Immune activation and neurotoxicity in patients with malignant melanoma undergoing IL-2 immunotherapy

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We sought to determine whether IL-2 stimulated increases in peripheral IFN-g plasma concentrations would be associated with increases in IL-6 plasma levels and decreases in FACT/GOG-Ntx Scores in stage IV malignant melanoma patients undergoing high-dose IL-2 therapy. IL-2 treatment is the standard of care in the United States for patients with stage IV melanoma. Although in 10-15% of cases it is effective in extending the survival of the patient it also induces many detrimental side effects including depressive, neurotoxic and even psychotic symptoms [1]. A lot of the times, these symptoms interfere with the continuation of this potentially life-saving therapy. These complications of IL-2 therapy have been posited to be caused by the activation of “secondary” cytokines through IL-2-induced stimulation of both the T-cells and B-cells of the immune system [2]. We believe that release of IFN-g, induced by IL-2 treatment, plays a significant role in the incidence of these symptoms as IFN-g activates the catabolism of the protein tryptophan. After giving informed consent, patients with Stage IV malignant melanoma were recruited. Prior to, during, and after IL-2 administration we measured plasma concentrations of IFN-g, neurobehavioral symptoms, cognitive function, and tolerance of IL-2 treatment. The Friedman test, Wilcoxon signed-rank test and Spearman’s correlation were used in the analysis. IFN-g levels were undetectable until about two hours post injection. The neurotoxicity scores and IFN-g levels correlate during cycle 4 and the Ntx scores reach a low at the same time point that the IFN-g levels reach their peak. Our findings support our proposed model but further analysis of levels of TNF-a, tryptophan and quinolinic acid are still needed. Recruitment of more patients will also allow for more accurate and visible correlations.
[1] Legha S. 2009. Oncology, 23(6), 488-496