PURPOSE: 130-nm albumin-bound paclitaxel (nab-paclitaxel) is a novel solvent-free albumin-bound paclitaxel, designed to avoid solvent-related toxicity. Nab-paclitaxel has been successfully introduced into the clinic but its radiation-enhancing potential has not yet been evaluated. We conducted a preclinical evaluation of the radiation-modulating effects of nab-paclitaxel in tumor and normal tissues. EXPERIMENTAL DESIGN: Mice bearing syngeneic ovarian or mammary carcinomas were treated with nab-paclitaxel, radiation, or combination of both. Nab-paclitaxel was administered at 90 mg/kg, 1.5 times the maximum tolerated dose for solvent-based paclitaxel. End points were antitumor efficacy (growth delay, radiocurability, and cellular effects) and normal tissue toxicity (gut and skin). RESULTS: Nab-paclitaxel showed single-agent antitumor efficacy against both tumor types and acted as a radiosensitizer. Combined with radiation, nab-paclitaxel produced supra-additive effects when given before radiation. Nab-paclitaxel significantly increased radiocurability by reducing the dose yielding 50% tumor cure (TCD(50)) from 54.3 to 35.2 Gy. Tumor histology following nab-paclitaxel treatment was characterized by pronounced necrotic and apoptotic cell death and mitotic arrest. Nab-paclitaxel did not increase normal tissue radioresponse. CONCLUSIONS: Nab-paclitaxel exhibited strong antitumor efficacy
against both tumors as a single agent and it improved radiotherapy in a supra-additive manner. These improved effects were achieved without increased normal tissue toxicity to either rapidly or slowly proliferating normal tissues although the drug dose was 1.5 times higher than the maximum tolerated dose of solvent-based paclitaxel. These preclinical findings show that combining nab-paclitaxel with radiotherapy would improve the outcome of taxane-based chemoradiotherapy. This novel taxane is thus a good candidate for testing in clinical chemoradiotherapy trials.

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