

EFFECTS OF IL-2 AND GM-CSF IMMUNOTHERAPY IN IMMUNE RESTORATION DISEASE AND ON HIV-1-SPECIFIC T-CELL RESPONSES AFTER ANTIRETROVIRAL THERAPY

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BACKGROUND: In late-stage disease, effective ART although controlling viral replication and allowing some immune reconstitution, does not allow restoration of anti-HIV-1 T-cell responses. In some cases, lack of response to other pathogens allows for emergence of severe immune reconstitution disease (IRD). Augmentative IL-2 + GM-CSF immunotherapy is being considered as an adjunct to ART in such patients.

METHODS: Individuals with late-stage infection on ART (VL BLD, CD4 <108) presenting with MAC IRD were subdivided into those receiving ART alone (Group 1) or ART + IL-2 + GM-CSF immunotherapy (group 2). Group 2 received IL-2 at 5 MU subcutaneously bd for five days for 3 and 4-weekly cycles. During the third cycle concomitant GM-CSF was administered subcutaneously at 150 ug daily for 5 days. Chronically infected patients receiving ART with no IRD were used as controls (group 3).

RESULTS: Median CD4 T-cell numbers in IRD patients (group 1 and group 2) rose from baseline 22 cells/ μ l of blood, before initiation of ART, to 108 cells/ μ l after 6 months of therapy, coinciding with IRD diagnosis. This is in comparison with group 3, who had median CD4 76 cells/ μ l at baseline, rising to 249 cells/ μ l at 6 months post-ART, which coincided with strong pathogen-specific responses and no IRD. Both group 1 and group 2 had significantly lower levels of naïve CD4 T-cells ($P < 0.005$), increased expression of immune-activation markers (HLA-DR and CD38, $P < 0.005$ and $P < 0.05$ respectively), and weak or absent pathogen-specific T-cell responses, compared with group 3. Augmentative IL-2 + GM-CSF induced immediate and strong pathogen-specific T-cell responses in group 2 IRD patients.

CONCLUSIONS: This immunotherapeutic approach resulted in resolution of IRD and clinical recovery.

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