Pre-clinical Investigation Of CAVATAK™ (Coxsackievirus A21) As A Potential Treatment For Pancreatic Cancer

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Background
Pancreatic cancer is a lethal cancer displaying a 5-year survival rate of 6%. Up to 90% of patients present with advanced unresectable disease due to symptoms developing in later stages. Approximately 85% of patients who undergo surgical resection relapse and succumb to the disease due to micrometastases already present at the time of surgery. Patients with metastatic disease exhibit a median survival of 6 months. Current therapies, including gemcitabine, are ineffective at controlling the disease and frequently cause severe toxicity. CAVATAK™, an oncolytic immunotherapy, is a bio-selected oncolytic strain of Coxsackievirus A21. Following intratumoral (i.t) injection, CAVATAK™ preferentially infects ICAM-1 expressing tumor cells, resulting in viral replication, cell lysis, and a systemic anti-tumor immune response (Figure 1). In general, metastatic pancreatic cancers express elevated levels of surface ICAM-1 and in vitro cultures of human pancreatic cells are susceptible to CAVATAK™-mediated oncolysis. In this presentation we investigate CAVATAK™ as a potential treatment for pancreatic cancer in an orthotopic mouse model both as a single agent and in combination with gemcitabine.

Mode of Action

CAVATAK™ (Coxsackievirus A21) and cancer modes of action

Figure 1. Proposed mode of action of intratumoral delivered CAVATAK™

Methods

• Pan-1 IAC+ cells were directly implanted into the pancreas of female BALB/c athymic nude mice and allowed to propagate for 58 days.
• Palpable tumors were intratumoral injected with CAVATAK™ (1x 10^9 TCID_50) twice over three weeks, and subsequently administered gemcitabine (120mg/kg) intraperitoneally (i.p) four times over 12 days in the combination treatment arm.
• Tumor burden was assessed by routine bioluminescence imaging and mice excluded from analyses if a >10% weight loss observed, or a tumor volume of 5 x 10^6 flux recorded during bioluminescent imaging.
• Sequential serum samples were collected weekly for analyses of viral load and neutralizing antibodies to CAVATAK™.
• Immunohistochemistry was performed on excised tumors to assess levels of CAVATAK™ replication within the tumor micro-environment.

Results

Tumor Response

Discussion

• CAVATAK™ as a single agent, and in combination with gemcitabine was well tolerated and induced notable tumor reduction and/or stabilization as assessed by bioluminescent imaging in a number of animals.
• Anti-tumor activity mediated from single agent or combination CAV21 treatment regimes, translated into statistically significant increases in survival rates (p<0.002 and p<0.008, respectively) compared to mice treated with gemcitabine alone.
• Taken together, the presented pre-clinical data suggest that CAVATAK™ may have potential anti-tumor activity in human pancreatic cancer.

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