

Poster Session 75

Biologics and immune regulation

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Long-term follow up (5 7 years) of omalizumab treatment in patients with indolent systemic mastocytosis

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Background: Several case studies have presented evidence that omalizumab treatment controls spontaneous and venom immunotherapy (VIT) induced anaphylactic reactions in systemic mastocytosis patients; the follow up period in these studies has been limited to 2 years or less. The aim of this study is to present a 5 7 year follow up of continuous omalizumab treatment in three patients with indolent systemic mastocytosis (ISM).

Method: Three adult patients (2 males, 1 female, aged 45, 48 and 44, respectively) with life threatening venom induced anaphylaxis were studied. Bee venom sensitisation (positive skin tests and RAST/CAP) was confirmed in the first male and vespid in the female patient; the second male with three of unprovoked and three bee venom induced life threatening anaphylaxis episodes was found to be IgE negative for venom allergy. On further workup, which included bone marrow biopsies and genetic studies too, they fulfilled the WHO criteria for ISM. A trial of VIT in the first two patients failed because of systemic reactions. All three patients consented to omalizumab treatment (+VIT in the 2 patients); 300 mg has been administered at monthly intervals through today (the first 2 year follow up has already been published).

Results: Patients have been free of anaphylaxis (spontaneous or VIT induced) and have tolerated omalizumab without any adverse effect. A stage I renal cell carcinoma was diagnosed post nephrectomy in the IgE negative patient at 2.5 years of omalizumab treatment; general anaesthesia was well tolerated despite his previous history of three unprovoked anaphylaxis episodes. Patient remains free of any recurrence 2.5 years post nephrectomy. All three have been repeatedly stung by the offending insects (H.bee, Vespids) without

reactions. Routine laboratory evaluation is within normal limits; serum tryptase (ImmunoCAP) remains lower than the pre omalizumab values and has normalised (<15 µg/l) in the longest treated patient (7 years).

Conclusion: Long term (5 7 years) omalizumab treatment in patients with systemic mastocytosis and venom induced anaphylaxis with or without demonstrable specific IgE appears to be a well tolerated and efficacious treatment.

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Improving anti-tumor immune response in breast cancer patients using dendritic cell based immunotherapy

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Background: Antitumor cellular immune response in patients with breast cancer is impaired. Dendritic cell function and tumor antigen presentation to CD4+ and CD8+ T cell subsets are very important in the disease course and prognosis. This study assesses anti tumor immune response in patients during dendritic cell (DC) based adjuvant immunotherapy.

Method: Since 2010 there were 43 patients included in the trials, 19 patients in the main group (treated with DC) and 24 patients in the control (C) group. DC were obtained from peripheral blood monocytes, primed with four p53 peptides and injected into the patient sub cutaneously three times. T regs and antigen specific T cell (ASC) count was evaluated before and 6 months after the therapy in 14 patients from the main group and 12 patients from the C.

Results: The median number of ASC was 0.29 (0.06 0.77)% in the DC treated group and 0.53 (0.14 0.89)% in the C ($P = 0.28$). The increase of ASC was seen in $80.0 \pm 12.6\%$ of patients after the DC immunotherapy. After the treatment the number of ASC increased in the DC treated group up to 0.81 (0.38 1.47)% ($P = 0.001$), while in the C there was no significant

difference before and after treatment ($P = 0.21$). The level of T regs before the treatment was 4.7 (2.9 6.7)% in patients from DC treated group and 3.6 (1.7 4.6)% in the C ($P = 0.06$). During course of DC immunotherapy T regs in these patients were decreased in $71.40 \pm 12.1\%$ ($P = 0.006$) and only in $25.0 \pm 12.5\%$ of the C ($P = 0.2$). The ratio of ASC/T regs in patients from the DC treated group was 0.04 (0.01 0.06)% before and 0.23 (0.19 0.43)% after the DC treatment ($P = 0.001$). However in the C group ASC/T regs ratio did not change significantly during treatment period being 0.06 (0.01 0.32)% and 0.02 (0.00 0.21)% ($P = 0.67$).

Conclusion: Elevated numbers of T regs in cancer patients correlate with worse survival while a decrease of T regs with treatment is a good prognostic factor. These results indicate the restoration of anti tumor immune response in the patients with breast cancer due to treatment with the dendritic cells vaccine.

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Acute infusion reactions to infliximab: safety and efficacy of a standardised rapid desensitisation protocol

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Background: Infliximab is a chimeric anti TNF α monoclonal antibody useful in the treatment of chronic inflammatory diseases. The Acute Infusion Reactions (AIRs) reported at its administration, represent a treatment impediment, compelling alternative, usually less efficient therapeutic choices. The aim of our study was to provide data on the efficacy and safety of re-administering infliximab to a well selected population by applying a standardised Rapid Desensitisation (RD) protocol.

Method: Patients (pts) selected for RD fulfilled the following inclusion criteria: (i) AIR clinically consistent with immediate hypersensitivity reaction, during or within 1 h after a slow rate (≥ 2 h) infliximab infusion, (ii) documented moderate or severe systemic (Brown grading system for hypersensitivity