

## **Leukemia and Oxidative Therapies Including Intravenous Ascorbic Acid**

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A seeming conundrum regarding the ability of some leukemic cells (i.e. CLL) to sequester ascorbate (ASC) has led to confusion regarding the safety and utility of high dose ascorbate delivered via IV (IVAA). This has led to some apparent confusion between this concern and the apparent positive benefits of IVAA seen in clinical practice.

As mentioned it is known that CLL cells can sequester ASC and that this may allow them some additional benefit in an oxidant milieu [1]. Added to this information is the data showing that CLL is a polymorphic disorder that likely has a variety of windows of sensitivity to oxidant therapies as well as immunologic resistance to oxidation [2,3].

Case reports from physicians employing IVAA (such as the author and others) have mostly been either neutral (no response) or positive (stabilization or regression) with respect to CLL. This response variety is common to most cancer types which seem responsive to IVAA. The likely reason that the dichotomy between earlier basic science concerns regarding ASC and CLL families and the apparent clinical response lies in the sensitivity of these cells to oxidants. As mentioned [1] CLL cells sequester ASC as an apparent antioxidant, but this is not enough redox buffer in the face of oxidative therapies. Two papers [4,5] show that CLL cells are sensitive to H<sub>2</sub>O<sub>2</sub> damage and selective killing. Another paper showed that the use of dual oxidant therapy “(ROS) generating arsenic trioxide (ATO) and ascorbic acid” enhanced Hu1D10-mediated cell death in these cells [6].

One reaction mentioned by many clinicians employing IVAA among other therapies with leukemia and lymphomas is presentation of tumor pseudo-progression. In these cases the patient symptoms and signs may aggravate for one to five weeks in an apparent exacerbation of disease. In most of these cases the patient (if appropriately followed and managed) would have an immune exacerbation which would resolve with no apparent advancement in baseline cancer.

Although pseudo-progression is a known phenomenon in oncology its report in leukemia and lymphoma is largely anecdotal. In the cases of physicians employing IVAA in these cancers it, though anecdotal, should be reported and patients monitored for this eventuality. It is not a cause to discontinue therapy with IVAA but rather a potential clinical change to be watchful of.

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References:

1. L. LIEBES, R. KRIGEL, S. Kuo, D. NEVRLA, E. PELLE, AND R. SILBER. Increased ascorbic acid content in chronic lymphocytic leukemia B lymphocytes. Proc. NatL Acad. Sci. USA Vol. 78, No. 10, pp. 6481-6484, October 1981
2. Djurdjevic P, Zelen I, Ristic P, Jovanovic I, Jakovljevic V, Baskic D, Popovic S, Arsenijevic N. Oxidative stress accelerates spontaneous apoptosis of B-chronic lymphocytic leukemia lymphocytes. J BUON. 2009 Apr-Jun;14(2):281-7. PMID: 19650179
3. Danilov AV, Danilova OV, Klein AK, Huber BT. Molecular pathogenesis of chronic lymphocytic leukemia. Curr Mol Med. 2006 Sep;6(6):665-75. PMID: 17022736
4. Farber CM, Liebes LF, Kanganis DN, Silber R. Human B lymphocytes show greater susceptibility to H<sub>2</sub>O<sub>2</sub> toxicity than T lymphocytes. J Immunol. 1984 May;132(5):2543-6. PMID: 6609202
5. Silber R, Stahl RL, Farber CM, Kanganis D, Astrow A, Liebes LF. Chronic lymphocytic leukemia lymphocytes: membrane anomalies and H<sub>2</sub>O<sub>2</sub> vulnerability. Blood Cells. 1984;10(2-3):233-9. PMID: 6336165
6. Biswas S, Zhao X, Mone AP, Mo X, Vargo M, Jarjoura D, Byrd JC, Muthusamy N. Arsenic trioxide and ascorbic acid demonstrate promising activity against primary human CLL cells in vitro. Leuk Res. 2010 Jul;34(7):925-31. Epub 2010 Feb 19. PMID: 20171736