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Efficacy of low temperature-sensitive liposome encapsulated docetaxel compared to free docetaxel in a xenograft murine model of prostate cancer

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Introduction / Objective: Low temperature sensitive liposomes (LTSLs) containing doxorubicin, in conjunction with a heat source, have been shown to increase tumor cell death in a rabbit model. The objective of this study was to investigate the efficacy of LTSL encapsulated docetaxel in an in-vivo prostate cancer cell line and compare it to free drug.

Methods: Female athymic nude mice with human prostate PC-3M-luciferase cells grown subcutaneously into the right hind leg were randomized into six groups: saline with and without heat, free docetaxel with and without heat groups, and LTSL docetaxel (provided by Celsion Corp) with and without heat. Treatment (15 mg docetaxel/kg) was initiated via tail vein once tumors reached a size of 200-300mm^3. Mice that underwent hyperthermia were anesthetized and secured in a device that allowed only the leg with tumor to be submerged in 41-42 ^{0}C water for one hour. These conditions are necessary to mobilize drug payload from within liposomes. Mice were followed daily for 60 days, and tumor volumes and body weight were recorded. Mice were sacrificed if tumor reached 5 times its original size.

Results: Docetaxel treatment in combination with heat increased growth delay in the PC3M model. For a 5-fold increase in tumor volume, tumor growth delay were (mean±SEM) 8 ±1 day for LTSL alone, 15 ±5 days for free docetaxel alone, 34 ±8 days for free docetaxel with heat, and 36 ±8 days for LTSL in combination with heat. Adding heat to LTSL and free docetaxel treatment resulted in significantly greater survival and growth delay compared to other treatments ($p<0.05$).

Conclusions: The addition of hyperthermia to LTSL docetaxel or free docetaxel improved survival in our study. Future experiments involving either free or encapsulated docetaxel and a focal ablative heat source (i.e. interstitial laser or focused ultrasound) should be done to evaluate a possible benefit in local prostate tumor control.