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# Paclitaxel and Carboplatin in Combination with Low-Intensity Pulsed Ultrasound for Glioblastoma

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## Abstract

**Purpose:** We recently reported on clinical trials for patients with recurrent glioblastoma where low-intensity pulsed ultrasound and microbubbles (LIPU/MB) improved paclitaxel or carboplatin delivery into the brain. Here, we report variable local tumor control with paclitaxel at the maximal/target dose in our phase I trial ([NCT04528680](https://clinicaltrials.gov/ct2/show/study/NCT04528680)). To address this, we investigated the combination of paclitaxel with carboplatin in pre-clinical glioma models.

**Experimental design:** We performed MRI-based analysis to evaluate disease control in patients from our trial. We studied the cytotoxicity of paclitaxel and carboplatin against eleven human glioma lines as monotherapy and in combination at concentrations derived from human intraoperative studies. Synergy was assessed with the Loewe model and the survival benefit evaluated in two xenografts. We examined the effects on cell cycle progression, DNA damage, and apoptosis.

**Results:** We performed MRI-based analysis to evaluate disease control in patients from our trial. We studied the cytotoxicity of paclitaxel and carboplatin against eleven human glioma lines as monotherapy and in combination at concentrations derived from human intraoperative studies. Synergy was assessed with the Loewe model and the survival benefit evaluated in two xenografts. We examined the effects on cell cycle progression, DNA damage, and apoptosis.

**Conclusions:** Combining paclitaxel and carboplatin in gliomas may be more efficacious than monotherapy, as in other cancers, due to synergy and independent susceptibility to each drug. These results form the basis for an ongoing phase II trial ([NCT04528680](https://clinicaltrials.gov/ct2/show/study/NCT04528680)) where we investigate this combination with LIPU/MB.

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