

Supplemental Appendix for:

Is There a Role for Oral or Intravenous Ascorbate (Vitamin C) in Treating Patients With Cancer? A Systematic Review
Carmel Jacobs et al.

Supplemental Appendix 2: List of Excluded Studies

EXCLUDED DUE TO MULTIPLE INTERVENTIONS, INCLUDING BUT NOT LIMITED TO ASCORBATE. NO DATA RELATED SOLELY TO ASCORBATE.

Poole EM, Shu X, Caan BJ, Flatt SW, Holmes MD, Lu W, et al. Postdiagnosis supplement use and breast cancer prognosis in the After Breast Cancer Pooling Project. *Breast Cancer Res Treat* 2013;139(2):529-37.

Greenlee H, Kwan ML, Kushi LH, Song J, Castillo A, Weltzien E, et al. Antioxidant supplement use after breast cancer diagnosis and mortality in the Life After Cancer Epidemiology (LACE) cohort. *Cancer* 2012;118(8):2048-58.

Suhail N, Bilal N, Khan HY, Hasan S, Sharma S, Khan F, et al. Effect of vitamins C and E on antioxidant status of breast-cancer patients undergoing chemotherapy. *J Clin Pharm Ther* 2012;37(1):22-6.

Fuchs-Tarlovsky V, Bejarano-Rosales M, Gutierrez-Salmean G, Casillas MA, Lopez-Alvarenga JC, Ceballos-Reyes GM. [Effect of antioxidant supplementation over oxidative stress and quality of life in cervical cancer]. *Nutr Hosp* 2011;26(4):819-26.

Nechuta S, Lu W, Chen Z, Zheng Y, Gu K, Cai H, et al. Vitamin supplement use during breast cancer treatment and survival: a prospective cohort study. *Cancer Epidemiol Biomarkers Prev* 2011;20(2):262-71.

Birdsall TC, Cain L, Martin J, Birdsall SM, Wiersum L, Anderson K, et al. The effect of naturopathic and nutritional supplement treatment on tumor response, control, and survival in prostate cancer patients treated with radiation therapy. *J Clin Oncol*. 2009; 27(15 SUPPL. 1):e16088.

Tareen B, Summers JL, Jamison JM, Neal DR, McGuire K, Gerson L, et al. A 12 week, open label, phase I/IIa study using apatone for the treatment of prostate cancer patients who have failed standard therapy. *Int J Med Sci* 2008;5(2):62-7.

Berenson JR, Matous J, Swift RA, Mapes R, Morrison B, Yeh HS. A phase I/II study of arsenic trioxide/bortezomib/ascorbic acid combination therapy for the treatment of relapsed or refractory multiple myeloma. *Clin Cancer Res* 2007;13(6):1762-8.

Berenson JR, Boccia R, Siegel D, Bozdech M, Bessudo A, Stadtmauer E, et al. Efficacy and safety of melphalan, arsenic trioxide and ascorbic acid combination therapy in patients with relapsed or refractory multiple myeloma: a prospective, multicentre, phase II, single-arm study. *Br J Haematol* 2006;135(2):174-83.

Kennedy DD, Tucker KL, Ladas ED, Rheingold SR, Blumberg J, Kelly KM. Low antioxidant vitamin intakes are associated with increases in adverse effects of chemotherapy in children with acute lymphoblastic leukemia. *Am J Clin Nutr* 2004;79(6):1029-36.

Bruemmer B, Patterson RE, Cheney C, Aker SN, Witherspoon RP. The association between vitamin C and vitamin E supplement use before hematopoietic stem cell transplant and outcomes to two years. *J Am Diet Assoc* 2003;103(8):982-90.

Fleischauer AT, Simonsen N, Arab L. Antioxidant supplements and risk of breast cancer recurrence and breast cancer-related mortality among postmenopausal women. *Nutr Cancer* 2003;46(1):15-22.

Waddell WR, Gerner RE. Indomethacin and ascorbate inhibit desmoid tumors. *J Surg Oncol* 1980;15(1):85-90.

EXCLUDED AS ASCORBATE NOT AN INTERVENTION OF INTEREST

Held LA, Rizzieri D, Long GD, Gockerman JP, Diehl LF, de Castro CM, et al. A Phase I study of arsenic trioxide (Trisenox), ascorbic acid, and bortezomib (Velcade) combination therapy in patients with relapsed/refractory multiple myeloma. *Cancer Invest* 2013;31(3):172-6.

Bejanyan N, Tiu RV, Raza A, Jankowska A, Kalaycio M, Advani A, et al. A phase 2 trial of combination therapy with thalidomide, arsenic trioxide, dexamethasone, and ascorbic acid (TADA) in patients with overlap myelodysplastic/myeloproliferative neoplasms (MDS/MPN) or primary myelofibrosis (PMF). *Cancer*. 2012; 118(16):3968-3976.

Sharma M, Khan H, Thall PF, Orlowski RZ, Bassett RLJ, Shah N, et al. A randomized phase 2 trial of a preparative regimen of bortezomib, high-dose melphalan, arsenic trioxide, and ascorbic acid. *Cancer* 2012;118(9):2507-15.

Welch JS, Klco JM, Gao F, Procknow E, Uy GL, Stockerl-Goldstein KE, et al. Combination decitabine, arsenic trioxide, and ascorbic acid for the treatment of myelodysplastic syndrome and acute myeloid leukemia: a phase I study. *Am J Hematol* 2011;86(9):796-800.

Bael TE, Peterson BL, Gollob JA. Phase II trial of arsenic trioxide and ascorbic acid with temozolomide in patients with metastatic melanoma with or without central nervous system metastases. *Melanoma Res* 2008;18(2):147-51.

EXCLUDED AS LETTER TO THE EDITOR WITH NO ORIGINAL DATA

Hemil H. Randomised trials on vitamin C. *Br J Nutr*. 2011; 105(3):485-487.

Stephenson CM, Levin RD, Lis CG. Phase 1 trial of high-dose intravenous vitamin C treatment for patients with cancer. *J Am Osteopath Assoc* 2007;107(6):212-3.

EXCLUDED AS REPORTED NO OUTCOMES OF INTEREST TO US

Zirpoli GR, Brennan PM, Hong C-C, McCann SE, Unger JM, Budd GT, et al. Effect of physician recommendation on multivitamin and antioxidant supplement use during chemotherapy in an adjuvant trial for breast cancer (SWOG S0221). *Cancer Res.* 2011; 71(8 SUPPL. 1).

EXCLUDED AS PRE-CLINICAL STUDY

Michel L, Dupuy A, Jean-Louis F, Sors A, Poupon J, Viguier M, et al. Arsenic trioxide induces apoptosis of cutaneous T cell lymphoma cells: evidence for a partially caspase-independent pathway and potentiation by ascorbic acid (vitamin C). *J Invest Dermatol* 2003;121(4):881-93.

EXCLUDED AS PREVENTION STUDIES IN HEALTHY POPULATIONS

Jacobs EJ, Connell CJ, Patel AV, Chao A, Rodriguez C, Seymour J, et al. Vitamin C and vitamin E supplement use and colorectal cancer mortality in a large American Cancer Society cohort. *Cancer Epidemiol Biomarkers Prev.* 2001; 10(1):17-23.

Webb PM BCP. Gastric cancer, gastritis and plasma vitamin C: results from an international correlation and cross-sectional study. The Eurogast Study Group. *Int J Cancer.* 1997; [cited 1997 Nov];73(5):684.

STUDY NOT AVAILABLE IN ENGLISH

Ostendorf GM. [High dosage vitamin C in breast cancer?]. *Versicherungsmedizin* 2012;64(2):85.

Garin AM, Gorbunova VA, Gershanovich ML, Manziuk LV, Borodkina AG, Breder VV, et al. [Results of a phase I clinical trial of "theraphthal + ascorbic acid" catalytic system]. *Vopr Onkol* 2001;47(6):676-9.