Table 1: Randomized clinical trials of ginseng for cancer

Source: Horneber M, Ziemann J, Ritter C, CAM Cancer Consortium. Ginseng [online document]. http://cam-cancer.org/en/ginseng, 2020.

Study	Design	Participants	Treatment	Outcomes	Comments
Barton 2010	Randomised, double-blind, placebo-controlled, 4 arms	Included patients: 282 Patients with cancer-related fatigue (>4 in screening question, >1 month, no other explanations for fatigue).	Arm A (control): Placebo Arm B – D (intervention): Panax quinquefolius with different dosages over 8 weeks Arm B: 750mg/day Arm C: 1g/day Arm D: 2g/day	*Clinical outcomes*: Fatigue: Brief Fatigue Inventory with no statistically significant differences between the 4 groups with a trend towards a greater effect in arm C and D Quality of Life: SF-36 with no statistically significant differences between the 4 groups with a trend towards a greater effect in arm C and D *Adverse effects*: no statistically significant differences between the groups	Methodologically sound pilot trial with a dose-finding/confirmatory design; good reporting quality. Low risk of bias
Barton 2013	Randomised, double-blind, placebo-controlled, 2 arms	Included patients: 346 Patients with a cancer related fatigue (>4 in screening question, >1 month, no other explanations for fatigue) undergoing or having completed curative intent treatment.	Arm A (control): Placebo Arm B (intervention): Panax quinquefolius 2g/day	Clinical outcomes Fatigue (MFSI, subscales and POMS showed reduction of general and physical CRF after 8 weeks in intervention group)	Replication study of Barton 2010 with a sound methodology. Authors did not use the same questionnaire for fatigue as in the pilot trial. Low risk of bias

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Yennurajalingam 2017	Randomised, double-blind, placebo-controlled Study approved by institutional review board.	Included patients: 112 outpatients diagnosed with cancer and CRF with an average intensity of ≥4/10 on the ESAS (scale, 0–10) during the 24 hours before study enrollment. CRF also had to be present every day for most of the day for a minimum of 2 weeks.	Arm A (intervention): Panax ginseng capsules 400mg twice daily (commercially available, preparation from Panax ginseng C.A. Meyer root, hydroalcoholic extraction, standardized to contain ≥7.0% of ginsenosides and malonyl ginsenosides) Arm B (control): Placebo (colored capsules for similar appearance containing methylcellulose)	Clinical outcomes: FACIT-F, ESAS, and HADS, at baseline, day 15, and day 29. The GSE questionnaire was assessed on day 29. PG did not significantly improve QoL, anxiety, depression, cancer-related symptoms, patient-reported benefit of treatment on CRF, and physical function scores compared with placebo according to FACIT-F, HADS, ESAS, GSE, 6MWT, and HGS, respectively. There were, however, significantly fewer AEs in the PG group than in the placebo group.	Methods: Randomisation procedure not stated Participants: medium sample size Treatment: dose was based on the results of a preliminary study Outcomes: blinded assessment Low risk of bias
Martoni 2018	Multicenter, randomised, double-blind, placebo-controlled study. study	64 patients with no evidence of disease after adjuvant chemotherapy for solid tumours or with metastatic disease in progression after first-line treatment had to complain of fatigue with a score of ≥4 on the BFI. Patients with anaemia, clinical hypothyroidism, diabetes, or persistent insomnia, or who had undergone treatment with warfarin or anxiolytic therapy with a dose not yet stabilized were excluded.	Patients were randomised to receive PG at 250 or 500 mg/d or placebo for 8 weeks. Doses were given in 2 oral administrations of similar-looking capsules containing 250 mg of PG dried extract or placebo.	Patients were asked to complete a diary containing self-assessment scales including the BFI weekly and were seen in the outpatient clinic every 2 weeks. There was a gradual reduction of the median BFI score after the first 4 weeks and stabilization up to week 8 reported with no differences between the groups; 44% of the patients perceived the a high to moderate treatment benefit and 27% had a correct perception of the blinded treatment	Results published as a letter Enrolment was lower than expected, with only 64 patients randomised in 33 months, the study was discontinued. Unclear risk of bias

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Jiang 2017	Randomised, two arms, no treatment control	Included patients: 60 with advanced NSCLC (33 squamous cell carcinomas, 27 adenocarcinomas 42 with stage III, 18 with stage IV, 42 males and 18 females, mean age of 59 years old) during chemotherapy.	Arm A (intervention): fermented red ginseng (obtained from Korea Joongbu University, No. 081005) 3,000 mg daily for 60 days (first dose was given 7 days before chemotherapy) Arm B (control): no treatment Chemotherapy (both groups): gemcitabine (1.0 g/m2, days 1 and 8) plus cisplatin (25 mg/m2, days 1 to 3) chemotherapy every 3 weeks for 60 days.	Clinical outcomes: Fatigue Symptom Inventory (FSI), Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS), Chinese medicine (CM) symptoms, Karnofsky Performance Status Scale (KPS), and Functional Assessment of Cancer Therapy-Lung (FACT-L) Results: For NSCLC patients after chemotherapy, FRG extract significantly improved the FSI score, CM symptoms score, psychological status, physical conditions, and quality of life and reduced chemotherapy toxicity. Other outcomes: chemotherapy toxicity and tumor biomarkers	Methods: randomisation procedure unclear, open-label, Patients: uneven group sizes Treatment: ginseng preparation only partially described Outcomes: no blinding High risk of bias
Kim 2017	Randomised, double blind, placebo-controlled trial, two arms	Included patients: 30 women with epithelial ovarian cancer (placebo n = 15 and ginseng groups n = 15), who showed complete or partial response after surgery and six cycles of adjuvant taxane- and platinum-based chemotherapy after surgery.	Arm A (intervention): Panax ginseng: two capsules three times a day (a total of 3000 mg/day) for three months. (ginseng was prepared from grinded red ginseng, manufactured from steamed and dried roots of a 6-year-old Panax ginseng Meyer with known ginsenoside content). Arm B (control): Placebo (500 mg of corn starch)	Clinical outcomes: five-item subscales of the QLQ-C30 (EORTC QLQ-C30), Brief Fatigue Inventory (BFI), Brief Pain Inventory (BPI), Hospital Anxiety and Depression Scale (HADS) and Sleep Scale from the Medical Outcome Study (MOS-SS). Results: improved emotional functioning; decreased symptoms of fatigue, nausea and vomiting, and dyspnea; reduced anxiety and interference affecting life; improved daytime somnolence in ginseng group. Other outcomes: changes of genotoxicity and survival	Methods: pilot study, randomisation procedure unclear Patients: small study population, Treatment: well described intervention/placebo Outcomes: setting of instrument distribution unclear Unclear risk of bias

Kim 2020	Randomised, double-blind, placebo-controlled, parallel, multi-center trial.	Included patients: 219 Colorectal cancer patients who received adjuvant or palliative mFOLFOX-6	Arm A (intervention): Korean red ginseng 2000mg/day Arm B (control): placebo	Clinical outcomes: The intervention group had signicantly less fatigue (BFI, area under the curve) after 16 weeks compared to placebo (particularly in "Mood" and "Walking ability" (P = 0.038, P = 0.023, respectively). In the per-protocol group, KRG led to improved CRF in the global BFI score compared with the placebo (P = 0.019). Specifically, there were improvements in "Fatigue right now," "Mood," "Relations with others," "Walking ability," and "Enjoyment of life" at 16 weeks (P = 0.045, P = 0.006, P = 0.028, P = 0.003, P = 0.036, respectively). In subgroups of female patients, ≥60 years old, with high compliance (≥80%) or more baseline fatigue, the beneficial effects of KRG were more enhanced than that of placebo. Although neutropenia was more frequent in KRG than placebo, the incidence of all adverse events was similar.	Methods: block randomization Moderate risk of bias
Kim 2006	Randomised, double-blind, placebo-controlled, pilot study	Included patients: 53 (38 women and 15 men Patients with different cancer (gynecologic cancer n = 28, hepatobiliary cancer n = 13, other cancers n = 12)	Arm A (intervention): Panax ginseng, 1000mg three times daily (heat processed Panax ginseng, called “sun ginseng”, containing Rs4, Rs5, Rs6, Rs7) Arm B (control): Placebo Group ratio 3:2 (intervention: control)	Clinical outcomes: Difference in the mean change (week 12-baseline) of the quality of life scales WHOQOL-BREF and GHQ-12 between groups. No primary outcome measure stated. Results: Trend improvements in the GHQ-12 total score and WHOQOL-BREF psychological health. No improvement in WHOQOL-BREF social relationships	Methods: pilot study, randomisation procedure unclear Patients: small and heterogenous study population, Treatment: placebo not described Outcomes: setting of instrument distribution unclear High risk of bias

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High 2012	Randomised, double-blind, placebo-controlled	Included patients: 293 Disease: CLL, early stage, untreated	Arm A (intervention): 200mg twice daily of a P. quinquefolius extract (CVT-E002, patented mixture of polysaccharides; Afexa Life Sciences, Edmonton, Canada) for 8 weeks Arm A (control): Placebo (microcrystalline cellulose)	Clinical outcomes: Infectious complications (no significant reduction in incidence of Acute respiratory illness (ARI) in intervention group, but less moderate or severe ARI) Other Outcomes: More seroconversion to common viruses in treatment group	Methodologically sound trial with a confirmatory design; good reporting quality Low risk of bias
Younus 2003	Randomised, double-blind, placebo-controlled	Included patients: 20 Chemotherapy naive cancer patients	Arm A (intervention): Ginseng (not nearer described)r Arm B (control): Placebo (no further information provided)	Clinical outcomes: Quality of life (QLQ-C30, significant impro-vement in intervention group) Fatigue (brief fatigue inventory form, significant improvement of total fatigue level and average fatigue level in intervention group)	Only as abstract publication available High risk of bias
Pourmohamadi 2018	Randomised, double blind, placebo-controlled trial, two arms	Included patients: 113 with non-metastatic colon cancer (age range: 20-70 years old) referred for chemotherapy treatment. After the chemotherapy sessions, the patients were randomly divided into two groups.	The first group received daily dose of 100 mg Panax ginseng for 30 days and the second group received placebo medication	Clinical outcomes: A customized questionnaire with two parts (BEK test and the researcher-built test with the short-form inventory for fatigue, pain, degree of happiness, and sleep quality (answers were coded on the scale of 1 to 3 mild, moderate, and severe) Results: the symptoms of CRF including pain, appetite and QOL were significantly improved with ginseng	Methods: unclear randomisation procedure, low reporting quality Patients: small study population, Treatment: no details given for the ginseng preparation Outcomes: description of instruments unclear Unclear risk of bias

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