Table 2: Controlled clinical trials of Astragalus for cancer outcomes

Source: Author, CAM-Cancer Consortium. Astragalus spp. [online document]. http://cam-cancer.org/en/astralagus_spp, date 2020.

First author, year	Study design	Participants (number, diagnosis)	Interventions (experimental treatments, control)	Main outcome measures	Main results	Comments
Duan 2002	RCT	Mixed solid tumours N = 120	Astragalus injection (20mL in 250mL saline) + chemotherapy for 4 x 21d 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

Chen, 2012	Phase II, double-blind, placebo-controlled RCT	Patients with advanced cancer receiving palliative care, with mod-severe CRF N = 84	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)	Fatigue: Brief fatigue index (BFI), fatigue improve response rate Safety - AEs	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, FIRRs 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)	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.
Wang, 2019	RCT, multi-centre, double-blind, phase IV study	Patients with advanced cancer receiving palliative care, mod to severe cancer-related fatigue (BFI >4) N=310 enrolled, 214 in ITT analysis Lung, colon and breast were the most common cancers in both groups	IV PG2 High dose (500mg) vs low dose (250mg) Frequency and duration: 3x/week for 8 weeks	Fatigue – Brief Fatigue Inventory (BFI) weekly Safety - AEs	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 < 0.001) Adverse events possibly related to astragalus <9%, >80% were grade 1-2. AEs possible related to astragalus include rash, pyrexia, feeling cold, chills, hypersensitivity.	No control group, all participants received PG2 but different doses. Authors state no placebo due to ethical considerations for a phase IV study

Huang, 2019	RCT, double-blind, exploratory study. Subset of patients from Wang et al, 2019 study	Metastatic cancer, supportive care only (no active anticancer treatments) N=23	IV PG2 High dose (500mg) vs low dose (250mg) Frequency and duration: 3x/week for 8 weeks	Inflammatory Cytokines Measured at baseline, 4 weeks, 8 weeks QoL (EORTC QLQ C-30), BFI	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-γ, 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	*This data is from subset of patients from the Wang et al, 2019 study No control group, all participants received PG2 but different doses. Small study, exploratory in nature
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

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