C31

Clinical trial on the efficacy and safety of intratumoral injection of oncolytic virus for unresectable pancreatic cancer

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Outline of Research

Pancreatic cancer is the fourth leading cause of death from cancer and has a poor prognosis, as reflected by a 5-year survival rate of 7.9%. Approximately 70% of pancreatic cancer patients do not meet indications for surgery, and the latest chemotherapy provides an overall survival of only 8.5–13.5 months; these facts indicate the need for new therapies. Approved in Europe and the United States at the end of 2015, oncolytic viruses (OV) represent an innovative cancer treatment, but their utilization in pancreatic cancer has not yet been established. Correspondingly, this study was designed as an investigator-initiated phase I/II clinical trial of survivin-responsive, conditionally replicating adenoviruses regulated by tumor-specific factors (Surv.m-CRA-1) in patients with unresectable pancreatic cancer.

Survivin, which is an anti-apoptotic protein, is highly expressed in most cancers but not detected in normal tissues. The applicants independently developed a Surv.m-CRA-1 for tumor cell-selective cytotoxicity using the survivin gene promoter, which is abnormally active in most cancers. Surv.m-CRA-1 is superior to conventional OV in that it induces a potent cytocidal effect against all cancer cell fractions, especially in cancer stem cells. Surv.m-CRA-1 is already available as a bulk drug produced following good manufacturing practice (GMP) standards for drug and quasi-drug manufacturing and quality control. Using endoscopic ultrasound-guided fine-needle aspiration, this study evaluated the safety and efficacy of local administration of Surv.m-CRA-1 in unresectable pancreatic cancer patients.

Superiority

Surv.m-CRA-1, developed by the applicants and intended for practical application in this study, is an oncolytic adenovirus inducing tumor cell-selective cytotoxicity. Several types of cancers have been shown to express survivin at increased concentrations, and this drug selectively proliferates and induces cytotoxic effects in survivin-activated tumor cells, whereas the virus does not proliferate well in normal cells with low survivin activity. Moreover, this drug outperforms chemoradiotherapy and competing OV. GMP manufacturing/testing and International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use-compliant nonclinical studies have been completed by a foreign contract manufacturing organization and a contract research organization, respectively. An investigator-initiated, first-in-human phase I trial on bone and soft tissue tumors is now in progress in collaboration with the Institute for Advancement of Clinical and Translational Science (iACT), Kyoto University Hospital, with interim results demonstrating high safety and favorable outcomes in humans.

Example of Practical Application

Highly expressed survivin has been noted in pancreatic cancer, and Surv.m-CRA-1 administered locally is expected to induce cytotoxic effects specific to pancreatic cancer cells. Thus, unlike the conventional chemoradiotherapy, this product is a new tumor-selective therapy for advanced pancreatic cancer (unresectable pancreatic cancer) with reduced side effects.

Patent Information

- WO2005/115476
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- WO2012/133674