

3. THE NON-TECHNICAL ABSTRACT

In the Phase 1 clinical trial, 15 subjects with androgen-independent advanced metastatic prostate cancer were treated with either single-dose (n=9) or two-doses (n=6) TLI in a Phase 1 dose-escalation study. Cohorts 1 through 3 (3 subjects per cohort) were treated with single infusions of 10^4 , 10^5 , and 10^6 transgenic lymphocytes, respectively. An additional 6 subjects were treated with 2 infusions of 5×10^5 transgenic lymphocytes 1 month apart, 1 cohort using a freshly prepared booster (Cohort 4a), the other, a frozen booster prepared from the same harvest as the priming dose (Cohort 4b). No treatment-related serious adverse events were observed and no clinically significant infusion reactions were noted.

For this multi-centre Phase 2 study, TLI will be tested as adjuvant therapy in 40 subjects with Stage III Melanoma with less tumor burden, and possibly a more intact immune system. As in the Phase 1 clinical trial, subjects will be infused with autologous lymphocytes transfected with plasmid DNA which codes for selected peptide sequences from the reverse transcriptase of human telomerase, an enzyme expressed in the vast majority (>85%) of cancer cells in humans.

Study objectives will assess the efficacy, safety, and immunological responses of TLI. The subjects will be given 3 infusions (a priming infusion and 2 booster infusions) of autologous lymphocytes that have been transfected *ex vivo*, using plasmid CB-10-01. These lymphocytes will serve as antigen-presenting cells with the aim of stimulating an immune response in the recipient against melanoma cancer cells expressing telomerase.

Subjects who meet all inclusion and exclusion criteria will undergo leukapheresis at the clinical site's leukapheresis unit to obtain a sufficient number of lymphocytes for 3 infusions (a priming infusion and 2 booster infusions) and specialized laboratory testing. The cell product will be sent to the assigned manufacturer for the transfection and dose preparation in accordance with Current Good Manufacturing Practices (cGMP). Transgenic lymphocytes for the priming infusion will remain unfrozen while cells for each booster infusion will be frozen separately and stored in sterile freezing vials under cGMP standards in a dedicated liquid N₂ tank. On Day 1, the patient will receive the priming infusion. Subsequently, the patient will receive two booster infusions approximately 28 days apart. Planned study enrollment is 40 subjects. Each booster infusion will be preceded by an intravenous infusion of cyclophosphamide (300 mg/m² IV) given 3 to 5 days prior to the TLI booster infusions. 20 subjects will be enrolled and followed for 2 years from primary surgery, after which time an interim analysis will be performed. If the primary clinical endpoint is met, then the remaining 20 subjects will be enrolled. Expected duration of the study, from the first subject, first visit through last subject, last visit, could be between 4 to 5 years. For each subject, there are a total of 19 regularly-scheduled visits over a total duration of approximately 2 years (until disease progression).