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PANCREATIC CANCER

VACCINE IS SAFE AND IMPROVES SURVIVAL

Much excitement has surrounded the remarkable clinical efficacy observed with immunotherapy agents that target cytotoxic T-cell lymphocyte antigen-4 or the programmed death-1 receptor in patients with multiple solid tumour types. Additional evidence has shown that immunotherapies are also active in patients with pancreatic ductal adenocarcinoma (PDAC)—a disease with a dismal prognosis that is rarely cured because it is usually diagnosed at an advanced stage.

GVAX and CRS-207 have been assessed in early clinical trials in patients with PDAC. GVAX is an irradiated, GM-CSF allogeneic PDAC cell line, administered with low-dose cyclophosphamide (Cy). CRS-207 is a recombinant, live-attenuated form of *Listeria monocytogene* that expresses mesothelin to induce innate and adaptive immunity. On the basis of preclinical synergy of the GVAX and CRS-207 vaccines, a multicentre, randomized, phase II study was initiated; crucially, extended overall survival and minimal toxicity were demonstrated for the vaccine combination in patients with metastatic PDAC.

Patients were randomly assigned in a 2:1 ratio to either two doses of Cy/GVAX and four doses of CRS-207 (arm A) or six doses of Cy/GVAX alone (arm B). Overall survival was significantly longer in patients receiving the vaccine combination (6.1 months) compared with those treated with Cy/GVAX alone (3.9 months). This 56% improvement in overall survival is meaningful in a previously treated patient population. Grade 3 and above adverse effects included fever, lymphopenia, elevated liver enzymes, and fatigue. The study met the pre-specified criteria for early stopping, and patients in arm B were allowed to crossover to be offered arm A treatment. Regardless of the treatment arm and total doses of vaccine administered, patients treated with CRS-207 had an improved overall survival.

The authors conclude: “This is the first study to demonstrate a survival advantage using immunotherapy in PDAC. A follow-up study in previously treated patients with PDAC has been opened to compare this combination with chemotherapy and explore CRS-207 alone. Cy/GVAX and CRS-207 are being further explored as a treatment for PDAC.”

Lisa Hutchinson

Original article Le, D.T. *et al*. Safety and survival with GVAX pancreas prime and *Listeria Monocytogenes*–expressing mesothelin (CRS-207) boost vaccines for metastatic pancreatic cancer. *J. Clin. Oncol*. doi:10.1200/JCO.2014.57.4244