A Phase 2 Study of Saltikva (Salmonella-IL2) in Metastatic Pancreatic Cancer
Daniel Saltzman1, Eddie Moradian2

Saltikva (Salmonella-IL2)

Background
- Genetically engineered on Salmonella platform to release human Interleukin-2 (IL-2) within the tumor microenvironment
- Oral administration
- Safe: Non-toxic with no observed adverse events
- Targeted: Seeks and colonizes solid tumors and metastases with 1,000:1-10,000:1 ratio over normal tissues
- Immunostimulatory: NK cell activation following IL-2 expression; no systemic toxicity since IL-2 is only produced in dogs with tumors
- Immuno-stimulating adjutant therapy to any standard of care, reducing required chemotherapy dose for equivalent effect
- Extensively Published: Over 20 peer-reviewed publications

Mechanism of Action
- Saltikva infiltrates tumor cells and tumor microenvironment
- Saltikva produces IL-2 within tumors
- Saltikva causes cell death by inducing a bystander immunological response
- Expansion of NK cells from IL-2 production
- NK cells release granzyme and perforin for tumor lysis
- CDB T cells bind with cancer cells for direct tumor lysis

Preclinical Studies
- 17 published murine studies demonstrating significant anti-cancer effects:
  - Metastatic colorectal adenocarcinoma to the liver
  - Metastatic Osteosarcoma to Lung
  - Primary Pancreatic Carcinoma
  - Primary Neuroblastoma
  - Primary Hepatoma
  - Metastatic Breast Carcinoma

Phase 1 Companion Canine Study demonstrated significant anti-cancer effects:
- Metastatic Osteosarcoma

Completed Clinical Studies

A subject who was diagnosed with stage IV metastatic pancreatic cancer was given Saltikva in combination with FOLFIRINOX. The first subject has now reached their 24th month of survival. A Phase I study with stage IV metastatic pancreatic cancer, a disease with a median overall survival of just 11.1 months. This patient is receiving one dose (every 2 weeks) of Saltikva® with concomitant FOLFIRINOX on an ongoing basis. The patient has not experienced any toxic effects to Saltikva®, and was able to significantly reduce the dose of chemotherapy, has normalized CA19-9 levels, maintained their immunologic cell populations despite cytotoxic chemotherapy, demonstrated a strong NK cell response, and has a radiologic regression of metastatic tumor burden with a complete absence of tumor activity by PET scan.

Advantages of Bacterial Based Cancer Therapy:
- Bacteria selectively invade and colonize solid tumors at extremely high ratios over the normal tissue of colonization (liver and spleen). Because such bacteria are facultative intracellular organisms and seek out hypoxic areas, it is hypothesized that Salmonella are naturally drawn to colonize tumors because solid primary and metastatic tumor deposits are thought to be warmer and more hypoxic than normal tissues. Bacteria stimulate the innate immune system. Many types of bacteria are able to colonize and convert the tumor microenvironment through proinflammatory responses. This alters the immunosuppressive nature of these tumors and converts them to immune stimulating.
- Bacteria have the ability to host large amount of foreign DNA. Bacterial vectors can therefore be genetically engineered to produce cytotoxic proteins within the tumor. They can also be genetically altered to attenuate the strain and reduce systemic toxicity.
- Bacteria colonize and convert primary solid tumor tissue for nutrients following colonization. This accumulation of bacteria within the tumor can cause direct oncolysis. Due to Bacteria’s increased propensity to the tumor microenvironment, their immunostimulatory nature, and their ability to host large amounts of DNA, they become an attractive candidate for delivery of cytotoxic proteins to the tumor microenvironment in order to create a desired anti-cancer immune response. Salspera has a platform of bacterial based cancer therapies that is currently developing in various solid tumor indications.


N=1 Case Study of Saltikva in Metastatic Pancreatic Cancer

Saltikva 10th every 3 weeks

Figure 1: Saltikva’s mechanism of action includes targeted colonization and IL-2 production within the tumor microenvironment

Figure 2: Saltikva in preclinical models of hepatic metastasis

Figure 3: Kaplan Meier curves for disease free interval for dogs with osteosarcoma receiving Salmonella-IL2, doxorubicin or carboplatin and doxorubicin demonstrating superior DFI in the Saltikva group

Figure 4: CA 19-9 levels in Patient #1 with metastatic pancreatic cancer (Months 0 to 12)

Figure 5: CA 19-9 levels in Patient #1 with metastatic pancreatic cancer (Months 0 to 11)

Figure 6: Flow cytometric analysis demonstrating a significant increase in the percentage of circulating NK and NKT cells

Primary Objective:
- Identify safe therapeutic dose for expansion study

Published Outcomes:
- Non-toxic with no adverse events
- Significant increase in circulating NK and NKT cells
- 10th CFU dose chosen for Phase II Study

Secondary Outcome Measures:
- Degree of tumor regression as measured by percent change of tumor(s) volume
- Determination of CA19-9 levels
- Flow cytometric analysis

Ongoing Phase II Study in Metastatic Pancreatic Cancer (FPI Oct. 2020)

Objectives:
- Assess the efficacy of multiple dose oral administration of Saltikva in patients with metastatic pancreatic cancer on standard chemotherapy (either FOLFIRINOX or Gemcitabine/Abraxane and Saltikva)
- Patient Population:
  - Unresectable, metastatic pancreatic cancer patients 18 years of age or older

Primary Outcome Measures:
- Overall Survival: Survival from diagnosis to death from metastatic pancreatic cancer (months)
- Progression Free Survival: Survival from diagnosis to progression of metastatic pancreatic cancer (months)

Secondary Outcome Measures:
- Biological response: Determination of CA19-9 levels (units per millimeter)
- Radiologic response: Degree of tumor regression as determined by serial radiologic imaging (CT Scan, PET Scan, and/or MRI - percent change of tumor(s) volume (cubic millimeters)

Salspera’s Microbial Immunotherapy Platform

Contact Us: info@salspera.com