### Table 2: Controlled clinical trials of Astragalus for cancer outcomes


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<th>First author, year</th>
<th>Study design</th>
<th>Participants (number, diagnosis)</th>
<th>Interventions (experimental treatments, control)</th>
<th>Main outcome measures</th>
<th>Main results</th>
<th>Comments</th>
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| Duan 2002          | RCT          | Mixed solid tumours N = 120      | Astragalus injection (20mL in 250mL saline) + chemotherapy for 4 x 21-day cycles  
Control: chemotherapy only | Chemotherapy toxicity, immune function  
Performance status (KPS) | WBCs and platelet count had a significantly lesser decline in the Astragalus group (p < 0.05)  
Astragalus group had a significantly lower CD8 (P < 0.05), increased CD4/CD8 ratio (p < 0.01), higher IgG and IgM levels (p < 0.05)  
KPS elevated in astragalus arm compared to control | Only abstract was reviewed as article is in Chinese language. Full data including methods was not reviewed. |
| Guo, 2012         | RCT, open label | Advanced (stage IIIb of IV) non-small cell lung cancer (NSCLC) N = 136 | Treatment: 250mg Astragalus polysaccharide injection (APS) on days 1-7 of each 28-day cycle of chemotherapy (vinorelbine and cisplatin)  
Control: vinorelbine and cisplatin  
Duration: 3 cycles | Tumour response, survival QoL (EORTC QLQ-C30 and LC13)  
Toxicity | No significant differences in APS versus control arm for tumour response (42.64% vs 36.76%), median survival (10.7 and 10.2 months), or 1-year survival rate (35.3% and 32.4%).  
Significant improvement in overall QoL (p = 0.003), physical function (P = 0.01), fatigue (P < 0.001), nausea and vomiting (P < 0.001), pain (P = 0.007) and loss of appetite (P = 0.023) with APS.  
No significant difference in grade 3 and 4 toxicities between groups | Study was open label |
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<th>Chen, 2012</th>
<th>Phase II, double-blind, placebo-controlled RCT</th>
<th>Patients with advanced cancer receiving palliative care, with mod-severe CRF N = 84</th>
<th>Treatment: IV PG2 500mg 3x/week for 4 weeks (cycle 1) Control: IV saline 3x/week for 4 weeks (cycle 1) All participants received PG2 for an 4 weeks in open-label extension (cycle 2)</th>
<th>Fatigue: Brief fatigue index (BFI), fatigue improve response rate Safety - AEs</th>
<th>Cycle 1: Fatigue improvement response rate (FIRR) was greater in PG2 group compared to placebo after week 1, (57% vs 32%, p = 0.043), but no significant difference after weeks 2-4. Cycle 2 (open-label): In group receiving saline in first cycle, FIRR increased significantly after cycle 2 (p = 0.02). Safety: no difference in AEs between PG2 and placebo group. No SAEs attributed to PG2. AEs included: rash (n=3), eczema (n=2), pruritus (n=2)</th>
<th>The better response in the open-label cycle may indicate a placebo-effect. Authors do not mention this, they mention that the longer duration of PG2 administration may improve outcomes.</th>
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<tr>
<td>Wang, 2019</td>
<td>RCT, multi-centre, double-blind, phase IV study</td>
<td>Patients with advanced cancer receiving palliative care, mod to severe cancer-related fatigue (BFI &gt;4) N=310 enrolled, 214 in ITT analysis Lung, colon and breast were the most common cancers in both groups</td>
<td>IV PG2 High dose (500mg) vs low dose (250mg) Frequency and duration: 3x/week for 8 weeks</td>
<td>Fatigue – Brief Fatigue Inventory (BFI) weekly Safety - AEs</td>
<td>Fatigue: 65% of participants had a ≥10% improvement in BFI at 4 weeks (73% in high dose, 67% in low dose, not stat sig different) Patients with higher Karnofsky Performance Status at baseline were more likely to be responders (p &lt; 0.001) Adverse events possibly related to astragalus &lt;9%, &gt;80% were grade 1-2. AEs possible related to astragalus include rash, pyrexia, feeling cold, chills, hypersensitivity.</td>
<td>No control group, all participants received PG2 but different doses. Authors state no placebo due to ethical considerations for a phase IV study</td>
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<td>Huang, 2019</td>
<td>RCT, double-blind, exploratory study. Subset of patients from Wang et al, 2019 study</td>
<td>Metastatic cancer, supportive care only (no active anticancer treatments)</td>
<td>N=23</td>
<td>IV PG2  High dose (500mg) vs low dose (250mg)  Frequency and duration: 3x/week for 8 weeks</td>
<td>Inflammatory Cytokines  Measured at baseline, 4 weeks, 8 weeks  QoL (EORTC QLQ C-30), BFI</td>
<td>EORTC: Significant improvement in global QoL in both high and low dose (p =0.01 and 0.02 respectively), significant improvement in pain, nausea (high-dose), fatigue (high-dose), sleep (high dose), appetite (high dose)  Inflammatory markers: suppression of pro-inflammatory IL-1b, IL-4, IL-6, IL-13, IL-17, monocytes chemotactic protein (MCP)1, GM-CSF, VEGF, TGF-B1, IFN-y, IL-10, IL-12 in both low and high dose  Univariate and multivariate analyses revealed that IL-1β, IL-13 and GM-CSF are independent prognosticators of improved QoL</td>
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| Hsieh, 2020 | Phase II, double-blind, placebo-controlled RCT | Patients (n=17) with advanced head and neck squamous cell carcinoma (HNSCC) receiving concurrent chemo-radiotherapy | Treatment: IV PG2 500mg 3x/week  Control: placebo  Concurrent treatment: Chemotherapy (Cisplatin, tegafur-uracil and leucovorin) and external bean radiation | AEs (CTCAE v 4.0)  Fatigue (BFI)  QoL (EORTC QLQ-C30 and H&N)  Overall survival, disease-specific survival, tumor response | Percentage of grade 3-4 AEs were generally lower in PG2 arm compared to placebo.  Anaemia 0% vs 12.5%, vomiting 0% vs 25%, mucositis 55.6% vs 62.5%, liver dysfunction 0% vs 12.5%, dermatitis 33.3% vs 37.5%, diarrhoea 22.2% vs 0%.  Fatigue: moderate trend of amelioration of fatigue in treatment group.  QoL remained more stable in PG2 group compared to placebo on a number of EORTC items, but most were not statistically significant. Statistically significant difference in pain (p = 0.03).  Tumour response 3 months after completion: 83.3% in placebo group and 100% in PG2 group  At 59 months, no significant difference in OS and DSS | Small study, was discontinued prematurely as a new formulation of PGE2 was approved. Most outcomes did not reach statistical significance. |

Legend: AE = adverse event, KPS – Karnofsky performance status, PS = performance status, QoL = quality of life, ITT = intention to treat, PP = per protocol, NSCLC = non-small cell lung cancer
References: