IL-12 Protein Expression Initiation of Local Phase 1 Melanoma internal tumor, where they are capable of anchoring to the neoplasm, injecting a plasmid DNA payload, and deploying electrodes. As a majority of malignant tumors occur within the body, OncoSec Medical has begun developing catheter-based devices to perform minimally invasive intratumoral immunotherapy. These devices are guided by an endoscope to an internal tumor where they are capable of anchoring to the neoplasm, injecting a plasmid DNA payload, and deploying electrodes to perform electroporation. Performing each of these steps with one catheter-based device increases the co-localization of exogenous therapeutic DNA with the electric field, improving the therapeutic outcome of the treatment. This catheter-based device will enable minimally invasive treatment of cancers of the lung, liver, stomach, esophagus, pancreas, and others.

OncoSec Medical is an immuno-oncology company developing plasmid-based intratumoral immunotherapies for the treatment of advanced-stage cancers. Delivery of these therapeutic entities relies on the concomitant application of an electric field to traditional electroporation to advance the treatment of advanced-stage cancers. Delivery of these therapeutic entities relies on the concomitant application of an electric field to traditional electroporation to advance the treatment of advanced-stage cancers.

Clinical evidence supports intratumoral delivery of IL-12 can induce local and systemic immune responses.

IN VIVO ELECTROPORTATION

1. Cancer Cells
2. DNA - Uninjected
3. Electroporation
4. DNA - IL-12 Injected
5. IL-12 Protein Expression
6. Initiation of Local Pre-Inflammatory Process
7. Targeted Anti-Tumor Immune Response & Lymphocyte Education
8. Systemic Anti-Tumor Immune Response

INTRATUMORAL "IN-SITU VACCINATION" CAN PROMOTE ANTITUMOR IMMUNE CD8 RESPONSES

- Effective adaptive immune responses: "good" antigen + "danger signal" → immunostimulatory APC
- TRIL (cell-mediated response) appears to be the most effective type of anti-tumor immunity
- IL-12 (Th1 cell-mediated response) seems to best promote 
  adaptive responses and specifying TRIL (cell-mediated response)
- In-Situ vaccination: immunogenic cell death exposure all antigens (including mutation derived "private" neoantigens) obviating the need to choose "good antigen" a priori

INTRATUMORAL IL-12 EP RESULTS IN LOCAL NECROSIS AND CD8 INFILTRATION

Baseline Post-treatment (Day 22)

70% treated lesions with >20% necrosis

E-FIELD GENERATED

CATHERETER-BASED DELIVERY OF pDNA

Luminous images acquired through the skin 24 hours after catheter-based delivery of a luciferase expressing plasmid injected animals treated with (A and B) 50 μg of plasmid DNA delivered by electroporation; (C) no treatment; (D and E) injection of 50 μg of plasmid DNA only.

LIMITATIONS OF CURRENT TECHNOLOGY

- Clinical evidence supports intratumoral delivery of IL-12 can induce local and systemic immune responses.
- Without invasive procedure, current state of technology limited to superficial treatments due to applicator size.

PHASE II: PIL-12 EP MONOTHERAPY DEMONSTRATES ANTI-TUMOR ACTIVITY IN METASTATIC MELANOMA

DEVELOPMENT OF A CATHETER-BASED APPLICATOR FOR IMMUNO-ONCOLOGY

CATHETER DEVELOPMENT

- Catheter being developed to treat lesions of the lung, liver, stomach, esophagus, and others
- Device deployed through Lumen in endoscope, trocar, guide catheter, or sheath

- Distal catheter features:
  - Designed to fit 2 Fr or 3 Fr needles
  - Distal needle allows local delivery of plasmid DNA encoding cytokines
  - Electrodes deploy around target site for precise electroporation

- Proximal catheter features:
  - Distal deployment of central needle and electrodes
  - Object penetration depth for needles and electrodes
  - Visualize and control passage of catheter

- Precision control over electroporation processes

CONCLUSIONS

- Clinical evidence supports intratumoral delivery of IL-12 can induce local and systemic reduction in tumor burden
- Catheter-based technology will enable intratumoral gene electrotransfer to tumors that are inaccessible with current technology
- Fully adjustable needle and electrode penetration depth on catheter handle allows clinician to optimize treatment for tumors of varying dimensions
- Combining electrodes and needles improves co-localization of the therapeutic agent with electric field
- Combination therapy with other agents, such as anti-PD1 drugs, have the potential to improve response rates by increasing tumor infiltrating lymphocytes

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