

A200 LONGITUDINAL IMMUNOMONITORING FOLLOWING TOCILIZUMAB IN RHEUMATOID ARTHRITIS

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Introduction Tocilizumab is a humanised anti-interleukin (IL)-6 receptor monoclonal antibody, which binds to circulating soluble IL-6 receptor and membrane-expressed IL-6 receptor, inhibiting IL-6 binding to both forms of IL-6 receptor. Tocilizumab is an efficient therapy for adults with moderate to severe rheumatoid arthritis (RA) in whom disease-modifying antirheumatic drugs or a tumour necrosis factor (TNF) inhibitor has failed. However, the impact of tocilizumab on several immune populations such as lymphocytes, monocytes, dendritic cells is still unknown. In order to longitudinally analyse the variations in frequencies as well as the activation status of these populations, the authors designed several panels specific for immune cells and performed immunomonitoring by FACS analyses.

Patients and methods 20 patients with severe and active RA, refractory to methotrexate or anti-TNF therapies were recruited and treated with 8 mg/kg of tocilizumab monthly. Peripheral blood was recovered for each patient at day 0, as well as 1 and 3 months after informed consents. Staining was performed on whole blood and peripheral blood mononuclear cells were purified for intracellular cytokine staining following CD3-CD28 overnight stimulation. The data were acquired on a FACS Canto II (eight colours) and analysed using DIVA software. Ten panels specific for subpopulations of T cells (Th1, Th2, Th17), B cells (naïve, memory and transitional), monocytes (classical, inflammatory and non-classical) dendritic cells (myeloid and plasmacytoid), Tregs (natural and induced) were designed. The activation status of the T, B and DC was also monitored.

Results According to the cytokinic secretion of the T cells following ex vivo activation, the authors observed various profile of patients: Th1, Th17 or Th1/Th17. The frequencies of these proinflammatory cytokine secreting T cells were found to be decreased following treatment with tocilizumab. Concerning the longitudinal analyses of the B cell populations, an increase of the transitional B cells (CD24^{high}CD38^{high}) was observed in non-responder patients and in contrast an increase of non-classical monocytes was observed in good responders. Concerning the Treg population, the high heterogeneity of the patients before treatment was confirmed. However the CD4CD25FoxP3 staining was confined to CD127^{low} and CD62L^{high} suggesting the induction of induced Tregs following Tocilizumab treatment as observed after infliximab treatment.

In conclusion, the design of specific panels to analyse the frequencies and the activation status of several subpopulation of immune cells, allows a longitudinal monitoring of the major effector populations in RA patients following cytokine blockade.