Table 1: Controlled clinical trials of Pomegranate for cancer

Source: Karen Pilkington, CAM-Cancer. Pomegranate (Punica granatum) [online document]. January 2019.

First author, year, (ref)	Study design	Participants	Interventions (experimental treatments, control)	Main outcome measures	Main results	Comments
Pantuck 2006[22] (included in SR by Vlachojannis et al[30])	Phase II clinical trial (open-label, single-arm)	46 men with rising PSA after surgery or radiotherapy (mean initial PSA 1.05 ng/ml; Gleason score of 7 or less)	6 to 8 ounces (180-240 mL) of pomegranate juice daily until disease progression	PSA doubling time (PSADT) Also serum-induced proliferation and apoptosis of prostate cancer cells, serum lipid peroxidation, and nitric oxide levels and safety	Mean PSA doubling time significantly increased with treatment from 15 months at baseline to 54 months posttreatment (P < 0.001). No serious adverse events reported; treatment well tolerated	Clinical effects were supported by in-vitro measures but lack of a control group limits the conclusions that can be drawn See Vlachojannis SR[30] for further comments
Freedland 2013[31] (included in SR[30])	RCT	70 men with prostate cancer	Pomegranate extract (POMx; Pom Wonderful) two tablets, POMx or placebo, daily up to four weeks before radical prostatectomy	Intraprostatic urolithin A, a pomegranate metabolite, benign and malignant 8-OHdG, and cancer pS6 kinase, NF-kappaB, and Ki67	POMx was associated with 16% lower benign tissue 8-OHdG, an oxidative stress biomarker, (P = 0.095); difference was not statistically significant	Effects on biomarkers only See Vlachojannis SR[30] for further comments
Stenner-Liewen 2013[32] (included in SR[30])	RCT	102 patients with advanced prostate cancer	500 ml of pomegranate juice or 500 ml of placebo beverage every day for a 4 week period; all patients received 250 ml of the pomegranate juice daily for another 4 weeks	PSA serum levels after one month of treatment	No differences between groups in PSA kinetics or pain scores. No grade 3 or higher toxicities reported within the study.	Randomised centrally with allocation concealed and the pomegranate juice and a placebo preparation were similar in taste and colour. Other ingredients may have also had an effect. See Vlachojannis SR[30] for further comments

Paller 2013[33] (included in SR[30])	Multicentre RCT	104 men with recurrent prostate cancer, a rising PSA and without metastases (median age of 74.5 years with a median Gleason score of 7)	1 or 3 g of pomegranate extract for up to 18 months (using capsules each containing 1g of polyphenol extract)	6-month on-study increase in PSADT from baseline in each arm	Median PSADT in the ITT population lengthened from 11.9 months at baseline to 18.5 months after treatment (P < 0.001); no significant difference between dose groups (P = 0.554); adverse effects: diarrhoea in 1.9% and 13.5% of the 1- and 3-g dose groups, respectively	Effects of different doses rather than the effects of pomegranate per se. 42% of patients discontinued treatment mainly because of a rising PSA. See Vlachojannis SR[30] for further comments
Kapoor 2015[38]	RCT	64 healthy postmenopausal women	8 ounces of either 100% commercial pomegranate juice (intervention) or apple juice (control) for 3 weeks.	Serum levels of estradiol, estrone, testosterone, androstenedione, and sex hormone binding globulin (SHBG).	Women in the intervention group did not experience any significant decline in serum sex hormones or SHBG compared to women in the control group	Cancer risk not cancer
Nunez-Sanchez 2015[37]	RCT	45 colorectal cancer patients	900 mg PE daily before surgery (35 patients) or no PE intake (10 control patients)	Effect on microRNAs (miRs) which are proposed as colorectal cancer (CRC) biomarkers	PE affects specific colon tissue miRs but also affected by surgery complicating interpretation	Effects on biomarkers only
Pantuck 2015[36]	RCT	183 men with rising PSA levels after primary therapy for prostate cancer	Pomegranate liquid extract versus placebo (extract N=102; placebo N=64; juice N=17)	Change in serum PSADT, safety and effect of a genotype	No statistically significant differences between groups in PSADT. Indication that men with MnSOD AA genotype may be more sensitive to antiproliferative effects. Majority of adverse effects mild or moderate.	Change from 3 arm to 2 arm trial due to poor recruitment. Power maintained. ITT analysis carried out. Groups matched at baseline and attrition similar. Pomegranate and matching liquid placebo provided by the study sponsor.

8-OHdG: 8-hydroxy-2' -deoxyguanosine, ITT: intention to treat (analysis), MnSOD: manganese superoxide dismutase, PE: pomegranate extract PSA: prostate-specific antigen, RNA: ribonucleic acid, SR: systematic review