

**ALL ASCO GU 2021 ABSTRACTS ARE UNDER EMBARGO AS PER CONGRESS
POLICY UNTIL 5:00 PM ET ON MONDAY, FEBRUARY 8, 2021.**

Fractionated Docetaxel and Radium 223 (Ra223) in Metastatic Castration-Resistant Prostate Cancer (CRPC): A Phase I Trial.

Authors: Brendan Connell, Edmund Folefac, Clara Hwang, Christian Lawlor, Paul Mathew

Background: Disease progression following highly-active androgen-axis therapy (HAAT) in CRPC remains bone-dominant and docetaxel-responsive. Combination bone-homing Ra223 isotope therapy with docetaxel would be a logical combination therapy to follow but myelosuppression is dose-limiting. With 3-weekly bolus schedules of docetaxel (D), dose-reduction to 60mg/m² Q3wkly and Ra223 to every 6 weeks has been required representing a reduction in the dose-intensity of both agents. Fractionated schedules of docetaxel Q2wkly (DQ2) have comparable activity to D 75mg/m² Q3wkly (DQ3) with mitigated myelosuppression. We hypothesize that a fractionated dose-schedule of DQ2 in combination with standard Ra223 dosing will be feasible without reduction in dose-intensity of Ra-223 or D.

Methods: Outcomes: The primary objective is to determine the feasibility and maximal tolerated dose (MTD) of the combination. Secondary objectives include PSA kinetics, objective response, bone marker outcomes, progression free and overall survival, and description of toxicity and quality of life. Eligibility: Progressive bone-metastatic CRPC, ECOG PS 0-2 with no prior Ra223, no prior docetaxel for CRPC, and no bulky visceral disease. Design: Phase I (6+6) design; 4 week lead-in with DQ2. Dose-level 1a: 40mg/m²; 2a: 50mg/m², both with PEGylated G-CSF on Day 16. If tolerated (\leq Grade 2 toxicity, ANC \geq 1500, Platelets \geq 100,000), lead-in is followed by C1D1 of DQ2 plus Ra223 Q4wkly x 6 doses. Dose level 1a has accrued 6 subjects without DLT. Enrollment to Dose Level 2a began in August, 2020. An expansion cohort of 25 subjects is planned after the MTD is determined.

Clinical trial information: NCT03737370.