IMMUNOSUPPRESSION – ONE FITS ALL VS. INDIVIDUALIZED SELECTION?

Marco Mattucci-Cerinic. University of Florence, Division of Rheumatology AOUC, Florence 50139, Italy

Systemic sclerosis (SSc) is an autoimmune disease characterised by skin, vascular and internal organ involvement leading eventually to tissue fibrosis and atrophy. The best control of the disease is usually achieved in the early phases which is characterised by a diffuse tissue inflammation and vasculopathy, of the tissues. In this phase an immunosuppressive strategy can in fact lead to disease remission even if some cases may escape control and progress inesorably to fibrosis. Classically, the clinical profile of the patient needs to be achieved. The subset, the disease activity and the main clinical features should be defined in order to have the precise profile of the disease. The knowledge of the clinical conditions may therefore help in deciding the drug and shaping the therapeutic regimen and its intensity. Usually, the use of Cyclophosphamide (CYC) and Micophenolate (MMF) may fit the necessity of the largest part of the SSc population. In practice, CYC may be employed as an induction treatment, either rorally or intravenous, while MMF may be used as a maintenance therapy. Both drugs have been demonstrated to be useful in the treatment of SSc either on the cutaneous or on the lung involvement.

However, the most severe and refractory cases may be today considered for a hematopoietic stem cell transplantation (HSCT). In this case, an individualised selection is performed before a patient can be considered fit to receive this kind of therapeutic regimen. Therefore, the treatment is strictly individualised and only after having a thorough clinical evaluation the patient can be accepted for the systemic conditions with high doses of CYC for bone marrow ablation. In conclusion, the treatment of SSc is today mainly centered on immunosuppression whose intensity must be decided and individualized according to the disease activity. New innovative targeted drugs are on the horizon in the effort to find the right immunosuppressive and anti-fibrotic therapeutic approach clinically tailored on the SSc patient.

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PREDICTING SHORT-TERM FRACTURE RISK: CAN WE FORESEE THE (CLOSE) FUTURE?

Nicholas Fuggle. University of Southampton, MRC Lifecourse Epidemiology Unit, Southampton, United Kingdom

A 60 year old female was under long-term follow-up for rheumatoid arthritis, for which she took methotrexate. Ten years previously she had been found to have a single vertebral fracture and her fracture risk, assessed using The WHO Fracture Risk Assessment Tool (FRAX®), was calculated as a 13% risk of major osteoporotic fracture over the next 10 years. According to The National Osteoporosis Guideline Group (NOGG) recommendations, she was considered as having a high fracture risk and underwent a bone mineral measurement (DXA) which demonstrated a bone mineral density T-score of -1.7 at the femoral neck. Lifestyle, vitamin D and calcium intake were optimised and follow-up was arranged for 6 months.

Prior to her next appointment she fell and sustained a fracture of the distal radius. On fracture liaison review her FRAX® risk of fracture was 14% (rising due to an increased year of age) despite the recent change in clinical circumstances. This case serves to emphasise the clinical conundra associated with imminent fracture risk (the 2 years after a fracture when the patient is at a significantly higher risk of fracture) and the difficulties with the decision to treat.

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CELL TRANSPLANTATION – ALL SCIENTIFIC QUESTIONS ANSWERED?

Jacob M. van Laar. University Medical Center Utrecht, Netherlands

Hematopoietic stem cell transplantation (HSCT) currently is the only disease modifying treatment for patients with poor prognosis diffuse cutaneous systemic sclerosis (dcSSc) based on three controlled clinical trials (ASSIST, ASTIS, SCOT). Nevertheless uptake of this intensive treatment modality is slow in most countries, while MMF may be used as a maintenance therapy. Both drugs have been demonstrated to be useful in the treatment of SSc either on the cutaneous or on the lung involvement. Nevertheless selection be optimised so as to avoid transplanting dcSSc patients with little chance of responding? Third, is there a window of opportunity where the immune system can be rebooted? Last but not least, how can potentially eligible dcSSc patients get access to HSCT? The latter may be the most (de)pressing one, as HSCT is only available in a small number of centres. Until efficacious disease-modifying drugs with a better risk-benefit ratio become available, HSCT will continue to be the only therapeutic option to reverse the disease course in dcSSc patients.

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PATIENTS WITH SCLERODERMA: TO CHOOSE OR NOT TO CHOOSE?

Cyrus Cooper. University of Southampton, MRC Lifecourse Epidemiology Unit, Southampton, United Kingdom

With an estimated 520,000 fragility fractures every year in the UK, delivering effective and efficient healthcare for this patient group has significant consequences for patients, families, the NHS, and society. A fragility fracture is a major risk factor for further fractures, and healthcare systems are now beginning to recognise the benefits of secondary fracture prevention. Despite this, less than 50% of patients receive effective secondary fracture prevention after a fragility fracture. This has led to national and international initiatives to improve clinical services by implementing fracture liaison services (FLSs). Successful funding of a new FLS is usually influenced by the number of fractures it is expected to prevent in the first few years after an index fracture. The expected number of fractures prevented is in turn determined by the baseline risk of subsequent fracture, the number of patients at high enough fracture risk to warrant anti-osteoporosis medication (AOM), and the degree of fracture risk reduction by AOMs. Underestimating fracture risk in the post-fracture period will lead to fewer expected fractures prevented and lower perceived benefit of the FLS by payers, and importantly also by patients, families, healthcare providers, and payers. Tools are available to determine the long-term risk of fracture based on patient factors, including previous fracture. Of these, FRAX and QFracture have been incorporated within UK NICE clinical guidance, and the FRAX-derived intervention threshold is used to guide recommendations for AOM in the NHS.

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