

**Table 1: IV VITAMIN C FOR CANCER MANAGEMENT; EVIDENCE SUMMARY**

Reference	Description	Outcomes
Systematic review of single or combination antioxidant therapy	Systematic review of 19 studies examining single or combination antioxidant therapy in combination with chemotherapeutic treatment regimens.	"From the 19 studies included in this review, no evidence was found that supported concerns that antioxidant supplementation given concurrently with ROS- generating chemotherapy diminished the efficacy of the chemotherapy in study populations comprising mostly advanced or relapsed patients. In contrast, 17 of the RCTs included in this review showed either a statistically significant advantage or non- statistically higher survival and/ or treatment response in those patients given antioxidants."
Block KI, Koch AC, Mead MN, Tothy PK, Newman RA, Gyllenhaal C. Impact of antioxidant supplementation on chemotherapeutic efficacy: a systematic review of the evidence from randomized controlled trials. <i>Cancer Treat Rev.</i> 2007; 33(5):407-18.	Systematic review of single or combination antioxidant therapy	Objective responses were observed in 6 (27%) of subjects. 12- months progression- free survival rate was 34%. Overall survival rate was 74%.
Berenson et al. A phase I/II study of arsenic trioxide/bortezomib/ ascorbic acid combination therapy for the treatment of relapsed or refractory multiple myeloma. <i>Clin Cancer Res.</i> 2007; 13(6):1762-8.	22 patients with multiple myeloma having failed 3-9 prior therapies received in open label design arsenic trioxide, bortezomib, and a fixed dose of ascorbic acid (1 g) i.v. on days 1, 4, 8, and 11 of a 21-day cycle for a maximum of eight cycles.	Functional scores demonstrating statistically significant improvement included physical, emotional, and cognitive function. Symptom scores demonstrating significant improvement included fatigue, nausea/ vomiting, pain, and appetite loss. Other function and symptom scales were not significantly improved following administration of vitamin C.
Yeom CH, Jung GC, Song KJ. Changes of terminal cancer patients' health-related quality of life after high dose vitamin C administration. <i>J Korean Med Sci.</i> 2007;22(1):7-11.	39 terminal cancer patients were administered 10000mg IV vitamin C twice over a one- week period, with coadministration of 4000mg per day oral vitamin C.	Objective responses occurred in 31 of 65 (48%) patients, including two complete, 15 partial and 14 minor responses. Median progression-free survival and overall survival were 7 and 19 months respectively. Twenty-two patients had elevated serum creatinine levels (SCr) at baseline, and 18 of 22 (82%) showed decreased SCr levels during treatment. Specific grade 3/4 haematological (3%) or cardiac adverse events occurred infrequently.
Berenson JR, Boccia R, Siegel D, 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. <i>Br J Haematol.</i> 2006;135(2):174-83.	EORTC QLQ-C30 quality of life scale served as the main endpoint measure.	"Recent evidence shows that oral administration of the maximum tolerated dose of vitamin C (18 g/d) produces peak plasma concentrations of only 220 µmol/L, whereas intravenous administration of the same dose produces plasma concentrations about 25-fold higher. Larger doses (50–100 g) given intravenously may result in plasma concentrations of about 14 000 µmol/L."
Padayatty SJ, Riordan HD, Hewitt SM, Katz A, Hoffer LJ, Levine M. Intravenously administered vitamin C as cancer therapy: three cases. <i>CMAJ.</i> 2006;174(7):937-42.	65 multiple myeloma patients who failed at least two previous therapies received melphalan, arsenic trioxide (ATO) and ascorbic acid (AA) (1 g i.v) (MAC) combination therapy. The intervention was administered twice weekly for 6 weeks.	"At concentrations above 1000 µmol/L, vitamin C is toxic to some cancer cells but not to normal cells in vitro."
	The paper reviews the basis for intravenous versus oral route of administration for vitamin C, and reports on 3 cases of advanced cancer demonstrating exceptionally long survival following intravenous vitamin C.	"We found 3 well-documented cases of advanced cancers, confirmed by histopathologic review, where patients had unexpectedly long survival times after receiving high-dose intravenous vitamin C therapy. We examined clinical details of each case in accordance with National Cancer Institute (NCI) Best Case Series guidelines. Tumour pathology was verified by pathologists at the NCI who were unaware of diagnosis or treatment. In light of recent clinical pharmacokinetic findings and in vitro evidence of anti-tumour mechanisms, these case reports indicate that the role of high-dose intravenous vitamin C therapy in cancer treatment should be reassessed."
		A clinical response was seen in 8 of 20 patients (40%). The median duration of response was 5 months. The median progression free survival was 4 months and the median overall survival was 11 months. -

## FEATURE

Reference	Description	Outcomes
Wu KL, Beksac M, van Droogenbroeck J, Amadori S, Zweegman S, Sonneveld P. Phase II multicenter study of arsenic trioxide, ascorbic acid and dexmethasone in patients with relapsed or refractory multiple myeloma. <i>Haematologica</i> . 2006;91(12):1722-3.	20 patients having failed 1-8 prior therapies (mean 4) were assigned to receive arsenic trioxide, dexmethasone, and ascorbic acid combination therapy for 4, 4 week cycles. 1000mg intravenous vitamin C was administered on 5 separate days during week one of the first cycle, and on 2 separate days each week thereafter.	A clinical response was seen in 8 of 20 patients (40%). The median duration of response was 5 months. The median progression free survival was 4 months and the median overall survival was 11 months.
Abou-Jawde RM, Reed J, Kelly M, Walker E, Andressen S, Baz R, Karam MA, Hussein M. Efficacy and safety results with the combination therapy of arsenic trioxide, dexmethasone, and ascorbic acid in multiple myeloma patients: a phase 2 trial. <i>Med Oncol</i> . 2006;23(2): 263-72.	Twenty patients in whom no more than two previous therapies had failed were enrolled. The regimen consisted of 14- or 15-wk cycles, with the first cycle considered induction, followed by one or two consolidation cycles with a reduced steroid schedule and then a maintenance cycle in responding patients	The overall response rate was 30%, with at least stable disease in 80% of patients. Median progression-free survival was 316 d in all patients and 584 d in those with a response. The regimen was well tolerated, with most adverse events being mild or moderate.
Riordan HD, Casciaro JJ, González MJ, Riordan NH, Miranda-Massari JR, Taylor P, Jackson JA. A pilot clinical study of continuous intravenous ascorbate in terminal cancer patients. <i>P R Health Sci J</i> . 2005;24(4):269-76.	Twenty-four late stage terminal cancer patients were given continuous infusions of 150 to 710 mg/kg/day vitamin C for up to eight weeks.	The most common adverse events reported were nausea, edema, and dry mouth or skin; and these were generally minor. One patient with a history of renal calculi developed a kidney stone after 13 days of treatment. Blood creatinine, BUN, glucose, and uric acid concentrations decreased or remained stable during therapy, suggesting that ascorbate infusions did not adversely affect renal function.
Drisko JA, Chapman J, Hunter VJ. The use of antioxidants with first-line chemotherapy in two cases of ovarian cancer. <i>J Am Coll Nutr</i> . 2003;22(2):118-23.	2 cases of remission of advanced stage ovarian cancer (one patient had Stage IIIC papillary serous adenocarcinoma, and the other had Stage IIIC mixed papillary serous and seromucinous adenocarcinoma) are presented.	Both patients had remained disease free at the time of publication. One patient had been followed for 3.5 years, the other patient for 3 years.
Bahlis et al. Feasibility and correlates of arsenic trioxide combined with ascorbic acid-mediated depletion of intracellular glutathione for the treatment of relapsed/refractory multiple myeloma. <i>Clin Cancer Res</i> . 2002;8(12):3658-68.	60g intravenous vitamin C was administered twice weekly complimentary to carboplatinum/ paclitaxel chemotherapy. Six patients with stage IIIA relapsed/refractory myeloma were studied. 0.25 mg/kg/day arsenic trioxide + 1,000 mg/day IV ascorbic acid (AA) was administered for 25 days over a 35 day period.	Two patients had partial responses; four patients achieved stable disease. Dose-limiting toxicity did not occur in any patient.
Cameron E, Campbell A. Innovation vs. quality control: an 'unpublishable' clinical trial of supplemental ascorbate in incurable cancer. <i>Med Hypotheses</i> . 1991;36(3):185-9.	Over a 4.5 year treatment period at three different cancer treatment centers, 1826 cases of "incurable" cancer were followed with 294 of these patients administered vitamin C orally, IV, or both. Oral protocol called for 10000mg per day. IV protocol called for cycles of 10000mg per day for 10 days. Standard practice in these treatment centers was not to administer chemotherapeutic agents for most adult cancers.	The coadministration of ascorbic acid did not alter the pharmacokinetics of Arsenic trioxide. Serial in vitro studies demonstrated continued sensitivity of patient myeloma cells to arsenic trioxide + AA. Mean survival was calculated as date of first hospital admittance until date of study conclusion (among subjects still alive) or death. Kaplan-Meier survival curves revealed mean survival among control patients of 180 days. Mean survival among vitamin C supplemented patients was 343 days. Identical dosing regimens produced significant variability in plasma ascorbate levels achieved. A clear linear relationship was observed for maximum plasma ascorbate level achieved and survival time. Plasma ascorbate levels greater than 3mg/dl were considered "particularly desirable".

Reference	Description	Outcomes
Campbell A, Jack T, Cameron E. Reticulum cell sarcoma: two complete 'spontaneous' regressions, in response to high-dose ascorbic acid therapy. A report on subsequent progress. <i>Oncology</i> . 1991;48(6):495-7.	A case report of terminal reticulum cell sarcoma managed with intravenous vitamin C is presented.	Spontaneous regression of a case of histologically proven widely disseminated reticulum cell sarcoma was observed, with 17 years of disease free follow-up at the time of publication of the report.
Cameron E, Pauling L. Supplemental ascorbate in the supportive treatment of cancer: Prolongation of survival times in terminal human cancer. <i>Proc Natl Acad Sci U S A</i> . 1976;73(10):3685-9.	100 patients with "untreatable" cancers were managed with a course of intravenous vitamin C (10g per day for 10 days) followed by oral dosing of 10g per day thereafter. Survival times were compared to 1000 disease matched controls.	The mean survival time for vitamin C treated subjects was 210 days, versus 50 days in disease matched controls. 90% of vitamin C treated subjects had survival times approximately 3-fold greater than controls. 10% of vitamin C treated subjects had survival times more than 20-fold greater than controls.

**Table 2; Commonly administered protocol of intravenous vitamin C in complimentary cancer management**

<p>Introductory dosing regime:</p> <ul style="list-style-type: none"> <li>• 250ml Sterile Water</li> <li>• 4ml Magnesium Sulphate (500mg/ml)</li> <li>• 2ml B12 (1000mcg/ml)</li> <li>• 2ml B6 (100mg/ml)</li> </ul>	<ul style="list-style-type: none"> <li>• 20 ml Ascorbic Acid (500mg/ml)</li> <li>• 5ml Potassium Chloroide (2meq/ml)</li> <li>• 1ml B-C-Complex (100mg/ml)</li> <li>• 4ml Sodium Bicarbonate 8.4%</li> </ul>
<p>If the formula is well-tolerated, increase dosages of constituents as follows;</p> <ul style="list-style-type: none"> <li>• 500ml Sterile Water (drain 100ml)</li> <li>• 20ml Calcium Gluconate (100mg/ml)</li> <li>• 5ml Potassium Chloroide (2meq/ml)</li> <li>• 2ml B12 (1000mcg/ml)</li> <li>• 2ml B6 (100mg/ml)</li> <li>• 2ml Multitrace (Zn 1mg, Cu .4mg, Mn .1mg, Cr 4mcg, Se 20mcg, I 25mcg, Mo 25mcg)</li> <li>• 1ml Zinc Sulphate (10mg/ml)</li> </ul>	<ul style="list-style-type: none"> <li>• 100 ml Ascorbic Acid (500mg/ml)</li> <li>• 4ml Magnesium Sulphate (500mg/ml)</li> <li>• 2ml B5 (250mg/ml)</li> <li>• 2ml B-C-Complex (100mg/ml)</li> <li>• 2ml Selenium (200mcg/ml)</li> </ul>
<p>If the formula is well-tolerated, increase dosages of constituents as follows;</p> <ul style="list-style-type: none"> <li>• 1000ml Sterile Water (drain 250ml)</li> <li>• 25ml Calcium Gluconate (100mg/ml)</li> <li>• 7.5ml Potassium Chloroide (2meq/ml)</li> <li>• 2ml B12 (1000mcg/ml)</li> <li>• 2ml B6 (100mg/ml)</li> <li>• 2ml Multitrace (Zn 1mg, Cu .4mg, Mn .1mg, Cr 4mcg, Se 20mcg, I 25mcg, Mo 25mcg)</li> <li>• 1ml Zinc Sulphate (10mg/ml)</li> </ul>	<ul style="list-style-type: none"> <li>• 150 ml Ascorbic Acid (500mg/ml)</li> <li>• 6ml Magnesium Sulphate (500mg/ml)</li> <li>• 2ml B5 (250mg/ml)</li> <li>• 2ml B-C-Complex (100mg/ml)</li> <li>• 2ml Selenium (200mcg/ml)</li> </ul>
<p>Therapy is initiated at low dosage, slow infusion, gradually working up to 50- 75g of vitamin C. Dosages greater than 50g should only be administered if access is available to a PICC line. Larger dosages into peripheral veins will result in sclerosis. Therapy is performed three times per week, pending objective demonstration of improvement (blood work, ultrasound, CAT scan, MRI). Treatment is reduced to twice weekly, and again to once weekly, as objective demonstration of improvement progresses. Once weekly treatment is typically maintained for at least months.</p>	