

Table 1: Human Studies of High-Dose Vitamin C in the Treatment of Cancer-Associated Depression

Authors, Year	Methodology	Sample size	Cancer Type(s)	Dose of vitamin C	Concomitant Therapy	Depression Scale Used	Outcome for Depression	Other Outcomes
Yeom 2007	Prospective Observational Study	39	Stage IV terminal cancer (estimated survival <6 months)	IV administration of 10g vitamin C twice with a 3-day interval and an oral intake of 4 g vitamin C daily for a week	None but they all had previous conventional therapy	EORTC QLQ-C30	Patients had significantly increased scores in emotional function after IVC therapy ($p>0.005$).	Significant improvements in QoL/global health scale as well as improvements in sleep, fatigue, N/V, pain, appetite loss and cognitive function ($p>0.005$). Patients had significantly increased scores for physical, cognitive and social function post-IVC therapy ($p>0.005$). No patients ceased IVC due to adverse effects.
Takahashi 2012	Prospective Observational Study	60	Any cancer with malignant tumours	Riordan IVC protocol; initial dose 12.5-15 g; 2nd dose 25 g; 3rd dose 50 g; 4th and additional dosing was calculated to maintain serum concentrations of 350-400 mg/dL. As well, vitamin C oral intake of 2-4 g daily	No restrictions were placed (i.e. patients were allowed to engage in concomitant conventional treatment)	EORTC QLQ-C30	There was a significant improvement in emotional function at four weeks ($p<0.05$).	Significant QoL improvements were observed from baseline where an average 8.6-point increase was observed at weeks 2 ($p<0.05$) and a 16.8-point improvement at week 4 ($p<0.01$). There were significant improvements in physical, role, cognitive, and social function at four weeks ($p < 0.05$). There were significant reductions ($p<0.01$) in fatigue and insomnia at 4 weeks compared to baseline by almost 50% as well as significantly decreased pain and constipation ($p<0.05$). No patients ceased IVC due to adverse effects.
Vollbracht 2011	Retrospective Observational Study	125	Breast cancer stage (IIa-IIIb)	Standard therapy + IVC (7.5 g Pascorbin once weekly)	Standard chemotherapy and radiation	Used a 3-point scale to assess the intensity of complaints (0=no complaints, 1=mild complaints, 2=severe complaints)	The IVC (n=53) treatment group had significantly reduced scores of depression ($p=0.017$).	There were significant reductions in cancer- and chemo/radiation-associated side effects during the adjuvant stage, such as fatigue ($p=0.004$), sleep disorders ($p=0.005$), and loss of appetite ($p=0.046$). No adverse effects associated with IVC were documented and there were no significant interactions between IVC and adjuvant therapy ($p=0.255$ for chemotherapy and $p=0.905$ for radiotherapy).
Bazzan 2018	Retrospective Observational Study	86 (32 had IVC only and 54 had IVC and chemo)	Variety of different kinds and stages	At least 5 doses of 50-150 g of IVC given over 2-3 hours	Chemotherapy (different kinds)	Used a 3-point scale to assess the efficacy of IVC treatment (improved, stable or worse) during the adjuvant therapy phase and aftercare phase	6 of the 7 patients in this study that had mood disturbances reported significant improvement and the last patient reported mood stability.	The most common adverse events related to IVC were temporary nausea and local discomfort at the site of injection. All adverse events reported in the IVC alone group were associated with less than 3% of the total number of infusions. Patients also reported improvements in fatigue and pain while receiving IVC.