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RETROVIROLOGY

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The combination of arsenic, interferon-alpha, and zidovudine restores an "immunocompetent-like" micro-environment in patients with adult T-cell leukemia lymphoma

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HTLV-I associated adult T-cell leukemia/lymphoma (ATL) carries a dismal prognosis due to chemo-resistance and immuno-compromised micro-environment. The combination of zidovudine and interferon-alpha (IFN) significantly improved survival in ATL. Promising results were reported by adding arsenic trioxide to zidovudine and IFN. Here we assessed Th1/Th2/T_{reg} cytokine gene expression profiles in 16 ATL patients before and 30 days after treatment with arsenic/IFN/zidovudine, in comparison with HTLV-I healthy carriers and sero-negative blood donors. ATL patients at diagnosis displayed a T_{reg}/Th2 cytokine profile with significantly elevated transcript levels of Foxp3, interleukin-10 (IL-10), and IL-4 and had a reduced Th1 profile evidenced by decreased transcript levels of interferon-γ (IFN-γ) and IL-2. Most patients (15/16) responded, with $CD4^+CD25^+$ cells significantly decreasing after therapy, paralleled by decreases in Foxp3 transcript. Importantly, arsenic/IFN/zidovudine therapy sharply diminished IL-10 transcript and serum levels concomittant with decrease in IL-4 and increases in IFN-γ and IL-2 mRNA, whether or not values were adjusted to the percentage of $CD4^+CD25^+$ cells. The observed shift from a T_{reg}/Th2 phenotype before treatment toward a Th1 phenotype after treatment with arsenic/IFN/zidovudine may play an important role in restoring an immuno-competent micro-environment, which enhances the eradication of ATL cells and the prevention of opportunistic infections.

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