Ultrasound activated microbubbles enhance the activity of standard of care therapeutics in pancreatic cancer

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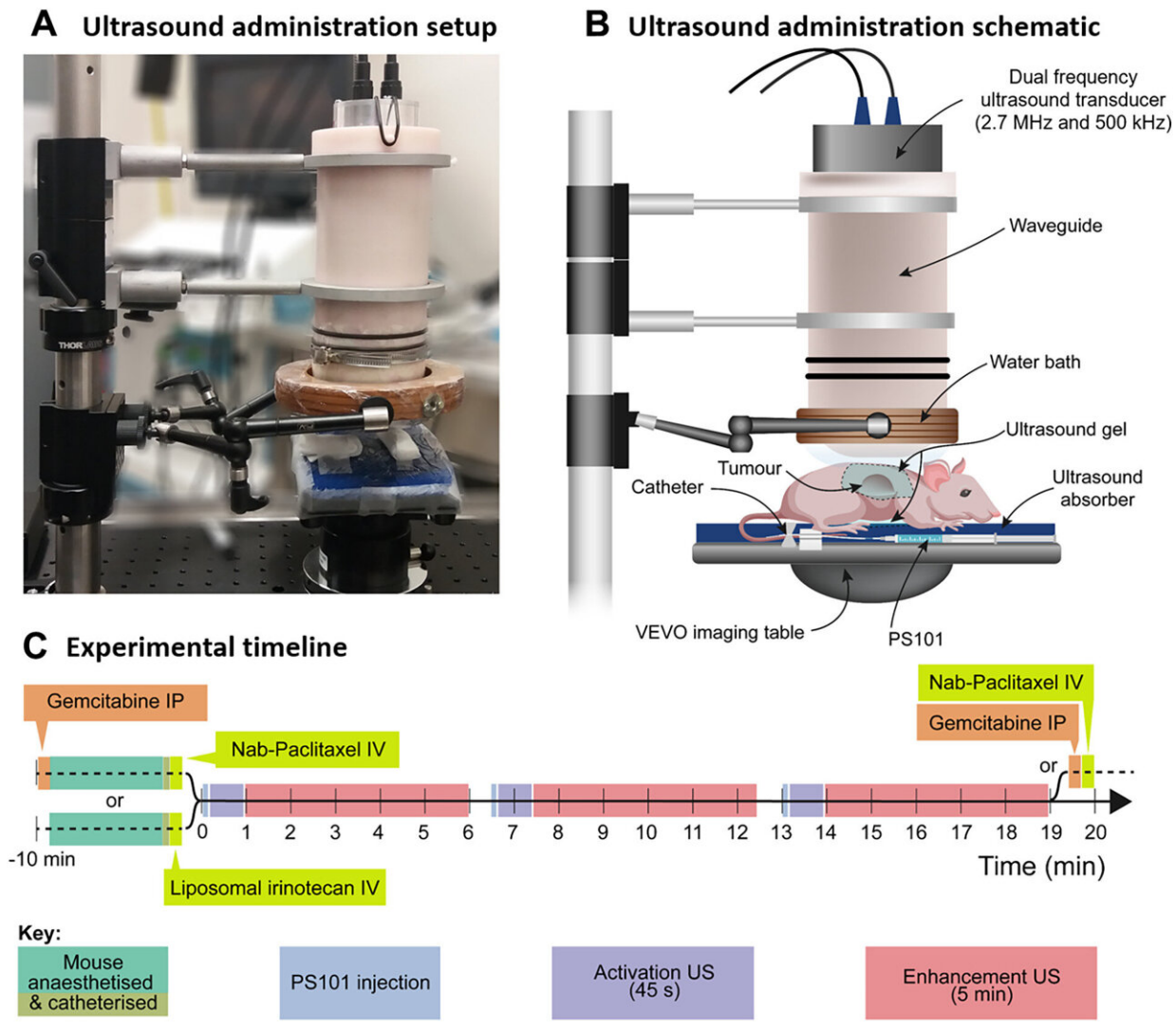

Ultrasound administration setup and drug dosing timeline. A. Photograph of the

ultrasound administration setup; B. Schematic depiction of the ultrasound administration setup; C. Experimental treatment timeline for groups that included PS101. The acoustic cluster therapy, which includes the injection of PS101, activation ultrasound, and enhancement ultrasound, was applied over a 19-min period either after or before the chemotherapeutics (gemcitabine/Nab-paclitaxel or liposomal irinotecan). IP, intraperitoneal; IV, intravenous; US, ultrasound. Credit: *Journal of Controlled Release* (2022). DOI: 10.1016/j.jconrel.2022.11.016

Scientists at the Phoenix-based Translational Genomics Research Institute (TGen), part of City of Hope, and EXACT Therapeutics AS ("EXACT-Tx", Euronext Growth: EXTX), a Norwegian clinical stage precision health company, today report that the ultrasound based Acoustic Cluster Therapy (ACT) significantly enhanced the antitumor efficacy of standard care therapies in a preclinical model for pancreatic cancer.

The study, titled "Effect of Acoustic Cluster Therapy combined with chemotherapy in a mouse model of pancreatic cancer," was published in the *Journal of Controlled Release*.

The ACT technology is based on microclusters of microbubble-microdroplets and when sonicated, vaporization of the microdroplets lead to the formation of larger ACT bubbles. The formation and subsequent oscillation of the ACT bubbles in the microvasculature produces mechanical bioeffects that enhance drug delivery and efficacy.

TGen has evaluated the effectiveness of the technology in a preclinical pancreatic cancer model, and the results demonstrated that ACT significantly improved the therapeutic efficacy of two cornerstone treatment regimens in the management of pancreatic cancer. The best effect was seen when drug administration preceded the ACT treatment,

but interestingly the anti-tumor effect was almost maintained when the drugs were administered after ACT-treatment was finalized.

Previous studies have shown that the main effect of ACT is not on the drug itself, but rather affects the vasculature and tumor microenvironment to facilitate drug delivery and therapeutic response.

"Our study demonstrates that ACT can significantly improve the effect of two standard of care chemotherapeutic regimens in a patient-derived pancreatic cancer xenograft model. The ACT treatment resulted in a significant increase in tumor growth inhibition and a 7.2 times higher probability of having a complete remission of the tumor compared to the chemotherapeutics alone," said Haiyong Han, Ph.D., a Professor in TGen's Molecular Medicine Division and the study's senior author.

This year, more than 62,000 Americans will be diagnosed with pancreatic cancer, and nearly 50,000 will die from this disease, making it the third leading cause of cancer-related death. With the best treatments currently available, the median survival for patients with advanced disease is about 10 months following diagnosis, and the 5-year survival rate is less than 9 percent of all patients.

"Pancreatic cancer is known to be notoriously resistant to treatment, in part because of poor drug delivery." said Daniel Von Hoff, M.D., TGen's Distinguished Professor and one of the nation's leading experts in pancreatic cancer. "The results from the study are some of the most encouraging ones we have seen in preclinical models for pancreatic cancer, and we look forward to being involved in the further development of this promising technology."

Per Walday, Ph.D., CEO of EXACT-Tx, said, "We are very pleased to announce the publication of these encouraging results from our collaboration with the prestigious Translational Genomics Research

Institute in Phoenix, Arizona. These data are produced in a model with patient-derived material, which more closely resembles the tumor tissue characteristics of pancreatic cancer in man compared to cell-line based models."

"The results further underpin the established potential of ACT to enhance standard of care treatments for difficult to treat cancers and we look forward to progressing our clinical development program in this area."

More information: Serina Ng et al, Effect of acoustic cluster therapy (ACT®) combined with chemotherapy in a patient-derived xenograft mouse model of pancreatic cancer, *Journal of Controlled Release* (2022). DOI: 10.1016/j.jconrel.2022.11.016

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