Immunotherapy in Treatment of Pancreatic Cancer

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Inttroduction

The immune system (or defensive system) of the body is exploited by cancer. Immune cells are unable to recognise cancer cells as a threat. Cancer cells can thus avoid the immune system, multiplying and spreading throughout the body. Immunotherapy is a type of treatment that employs medications to assist the body's immune system in recognising and attacking cancer. The investigation on immunotherapy in treatment of pancreatic cancer is actively proceeding. The pancreas is one organ of digestive system that sits below the stomach, between the spleen and the small intestine. The two main functions of pancreas are; an endocrine function, which distributes insulin and glucagon into the bloodstream, and an exocrine function, which makes digestive enzymes and releases them into the small intestine. Early detection and diagnosis of pancreatic cancer are extremely difficult. Although several risk factors have been found, it frequently develops without early symptoms, and there is no widely utilised procedure for early identification (such as tobacco use, family history of pancreatic cancer, and a personal history of pancreatitis, diabetes, or obesity), few people with pancreatic cancer have risk factors that can be identified. When compared to other cancer types, pancreatic cancer is substantially more resistant to chemotherapy, leaving patients with fewer treatment options in the early stages of the disease.

Treatment options for pancreatic cancer

Surgical resection, radiation, ablative therapies, and chemotherapy are all conventional treatments for pancreatic cancer. Complete surgical excision of pancreas in only possible treatment for patients with pancreatic cancer.

Immune Checkpoint Inhibitors (ICIS)

In the presence of malignant cells, inhibitory and stimulatory signals known as immune checkpoints control the immune response from T cells (CD4+ and CD8+) via antigen recognition. Tumour cells can elude immune surveillance by producing inhibitory ligands. CTLA4 and its ligands B7-1 and B7-2, as well as programmed cell death receptor 1 (PD1) and its ligands PD-L1 and PD-L2, were the first immune checkpoints found. ICIs including ipilimumab, pembrolizumab, and durvalumab have helped patients with a range of solid cancers, but only showed limited success in pancreatic ductal adenocarcinoma (PDAC) patients.

For a tiny subset of patients with unresectable pancreatic cancer, there is now one FDA-approved immunotherapy treatment, and others are being investigated in clinical studies.

Pembrolizumab (Keytruda®)

This is a checkpoint inhibitor targeting the PD-1/PD-L1 pathway. It has been approved in treatment with advanced pancreatic cancer in patients with high microsatellite instability (MSI-H), DNA mismatch repair deficit (dMMR), or a high tumour mutational burden (TMB-H).

Therapeutic Vaccines

Another option under consideration is the use of therapeutic vaccinations to combat pancreatic cancer's immune desert. Vaccines have the potential to make PDAC tumours more immunogenic by activating particular T cells that can move into PDAC tumours. The vaccine is made out of inactivated pancreatic cancer cells, which means they can't develop. Altering these cells makes them produce a molecule that attracts immune cells to cancer cells. Vaccine therapy works by causing the body to target cancer cells in the pancreas as well as anywhere else in the body where the cancer has spread. Tumours have driver and passenger mutations, which can cause changes in amino acid sequences, resulting in mutant proteins produced by the tumours. T lymphocytes recognise these mutant proteins as foreign antigens because they are converted into short polypeptides and presented on the cell surface by the major histocompatibility complex (MHC). This distinguishing feature of a malignant cell from a normal cell may allow the immune system to target tumour cells while leaving normal cells alone.

GVAX is a whole cell vaccine made up of two human allogeneic pancreatic tumour cell lines that have been irradiated to release antigens. It's also genetically modified to release GM-CSF (granulocyte-macrophage colony-

stimulating factor) at the injection site. Dendritic cells are drawn to the GM-CSF location, where they phagocytose antigens produced by PDAC cells that have died. These dendritic cells subsequently go to draining lymph nodes, where they activate effector T-cells by presenting tumour antigens identified in vaccination PDAC cell lines.

Conclusion

In preclinical and early phase clinical trials, GVAX, a vaccine derived from PDAC tumour related antigens, demonstrated T-cell mediated anticancer efficacy. It's presently being studied in combination with ICIs.

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