A phase I/II study combining a TMZ-CD40L/4-1BBL-armed oncolytic adenovirus and nab-paclitaxel/gemcitabine chemotherapy in advanced pancreatic cancer: An interim report.

Benjamin Leon Musher, Brandon George Smaglo, Waisf Abidi, Mohamed Othman, Kalpesh Patel, James Jing, Nir Stanietzky, Jinyu (Jim) Lu, Amanda Brisco, Jessica Wenthe, Benjamin Brenner, Emma Eriksson, Ann M. Leen, Susan G. Hilsenbeck, Gustav J. Ullenhag, Eric Keith Rowinsky, Bambj Grilley, Angelica Sara Ingrid Loskog; Baylor College of Medicine, Houston, TX; Georgetown Lombardi Comprehensive Cancer Center, Washington, DC; Uppsala University, Uppsala, Sweden; Smith Breast Center At BCM, Houston, TX; Akademiska Sjukhus, Uppsala, Sweden; Rgenix, Inc., New York, NY

Background: Pancreatic ductal adenocarcinoma (PDAC) has been highly resistant to immunotherapeutics to date. LOAd703, an oncolytic adenovirus with transgenes encoding TMZ-CD40L and 4-1BBL, has been shown to lyse tumor cells selectively, induce anti-tumor cytotoxic T-cell responses, reduce myeloid-derived suppressor cell (MDSC) infiltration, and induce tumor regression in preclinical studies. Methods: In this phase I/II trial, patients with unresectable or metastatic PDAC are treated with LOAd703 intratumoral injections and standard nab-paclitaxel/gemcitabine (nab-P/G) chemotherapy. Starting on cycle 1 day 15 of nab-P/G, LOAd703 is injected with image guidance into the primary pancreatic tumor or a metastasis every 2 weeks for 6 injections. In the event of sustained tumor control, subjects are eligible to receive 6 more injections. Three dose levels of LOAd703 are being investigated using a BOIN dose escalation design. Primary endpoints are safety and feasibility. Secondary endpoints include response rate and overall survival. Results: To date, 13 subjects are evaluable for safety and feasibility. Three patients were treated at dose 1 (5x10^10 VP), 4 subjects at dose 2 (1x10^11 VP), and 6 subjects at dose 3 (5x10^11 VP). The most common adverse events (AEs) attributed to LOAd703 have been fever, chills, nausea, and increased transaminases. AEs have been transient and grade 1-2, with the exception of a grade 3 transaminase elevation in 1 subject receiving dose 3 (the only dose-limiting toxicity observed thus far). During protocol treatment, circulating MDSCs decreased in 8/13 subjects while effector memory T-cells increased in 10/13. ELISPOT analyses showed a rise in tumor antigen-specific T-cells in 10/13 subjects. At the lowest dose level, best response was stable disease, and 6/10 patients who received higher LOAd703 doses had partial responses. Only 1 patient has had progressive disease as best response. Conclusions: Adding LOAd703 to nab-P/G has been safe and feasible. Treatment-emergent immune responses have been demonstrated in most subjects, with a notable proportion having objective anti-tumor responses. Clinical trial information: NCT02705196. Research Sponsor: LOKON pharma, Other Foundation.