AXL INHIBITORS FOR THE TREATMENT OF PANCREATIC DUCTAL ADENOCARCINOMA

Camila Esposito (Jill Shea)
Department of Surgery, School of Medicine
University of Utah

Background: In the United States more than 46,000 people will be diagnosed with pancreatic cancer. Although it is relatively rare, pancreatic cancer is the 4th leading cause of cancer death in men and women. Gemcitabine, the most common treatment for pancreatic cancer has less than 10% partial response rate. Also, Gemcitabine resistance is common in pancreatic cancer patients. Therefore, there is a clinical need to improve outcomes for patients diagnosed with pancreas cancer. Many cancers, including pancreas cancer, overexpress Axl, a receptor tyrosine kinase, which may provide a survival advantage for the cancer cells.

Aim: The aim of the study was to determine the efficacy of an Axl inhibitor to treat patient derived pancreatic cancer xenograft tumors in a mouse model. Efficacy will be evaluated by determining if the analog can curb primary and metastatic tumor progression.

Methods: A pancreatic adenocarcinoma tumor was obtained from a patient undergoing a resection at the Huntsman Cancer Institute and was propagated as subcutaneous tumors in female SHO immunocompromised mice (IRB and IACUC approved). The expanded tumor was then implanted orthotopically into the pancreas of 40 SHO female mice. Two weeks later, after the tumor had established, the mice were randomly assigned to the following treatment groups: 1) control; 2) gemcitabine + abraxane; 3) Axl inhibitor low dose; and 4) Axl inhibitor high dose. The mice were treated for 4 weeks and then sacrificed. At harvest the primary tumor was weighed and areas of metastasis were identified.

Results: The gemcitabine abraxane group (0.03±0.02g) had statistically smaller tumors than the control group (2.0±1.6g), Axl Low (1.1±0.75g), and Axl High (1.2±1.0g)(p=0.008). The gemcitabine abraxane group (0%) also had a lower incidence of metastasis than the control (70%), Axl Low (30%), and Axl High (40%) groups (p=0.04).

Discussion: The greatest efficacy was observed in the tumors treated with gemcitabine abraxane. However, there was an inhibitory effect of treatment with the Axl inhibitor on both primary tumor growth and metastasis. Further studies are needed to determine if the efficacy of treating with an Axl inhibitor could be improved with a combination treatment approach, such as an Axl inhibitor along with gemcitabine or abraxane.