

A study of 7 days of water-only fasting or ketone supplementation in patients with prostate cancer

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Background: Immunotherapy is the most promising approach for durable control of metastatic cancer, however >95% of patients with prostate cancer do not respond. Studies of mouse models of cancer demonstrate that oxidation of ketone bodies enhances T cell stemness, IFN γ production, and antitumor function. Elevated systemic ketones (i.e., ketosis) can occur due to fasting-induced ketogenesis or dietary administration of ketone body supplements, which we hypothesize will enhance prostate cancer immunity. However, it is unknown whether prolonged fasting or ketone supplementation to result in sustained ketosis is safe or feasible in patients with prostate cancer.

Methods: To test the hypothesis that 7-days of water-only fasting or ketone supplementation is safe and feasible in patients with prostate cancer, we designed a phase 1, open-label, 4 cohort clinical trial (NCT06826924). Cohorts 1 and 3 enroll patients with local prostate cancer, while cohorts 2 and 4 enroll patients with recurrent/metastatic prostate cancer. Patients in Cohorts 1 and 2 perform 7-days of water-only fasting followed by a 3-day refeeding protocol. They may deviate to a very low calorie ketogenic diet at any time. Patients in Cohorts 3 and 4 consume their normal diet and a ketone supplement (80 grams of beta-hydroxybutyrate (BHB) and its precursor 1,3 butanediol sipped by mouth continuously over 12 hours) for 7 days followed by a 3 day no ketone supplement period. Each cohort will enroll 10 patients. All patients will wear continuous glucose, ketone, and activity monitors, provide research blood on days 1, 3, 7, and 10, provide tumor biopsies during screening and day 7 where feasible, and take a daily quality of life survey. The primary endpoints are the incidence and severity of adverse events and whether patients complete the protocol. Exploratory endpoints include effects of ketosis on metabolism and immunity.

Results: To date, 10 patients have enrolled (cohort 1—1; 2—8, 3—0, 4—1). The median age is 69 years, Grade Group 5, PSA 1.8 ng/ml, and ECOG 0. All participants completed the protocol. Adverse events were minimal and largely expected. In the fasting cohorts, the median blood BHB increased from 0.15 mM on day 1 (12-hours fasting) to 2.11 mM on day 3, 4.23 mM day 5, 5.57 mM day 7, while the glucose declined to a median value of 61 mg/dl on day 7. In the single patient in the ketone supplementation cohort, the blood BHB was 0.09 mM on day 1 (no supplement), 0.83 mM on day 3, and 0.96 mM on day 7, while the glucose did not change. BHB and glucose kinetics will be presented.

Conclusions: Interim analyses suggest that 7 days of water-only fasting or ketone supplementation is safe and feasible for this selected group of patients with prostate cancer.

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Conflicts of Interest: Abbott Lingo is providing glucose and ketone monitors free of cost for this study.