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Cancer Advances, Inc. announces new publication: "Gastrin Vaccine Improves Response to Immune Checkpoint Antibody in Murine Pancreatic Cancer by Altering the Tumor Microenvironment", in the journal Cancer Immunology, Immunotherapy

- *Inactivation of the growth peptide gastrin modulates the tumor microenvironment of pancreatic cancer rendering it more susceptible to immune checkpoint antibody therapy.*
- *Polyclonal Antibody Stimulator (PAS) monotherapy elicits both a humoral and a cellular immune response when used in immune competent mice bearing pancreatic tumors.*
- *PAS monotherapy produced a marked T-cell activation and influx of CD8+ lymphocytes into pancreatic tumors.*
- *When PAS was given in combination with PD-1 Ab, tumors had less fibrosis, fewer inhibitory regulatory T lymphocytes (Tregs) and fewer tumor-associated macrophages.*
- *This research provided the basis for a poster presentation at ASCO GI in January 2019.*

DURHAM, NC, November 11, 2019

Cancer Advances, Inc., a clinical stage biopharmaceutical company developing therapeutics for gastrointestinal cancers, today announced a new publication in the journal: Cancer Immunology, Immunotherapy.

The researchers set out to determine whether vaccination with Cancer Advances' anti-gastrin cancer vaccine, PAS (Polyclonal Antibody Stimulator) induces a gastrin-dependent T-cell response in immune competent mice with pancreatic cancer. The study also examined the impact of PAS monotherapy and PAS combined with a PD-1 immune checkpoint antibody on pancreatic tumor growth, and the tumor microenvironment.

Gastrin is a digestive hormone known to have growth-promoting effects in pancreatic and other gastrointestinal cancers. Prior clinical research with PAS demonstrated that blocking gastrin led to an increase in overall survival in patients who produced an antibody response following vaccination.

Pancreatic cancer has one of the lowest five-year survival rates of any cancer. Patients are often diagnosed in late stages of the disease once the cancer has already spread outside the pancreas. In addition, the tumor's microenvironment is densely fibrotic and resistant to the body's immune defenses, chemotherapy, and immune therapy.

In this study, male mice were exposed to pancreatic cancer cells and then randomized to one of six treatment groups: placebo, 2 different doses of PAS monotherapy, one dose of PD-1 antibody monotherapy, and combination PAS/PD-1 antibody at the 2 different doses of PAS. After four weeks researchers measured the impact of treatment on tumor volume, intra-tumor fibrosis, and immune cell activity in the tumor environment.

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The study showed that PAS monotherapy alone successfully induced a T-cell response to gastrin. Activated T-cells responded to gastrin by releasing cytokines. In addition, a significant decrease in tumor size was seen in mice treated with a higher dose of PAS monotherapy as well as in mice treated with combination therapy at both doses of PAS/ PD-1 antibody, lending support for the vaccine's efficacy.

The researchers also found that the combination of PAS and PD-1 antibody therapy resulted in reduced intra-tumoral fibrosis. Mice receiving combination therapy had a higher number of tumor suppressing immune cells (CD8+ Tumor Infiltrating Lymphocytes (TILS)) and a lower number of immune evading immune cells (Foxp3+ cells, Tregs, Tumor Activating Macrophages (TAMs)) than the placebo group.

PAS vaccination combined with PD-1 antibody therapy induced a synergistic effect to reduce tumor growth and to improve T-cell response when administered concomitantly at doses that had resulted in no effect when administered as monotherapy.

This work provides compelling support for both the efficacy of PAS vaccine monotherapy and for further research into the potential for improved patient outcomes with PAS and PD-1 antibody combination therapy.

To read the abstract, please go to: PMID: 31549214
https://www.ncbi.nlm.nih.gov/pubmed/?term=31549214

Print version: Gastrin Vaccine Improves Response to Immune Checkpoint Antibody in Pancreatic Cancer by Altering the Tumor Microenvironment, Cancer Immunol Immunother. 2019 Oct;68(10):1635-1648.

https://link.springer.com/article/10.1007/s00262-019-02398-6

About Cancer Advances, Inc.

Cancer Advances Inc. (Durham, NC) is a biotechnology company focused on impacting human health and preventing the progression of gastrointestinal cancers by enhancing the adaptive immune system. The company is led by an experienced management team and has a broad intellectual property portfolio.

Cancer Advances is a wholly owned subsidiary of Cato Bioventures. The company is planning a Phase 3 registrational study for its lead compound, Polyclonal Antibody Stimulator (PAS), a cancer vaccine, in gastric cancer.

About Polyclonal Antibody Stimulator (PAS)

Polyclonal Antibody Stimulator (PAS) vaccine is an immunomodulator potentially applicable in multiple cancer types including gastric, pancreatic, colorectal, and liver. The vaccine is a peptide-conjugate that includes an N-terminal epitope of human gastrin-17 (G17) linked to carrier diphtheria toxoid. PAS has already been studied in multiple clinical trials in 1,500+ subjects and has demonstrated

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an excellent safety and tolerability profile. Cancer Advances exclusively owns PAS and is funding and managing all aspects of the PAS gastrin vaccine program.

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