



MEETING ABSTRACT

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# Ascorbic acid has superior antiviral and antiproliferative effects over IFN-alpha in HAM/TSP PBMC ex vivo

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IFN-alpha and high dose ascorbic acid (AA) have a modest clinical benefit in HAM/TSP (Nakagawa, 1996). We investigated the effect of ex vivo and in vitro AA and IFN-alpha treatment on HAM/TSP PBMC and HTLV-1-infected cell lines, respectively.

We treated cells for 48-72h ex vivo and in vitro with low-high (10-100µg/ml) dose of AA and 1000U/ml of IFN-alpha and quantified lymphoproliferation by [<sup>3</sup>H] thymidine incorporation, tetraploid DNA content and PCNA expression (flow cytometry). Viral expression was measured at the RNA (tax, LTR) and protein (Tax, p19) level by RT-PCR, Western blot and ELISA, respectively. Apoptosis was quantified by subdiploid DNA content (flow cytometry). Th1/Th2/Th17 cytokines were quantified by cytometric bead array. AA induced a dramatic 95% decrease (control 3689±755 cpm vs. AA 121±52 cpm, p=0.001) in spontaneous, virus-driven lymphoproliferation and a decrease in tax and LTR transcription in HAM/TSP PBMC. In addition, AA decreased the exacerbated ex vivo IFN-gamma production in HAM/TSP PBMC. In HTLV-1 infected cell lines (MT-2 and MT-4), AA induced a dose-dependent increase in DNA fragmentation (p=0.02, p=0.005), paralleled by a decrease in PCNA (p=0.003), as well as p19 (p<0.001) and Tax levels. These effects appear virus-specific, since high-dose (100µg/ml) AA did not exert a significant antiproliferative or pro-apoptotic effect on PBMC of normal donors. On top, AA displayed a superior antiprolifera-

tive, antiviral and immunomodulatory effect over IFN-alpha in both cell lines and HAM/TSP PBMC. Considering the selective antiproliferative and antiviral effects of AA ex vivo and in vitro, the therapeutic potential of combination therapy with high dose AA in HAM/TSP should be further explored.

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