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A randomized phase 2 trial of ascorbic acid in combination with Docetaxel in men with metastatic prostate cancer

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Ascorbic acid is being used by complementary medicine practitioners to treat cancer, infections, and other conditions. Annual administration of more than 355,000 doses of intravenous (IV) ascorbic acid for more than 10,000 patients has been documented, although total industry sales are more than double that amount. The average prescribed dose is 28 grams every 4 days. Complications reported have been minimal, with fatigue reported in 1.2% of patients overall and rare reports of phlebitis and kidney stones. A long period of controversy over the efficacy of ascorbic acid in cancer patients began in 1976. Ewan Cameron with Linus Pauling published a retrospective study of untreatable cancer patients that demonstrated a survival benefit of 321 days with IV and oral ascorbic acid vs. 38 days for controls. In contrast, a 1979 Mayo Clinic study did not replicate this finding, although ascorbic acid was delivered only orally instead of IV. Phase 1 and 2 clinical trials in 2012, 2013, and 2014 demonstrated safety and anti-tumor activity for high dose IV ascorbic acid. These studies warranted testing the efficacy of IV ascorbic acid in randomized, placebo-controlled clinical trials. At high doses, ascorbic acid is very poorly bioavailable when delivery orally. Maximal oral administration has been shown to result in concentrations of no more than 0.2 mM, far below therapeutic levels.The effective therapeutic concentration of ascorbic acid is high, and can only be achieved with intravenous dosing. Thus the findings of the 1979 Mayo Clinic study, which used oral administration only, do not conflict with Cameron and Pauling's findings that used IV plus oral administration.

A recent study of high dose IV ascorbic acid in ovarian cancer patients indicated that ascorbic acid treatment combined with standard chemotherapy (paclitaxel) reduces certain toxicities associated chemotherapy and might increase survival.

Dr. Channing Paller is conducting a randomized phase 2 clinical trial comparing docetaxel plus IV ascorbic acid (1g/kg, 3 times per week) versus docetaxel plus IV fluid (placebo) in mCRPC patients. The primary outcomes will be PSA response and reduction of chemotherapy-related toxicities.Key secondary outcomes include radiographic progression free survival, safety, quality of life, and the need for dose reductions of docetaxel.Laboratory correlates including pharmacokinetics of ascorbic acid and docetaxel and oxidative stress levels. Biomarkers of resistance to docetaxel will also be investigated.This clinical trial activates in spring 2016 and will be conducted at Johns Hopkins University and partnering sites.

Biography:

Channing J Paller, M.D, is Assistant Professor of Oncology at the Johns Hopkins University School of Medicine. Dr. Paller earned her M.D. at Harvard Medical School and completed her medical residency at the Johns Hopkins Hospital, where she was a member of the Osler Housestaff Program, and her Fellowship in Medical Oncology at the Johns Hopkins Kimmel Cancer Center. As an investigator, Dr. Paller is focused on translational research and clinical trials of developmental therapeutics in prostate and other solid tumors. Dr. Paller actively participates in the Johns Hopkins Kimmel Cancer Center Phase I program, with a concentration on the rigorous evaluation of natural products. She focuses on novel clinical trials of immunotherapy (TGFBR inhibitor) and natural products in men with prostate cancer or other solid tumors including pomegranate, muscadine grape skin, vitamin C, and mistletoe.