

SurgeryNews

NEW VACCINE STUDY Offers Hope for Patients with PANCREATIC CANCER

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For patients with pancreatic cancer, the prognosis is poor. In 2008, approximately 37,680 people were diagnosed and 34,290 died, according to the American Cancer Society. These discouraging odds may change if a new anti-cancer vaccine clinical trial being conducted at Beth Israel Medical Center proves fruitful.

The non-toxic, yeast-based vaccine, genetically engineered to stimulate immune responses against the most common mutations found in pancreatic cancer, will be investigated in a double-blind, placebo-controlled, randomized Phase III trial.

The high mortality rate for pancreatic cancer occurs because early disease is often asymptomatic and goes undetected. When symptoms do appear, they are typically vague—unexplained weight loss, discomfort in the abdomen, and occasionally glucose intolerance. Jaundice develops only if the tumor causes blockage of the common bile duct. Conventional treatments have included surgery in combination with radiation therapy and chemotherapy. These may relieve symptoms or even extend survival, but seldom do they produce a cure, and additional treatments are frequently required.

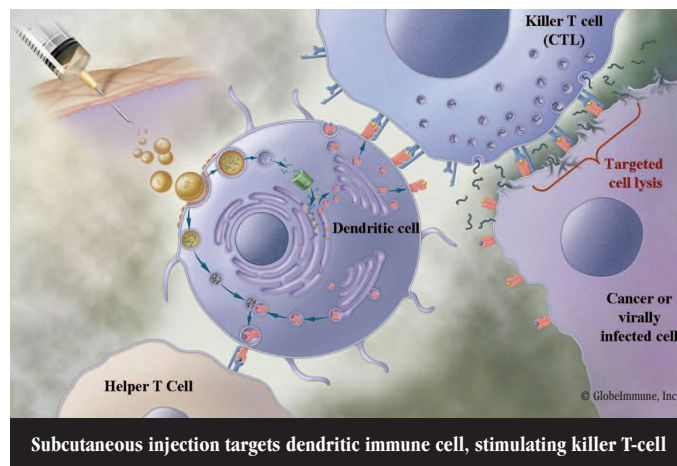
For years, interest in recruiting the body's own defenses to attack malignant cells has tempted researchers. Immune treatments for melanoma and renal cancers have met some success, but to date the only two approved cancer vaccines target the infections that result in cervical and some liver cancers. Recent drug developments take a different approach honing in on Ras protein mutations. Ras genes control signaling pathways and

regulate both normal cell growth and malignant transformation. Mutations cause these oncoproteins to remain active longer, resulting in overstimulation and, ultimately, tumor development. These Ras mutations occur in approximately 30 percent of all human cancers—and 90 percent of pancreatic cancers—making them a logical target for immunotherapy.

The study drug GI-4000, manufactured by GlobelImmune, is a recombinant, heat-inactivated *S. cerevisiae* yeast variant containing three of the five most common Ras oncogene mutations. Three separate vaccine configurations will be tested and it is hoped they will prompt the immune system to eliminate diseased cells containing gene product from the four mutations selected for investigation.

To be admitted to the GlobelImmune-funded study, patients must have resectable cancer, located in the head of the pancreas and Stage 1 through Stage 3 disease. One of the four selected mutations must be present and confirmed by genetic assay testing. Patients with microscopic positive margins can be enrolled, but those with cancer in or in close proximity to the spleen, or in the body or tail of the pancreas, will be ruled out.

Patients will be randomized to receive either vaccine with the chemotherapy drug (Gemcitabine) or placebo with Gemcitabine, the current standard of care. The drugs will be administered three times over six months. The advantage of this type of yeast-based monochromal (CONTINUED ON NEXT PAGE)



PANCREATIC CANCER VACCINE STUDY

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antibody therapy is that it elicits an immune response with each application so it remains effective if given repeatedly, rather than being diminished or extinguished over time.

Recurrence-free survival without metastases after 15 months will constitute a positive outcome. Researchers will record blood level changes in the biochemical tumor marker CA 19-9, and assess symptoms and quality-of-life measurements at the start and finish of treatment. Co-principal investigators at Beth Israel are Martin S. Karpeh, Jr., MD, Chairman of the Department of Surgery at Beth Israel, and hematologist/oncologist Peter Kozuch, MD, Attending Physician in the Department of Medicine.

The study is also being conducted at St. Luke's-Roosevelt Hospital Center, another member of Continuum Health Partners, Inc., the nonprofit hospital system that includes Beth Israel. Co-principal investigators at St. Luke's-Roosevelt are Byrne Lee, MD, and Fadi Attiyeh, MD.



For further information or to refer a patient, please call the Department of Surgery at Beth Israel Medical Center at (212) 420-4041.