EUROPEAN HEMATOLOGY ASSOCIATION

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ABSTRACT BOOK

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POSTER

Biology and preclinical

P02

MAJOR CHANGES IN LEVELS OF REGULATORY CYTOKINES AND FUNCTIONAL ANTIBODIES CONTRIBUTE TO SEVERE IMMUNODEFICIENCY OF MYELOMA PATIENTS AND PERSIST AT ONE YEAR POST DIAGNOSIS

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Introduction. Multiple myeloma is associated with severe immunodeficiency and increased susceptibility to infections. Bacterial infections are recurrent and a major cause of morbidity in myeloma patients. Cytokines interleukin-10 (IL-10) and -13 (IL-13) are regarded as anti-inflammatory which down regulate innate immune functions against infections. Interleukin-7 (IL-7) has been shown to promote myeloma growth through the inhibition of osteoblast differentiation. Acting together immunoparesis (a reduction in normal polyclonal immunoglobulin levels below the lower limit of normal) and the dysregulation of cytokine network may contribute to increased susceptibility to bacterial infections, perpetuation of inflammation and disease development. This study investigated functional antibodies levels and IL-7, IL-10 and IL-13 at disease presentation, in response to induction treatment and in remission in the UK Tackling Early Morbidity and Mortality in Myeloma trial (TEAMM). Method Serum samples at disease presentation, after 12 weeks of therapy and after 1 year were collected from 890 multiple myeloma patients (aged 35–90 years old) enrolled in TEAMM. Multiplex Luminex assay was used for the analysis of IgG antibody levels against 19 bacterial antigens (12 pneumococcal (Pn), 4 meningococcal (Men), haemophilus influenza b (HiB) polysaccharide, and diphtheria and tetanus toxoids) and of serum cytokines IL-7, IL-10 and IL-13. Anti-bacterial antibodies and cytokines levels from patients with myeloma were compared to healthy blood donors. Results A significantly lower proportion of myeloma patients demonstrated protective levels against all bacterial antigens compared to the healthy donors ($p<0.05$) (see Table attached). At disease presentation, less than 6% of multiple myeloma patients had serum IgG antibodies above the WHO 0.35 μg/mL protective threshold for at least 8 of the 12 investigated Pn serotypes. A higher proportion of patients aged < 65 years old were protected against Men serotypes, HiB and tetanus while more patients in the ≥ 65 age group were protected against Pn serotypes which may result from UK vaccination of 65 year olds with pneumovax. Following induction therapy, serum IgGs levels against all investigated bacteria were significantly lower than presentation levels ($p<0.01$). Regulatory cytokines IL-7, IL-10 and IL-13 were significantly higher in TEAMM patients compared to healthy volunteer ($p<0.05$) at disease presentation, after induction therapy and during remission. Patients who had suffered episodes of infection during TEAMM trial presented higher concentrations of IL-7 compared to patients without infection episodes ($p<0.05$). Discussion This study shows anti-bacterial immunological responses are severely compromised in a large population of multiple myeloma patients. The overwhelming majority of patients failed to meet protective levels of functional antibodies and after treatment these levels are significantly reduced even further. Regulatory cytokines were elevated in myeloma patients compared to healthy controls suggesting their involvement in the down-regulation of immune responses to bacterial infection and in multiple myeloma disease progression. This project is funded by the Efficacy and Mechanism Evaluation (EME) Programme, an MRC and NIHR partnership. The views expressed in this publication are those of the author(s) and not necessarily those of the MRC, NHS, NIHR or the Department of Health.