assays were performed with Treg and responder T cells from HC after preincubation of individual cell populations with CTLA-4Ig or with antibodies (Abs) against costimulatory B7 molecules.

Summary Proportions of $CD4^+$ T cells and Treg substantially increased 2 and 4 weeks after the initiation of CTLA-4Ig treatment. No differences were observed for the percentage of memory and naïve $CD4^+$ T cells. Phenotypic analyses revealed a downregulation of activation associated marker molecules and of CD95 on $CD4^+$ T cells and Treg. Likewise, preincubation of PBMCs from HC with CTLA-4Ig before stimulation led to a dose dependent downregulation of activation markers on CD4 cells and Treg in vitro. Moreover in vitro analyses of $CD4^+$ T cells and Treg from HC showed a dose dependent decrease in AICD after incubation with CTLA-4Ig. Functional analysis of isolated Treg from RA patients revealed a diminished suppressive capacity of Treg 4 weeks after treatment with CTLA-4Ig. However, only the preincubation of responder T cells, but not of Treg, from HC with CTLA-4Ig or with Abs against B7 molecules resulted in a decreased T cell suppression.

Conclusion Within our study the authors were able to demonstrate for the first time a direct effect of CTLA-4Ig on T cells in RA patients, which results in increased proportions of $CD4^+$ and Treg, the downregulation of CD95 and a decrease in AICD. Blockade of B7 costimulatory molecules on T cells by CTLA-4Ig leads to a diminished susceptibility of T cells for Treg suppression which might be counter balanced by increased Treg numbers.

22 ABATACEPT (CTLA-4IG) THERAPY PREVENTS ACTIVATION INDUCED CELL DEATH (AICD) OF REGULATORY T CELLS AND REDUCES THE SUSCEPTIBILITY OF T CELLS TO REGULATORY T CELL SUPPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background Abatacept (CTLA-4Ig) inhibits the binding of CD28 to the B7 ligands CD80/CD86 on antigen presenting cells (APC) and thereby effector T cell activation. Costimulatory molecules can also be expressed on T cells upon activation. Whether this allows CTLA-4Ig to directly affect distinct T cell subsets remains unclear. The authors therefore performed phenotypic and functional analysis of T cells in RA patients before and after CTLA-4Ig therapy.

Methods Peripheral blood mononuclear cells (PBMC) from RA patients (n=15) were analysed before, 2 and 4 weeks after the initiation of CTLA-4Ig therapy. Phenotypic analyses on different T cell subsets were performed by FACS. Apoptosis was induced in CTLA-4Ig incubated cells by anti-Fas antibody and DNA fragmentation was measured by TUNEL staining. $CD4^+CD25^+$ Treg were isolated from RA patients by cell sorting and analysed for their functional capacity. Suppression