A STUDY OF AUTOLOGOUS DENDRITIC CELL THERAPY TARGETING MUCIN 1 FOR TREATMENT OF PATIENTS WITH EPITHELIAL OVARIAN CANCER IN FIRST REMISSION

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BACKGROUND
Immunotherapy-based cancer treatments show great promise in stimulating the patient’s own immune system to fight cancer. When dendritic cells (DCs) are removed from a patient's blood and then exposed to a fusion protein (FP) containing immunogenic sequences from the mucin 1 protein, the DCs are primed to mount an immune response against the mucin 1 protein, which is overexpressed in many cancers. When these primed DCs, in the form of the drug product DC-M-FP, are injected back into a patient with a tumor overexpressing mucin 1, the immune system selectively attacks the cancer. Because the patient’s own cells are the basis of the therapy, there is minimal toxicity. Two clinical studies have been completed with DC-M-FP to date and have established that the treatment does stimulate a sustained cell-based immune response and is associated with only mild side effects (Karanikas 1997, 2000; Loveland 2006). Two clinical studies are underway. One is fully enrolled (CAN-003) and the other phase 3 trial is starting globally (CAN-004 or CANVAS).

PERSONALISED BIOThERAPEUTICS
DC-M-FP is composed of a patient’s autologous dendritic cells (DCs), which are obtained by monocellular neuron (MNC) collection. The DCs are pulsed ex vivo with a recombinant human fusion protein (mucin 1-glutathione S-transferase) coupled to oxidized polymannose. The DCs are then formulated into a finished product and reinjected into the patient to stimulate a T-cell cytotoxic response targeted at mucin 1-overexpressing tumor cells.

In this study, DC-M-FP will be evaluated for the maintenance treatment of epithelial ovarian, primary peritoneal, or fallopian tube cancer (EOC) patients in complete remission (CR) after first-line chemotherapy.

CLINICAL TRIALS TO DATE
CAN-001 - 10 adenocarcinoma patients
Incurable recurrent ovarian cancer; diagnosed by elevated CA-125 initial stabilization of CA-125 for 4 months after DC-M FP CA-125 stabilization for additional 18 months after further DC-M-FP injections
Patient survival >18 months is a significant outcome in this population Evidence of T-cell activation Determination of product safety

CAN-002 – 28 advanced/recurrent persistent ovarian cancer patients
4 of 21 evaluable patients responded (19%) to DC-M-FP (stabilization or reduction in CA-125 level from baseline) DC-M-FP well tolerated; no therapy-related toxicity

CAN-003 – 63 ovarian cancer patients
1 of 2nd remission
Randomized and controlled trial of DC-M-FP compared to observation

CAN-004 (CANVAS) – 800 ovarian cancer patients
1 in 1st remission Randomized & placebo-controlled to obtain robust clinical efficacy data Validation of manufacturing specifications and process at 3 global sites

STUDY STATUS
• Approximately 1000 patients are to be enrolled globally to ensure 800 patients proceed to treatment.
• In Europe 9 countries have EC approvals Austria, Estonia, France, Germany, Latvia, Lithuania, Poland, Romania, Ukraine
• Submissions to competent authorities are underway*
• In the US and Australia the study is approved and sites are undergoing site initiations.

METHODS
The current study CANVAS (Cancer Vaccine Study) was designed to assess the efficacy, in terms of PFS, of DC-M-FP as compared with placebo for the maintenance treatment of patients with EOC in CR following first-line chemotherapy. Secondary objectives are to assess the efficacy, in terms of OS, of DC-M-FP as compared with placebo for the maintenance treatment of patients with EOC in CR following first-line chemotherapy, to assess the safety and tolerability of DC-M-FP as compared with placebo and to assess health-related quality of life (QoL), related to DC-M-FP treatment as compared with placebo.

To be eligible for this study, patients must have stage II/IV mucin-1 positive EOC in first remission after optimal cytoreductive (< 1 cm residual disease) surgery and chemotherapy.
Patients who are in remission after chemotherapy will be randomized to DC-M-FP or placebo. Patients must undergo apheresis to obtain immature DCs needed for manufacture of DC-M-FP prior to chemotherapy, and after chemotherapy will receive DC-M-FP or placebo every 4 weeks for 3 doses, and every 12 weeks for 3 doses.

REFERENCES