assess the influence of etanercept on autonomic cardiovascular regulation in psoriatic patients; while Chimenti et al. evaluate the serum levels of the TNF- α inhibitor adalimumab in patients with psoriatic arthritis undergoing long-term therapy addressing the implications of the development of antidrug antibodies. Chimenti et al. also investigate serological markers associated with disease activity in patients with rheumatoid arthritis treated with rituximab, a genetically-engineered chimeric monoclonal antibody targeted to CD20+ B cells.

The third section examines the potential role of comorbidities in immune-mediated diseases, encompassing papers on suicide risk and psychiatric comorbidity by Pompili et al.; treatment of immunocompromised patients with psoriasis (De Simone et al.); and the long-term safety of etanercept in psoriasis, with particular emphasis on infections (Orsini et al.). Generali et al. analyse data from a longitudinal study in a large cohort of Italian subjects followed-up over a 13-year period to determine the prevalence of antinuclear antibodies and antiextractable nuclear antigens and their predictive value for the development of an autoimmune disease.

In the fourth section, the influence of obesity on treatment efficacy is addressed in a study by Giunta et al., which investigated the effect of body weight and body mass index on the efficacy of etanercept in patients with psoriasis.

The implications of immune-mediated diseases on cardiovascular risk are examined in the fifth section, in a case-control study from Erre et al. investigating the role of asymmetric dimethylarginine and arterial stiffness in rheumatoid arthritis patients; a review on the role of post-translational modifications – citrullination and carbamylation – in the pathogenesis of rheumatoid arthritis and atherosclerosis, by Spinelli et al.; and data from Murdaca et al. showing the beneficial effects of long-term treatment with bosentan on endothelial dysfunction in patients with systemic sclerosis and pulmonary arterial hypertension.

The final section reports the experiences of the contributing rheumatologists and dermatologists treating patients in 'real-life' clinical situations. In this section, Chimenti et al. describe the ability of anti-TNF therapy to induce remission and reduce disease activity in rheumatoid arthritis patients; Faleri et al. discuss the unmet needs in patients with psoriasis highlighting the importance of multidisciplinary assessment and

management; Babino et al. report comedication patterns in patients with psoriasis treated with etanercept; and Pezzolo et al. raise the issue of chronic kidney disease in patients receiving long-term therapy for psoriasis. De Santis et al. and Conti et al. investigated the value of nailfold videocapillaroscopy and speckled variance optical coherence tomography as diagnostic and monitoring tools in immune-mediated inflammatory diseases. The role of methotrexate as a concomitant therapy with etanercept in patients with rheumatoid arthritis is described in a paper by Becciolini et al.; and Anginelli et al. report

a case of the safe and successful treatment of scleromyxoedema with high-dose intravenous immunoglobulins.

We believe that this special supplement of *The Journal of International Medical Research* highlights a range of key issues surrounding the management of immune-mediated inflammatory diseases that will not only contribute towards a better understanding of the pathophysiology of these complex inflammatory conditions, but will be of practical value in informing the effective use of biological therapies in these chronic diseases.