Abstract #202873

Personalized vaccine for advanced HCC.

Wirote Lausoontornsiri, Michael Har-Noy, Jitraporn Wongwiwatcha, Miriam Bloch, Supaporn Suparak, Anucha Ahooja, Michael Bishop, Wattana Sukeepaisarnjaroen; National Cancer Institute, Bangkok, Thailand; Immunovative Therapies, Ltd, Jerusalem, Israel; Khon Kaen University Srinagarind Hospital, Khon Kaen, Thailand; Immunovative Clinical Research, Inc., Mesa, AZ; National Institutes of Health, Nonthaburi, Thailand; Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand

Abstract Text:

Background: The chronic inflammation and viral infection associated with HCC combined with liver tolerogenic mechanisms creates a profoundly immunosuppressive microenvironment. Modulating the microenvironment with checkpoint blockade benefits ~20% of patients. The non-responders and those with poor liver function are an unmet need. Checkpoint blockade requires effector cells to be resident within tumors. However, the majority of HCC lesions lack effector cells. Therefore, a strategy for amplifying the tumor-specific immune response, while counteracting the immunosuppressive mechanisms may provide an improved immunotherapy. Endogenous heat shock proteins (HSP) chaperone tumor neoantigens. A concentrated composition of calreticulin, hsp70, hsp90 and gr94/gp96 (CRCL) is purified from biopsy samples. In addition, a bioengineered allograft (BAG) derived from healthy blood donors with a Th1 memory phenotype, CD3/CD28-coated microbeads and high expression of CD40L has potent immunomodulatory and counter-regulatory properties. The combination of CRCL with BAG is being evaluated as a strategy to amplify tumor-specific immunity and counter-regulate the immunosuppressive microenvironment. **Methods:** An open-label Phase II clinical trial evaluating the safety and efficacy of CRCL+BAG vaccine in Child-Pugh A/B advanced/metastatic HCC w/o Sorafenib. Approximately 6-10 cores of tumor are collected at baseline. The tumor is lysed and CRCL purified using an isoelectric focusing technique. Subjects are primed with multiple intradermal injections of BAG cells alone to increase the titer of allo-specific Th1/Tc1 cells. Next, multiple intradermal injections of BAG+CRCL are administered to elicit increased titers of tumor-specific Th1/Tc1 cells. Subsequent intravenous infusions of BAG cells activate allo- and tumor-specific memory cells, enabling their infiltration into tumor lesions. The BAG allo-rejection response creates a type I cytokine storm which serves to down-regulate suppressor circuits. Response is evaluated by mRECIST and experimental biomarkers. Longitudinal CT scans with concurrent biopsies as well as multiple collections of PBMC and plasma permits immunomonitoring of these immune mechanisms. NCT02409524

Title:
Personalized vaccine for advanced HCC.

Submitter's E-mail Address:
harnoy@immunovative.com

Is this a late-breaking data submission?
No

Is this abstract a clinical trial?
Yes

Is this clinical trial registered?
Yes

Registry Name:
Clinicaltrials.gov

Registration Number:
NCT02409524