Background Unresectable tumor or incomplete surgical excision of solid tumors are risk factors for primary treatment failure. For those patients, treatment options to clear residual tumor cells following incomplete surgical excision which could be administered promptly and safely in an intraoperative setting would be beneficial. Approaches that could simultaneously clear positive margins without raising safety concerns and interfering with wound healing would be ideal. Here we have tested the hypothesis that the local, intraoperative use of chimeric antigen receptor (CAR) T cell therapy might be an effective surgical adjuvant, based on their emergence as an effective systemic immunotherapy for several hematological malignancies.

Methods We have optimized the use of tissue adhesives as a CAR T cell carrier, which could be applied intraoperatively on the wound surface without the need for intratumoral injection and have evaluated fibrin glue, a biologic tissue adhesive which was found to be an effective sealant and topical hemostatic agent. We then tested the feasibility of this approach in partial resection xenograft models of pancreatic adenocarcinoma and triple negative breast cancer using mesothelin-specific CAR T cells. In addition, we developed a novel in vivo toxicity model to evaluate safety of this approach and effects on wound healing in immunocompetent C57BL/6 mice.

Results We found that the local delivery of CAR T cells in a fibrin-glue based carrier (fibrin gel) applied within the resection cavity was effective in clearing residual cancer cells following incomplete surgical excision of subcutaneous tumors. This resulted in significantly longer overall survival when compared to mice treated with surgery and direct intracavitary CAR T cell injection without fibrin gel. Importantly, off-target toxicity was diminished compared to mice treated with systemically administered CAR T cells. In addition, wound healing complications were not seen in any of the immunocompromised or immunocompetent mice.

Conclusions In summary, CAR T cells can be effectively and safely used as a surgical adjuvant in adenocarcinomas that cannot be completely excised. Based on these promising observations, a clinical trial in patients with locally advanced breast cancer is planned.