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A Phase I study of docetaxel plus synthetic lycopene in metastatic, castration-resistant and chemotherapy-naïve prostate cancer patients

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Introduction & Objectives: Preclinical study showed that lycopene enhanced anti-prostate cancer efficacy of docetaxel. A Phase I trial (NCT0149519) was conducted to identify an optimum dose of lycopene in combination with docetaxel and to evaluate its effect on safety and pharmacokinetics of docetaxel in men with metastatic prostate cancer.

Materials & Methods: Participants were treated with 21-day cycles of 75 mg/m2 doctaxel, plus lycopene at 30, 90, or 150 mg/day. A Bayesian model averaging continual reassessment method was used to guid dose escalation. Pharmacokinetics of docetaxel and multiple correlative studies were carried out.

Results: Twenty-four participants were enrolled, 18 in a dose escalation cohort to define the maximum tolerated dose (MTD), and 6 in a pharmacokinetic cohort. Docetaxel plus 150 mg/day lycopene results in dose-limiting toxicity (i.e. pulmonary embolus) in 1 of 12 participants with estimated probability of 0.106 and thus is chosen as the MTD. The rate and severity of neuropathy (12.5%) and neutropenia (20.8%) were lower than expected docetaxel monotherapy. Lycopene increased the AUCinf and Cmax of plasma docetaxel by 9.5% and 15.1%, respectively. A reduction of >= 50% from baseline in IGF1R phosphorylation was observed in 60% patients. Levels of IGF-1, VEGF-A and circulating endothelial cells were suppressed by 30 mg/day lycopene, but not by 90 and 150 mg/day lycopene.

Conclusions: The combination of docetaxel and lycopene is of low toxicities and favorable in pharmacokinetics. The hormesis effects of lycopene on biomarkers suggest that the optimum dose for further trials may be determined by biochemical assays rather than by toxicity.