Can an intratumoral DNA-encoded immunotherapeutic device platform currently used in the management of cutaneous lesions be scaled in size to function in the treatment of visceral tumors through image-guided techniques? 

Authors: Dan Simon1, James Nitzkorski2, Michael Pritchett3, John Canty4, Daniel O’Connor5, Keir Loiacono5, Chris Twitty5, John Rodriguez5, and Kim Jaffe5 

Affiliations: 1VA of NJ and MCA of Maryland, 2Vassar Brothers Medical Center, Poughkeepsie, NY, 3FirstHealth of the Carolinas & Pinehurst Medical Clinic, Pinehurst, NC, 4University of Buffalo Clinical and Translational Research Center, Buffalo, NY, 5OncoSec Medical Incorporated, San Diego, CA and Pennington, NJ 

OBJECTIVE

The mobilization of the immune system as a therapeutic strategy has emerged as a transformative approach to the treatment of cancer. Intratumoral injection of plasmid IL-12, taakonogene telsaplastim (TAVO), and co-localized reversible electroporation has demonstrated safe and promising results in the over 200 patients enrolled in trials for melanoma (KEYNOTE-695), breast cancer (KEYNOTE-890), and SCCHN. This current delivery platform uses an applicator capable of reaching lesions no more than 1.5cm at or below the skin. Here, we evaluated the feasibility and performance of an applicator capable of delivering and electroporating DNA-based immunotherapy directly into the liver, lung, bone, and pancreas in a large animal model, thus paving the way for future visceral lesion treatment in humans. 

VISCERAL LESION APPLICATOR (VLA)

Tumors located inside the body have unique challenges. Patients are often diagnosed late when treatment options are limited. Current treatment options that change tumors from immunologically ‘cold’ to ‘hot’ do not drive strong systemic responses and ablative solutions can often lack efficacy especially when controlling metastatic tumor burden. IL-12 is a potent immunomodulatory cytokine that, when delivered intratumorally via electroporation (EP), can generate local and systemic immune responses that effectively convert immunologically cold tumors to hot tumors. Providing IL-12 intratumorally avoids the toxicities associated with systemic IL-12 (EP), can generate local and systemic immune responses that effectively convert immunologically cold tumors to hot tumors. Providing IL-12 intratumorally avoids the toxicities associated with systemic IL-12 delivery while still enabling the regression of both treated and untreated lesions throughout the body. 

INTRATUMORAL ELECTROPORATION OF IL-12 (TAVO)

IL-12 is a potent immunomodulatory cytokine that, when delivered intratumorally via electroporation (EP), can generate local and systemic immune responses that effectively convert immunologically cold tumors to hot tumors. Providing IL-12 intratumorally avoids the toxicities associated with systemic IL-12 delivery while still enabling the regression of both treated and untreated lesions throughout the body.

CLINICAL TRIAL EXPERIENCE - RESPONSES IN TREATED AND UNTREATED TUMORS

• KEYNOTE-695: Patient 2 (71 year old female with stage IVA melanoma)
  - Complete response (no longer being treated)
  - Prior treatment with checkpoint therapies single agent and combination (17 cycles).

• KEYNOTE-890: Patient #03 (35year old female with TNBC)
  - Partial response by RECIST v1.1 with a 66% reduction in SLD
  - Rapid relapse following neoadjuvant chemotherapy and rapid progression on 1st line chemotherapy
  - Resolution of chest wall disease and regression of distant hepatic and nodal disease

CONCLUSION

These results demonstrate feasibility of the device to reach high value tissue targets. The ability to deliver potent and safe immunotherapy directly to a tumor presents a meaningful opportunity to drive strong clinical responses in difficult to treat malignancies and offers a potentially new solution for interventional radiologists in managing these patients. We will next look to commence a safety study in an appropriate animal model to obtain the necessary data for filing with the FDA, allowing for initiation of a phase 1 human trial using this platform in combination with TAVO to target liver tumors.

VLA IN LIVER, LUNG, PANCREAS, & BONE

Large animal simulations of CT-guided procedures were performed in the liver, lung, pancreas, and femoral medullary cavity using a Siemens Somatom Flash CT Imaging Platform. Two Yorkshire pigs were placed under general anesthesia and monitored in accordance with an approved IACUC protocol. Following rigid applicator placement and confirmation in the respective target organs, the applicator tip (injection port and electroporation tines) was deployed and electroporation commenced. CT images below show the applicator tip deployed in liver, pancreas and lung.

REFERENCES

Acknowledgements: Special thanks to the study participants, their families, the institutions participating in KEYNOTE 695 & 890 and to the Skirball Center for Innovation team. 


Contact: Keir Loiacono kloiacono@oncosec.com or Kim Jaffe kjafee@oncosec.com