

Non-technical Abstract

Phase Ib, Open Label Trial to Define The Safety, Tolerance, Transgene Function, and Immunological Effects of Intratumoral Injection(s) of Adenoviral Transduced Autologous Dendritic Cells Engineered to Express hIL-12 Under Control of The RheoSwitch[®] Therapeutic System in Subjects With Stage III and IV Melanoma

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A phase I study involving study subjects with stage III and IV melanoma will be conducted in two cohorts (groups) of subjects, each subject receiving a single injection (into a melanoma tumor) of adenoviral (a group of viruses from the *Adenoviridae* family) transduced autologous (reinserted into the same subject that they came from) dendritic cells (DCs) engineered to express human interleukin-12 (hIL-12) in combination with 14 once daily oral doses of Activator Drug. The study will use injections of dendritic cells transduced (after the cells are removed from the subjects) with adenoviral vector for inducible expression of human IL-12. The IL-12 production is “turned on” from the injected DCs through the activation of the RheoSwitch[®] Therapeutic System (RTS) by the oral administration of the Activator Drug (RG-115932). Safety and tolerance is to be assessed by physical examinations (including ECOG performance status), vital signs, serum chemistry, urinalysis, hematology, adverse events “side-effects”, and antibodies and cellular immune response to the adenovirus and the Activator Drug. In addition, the study will analyze hIL-12 levels and cellular immune response (T cells) in biopsies of the target tumors, draining lymph nodes, and peripheral circulation, as well as a serum cytokine profile.

Forty subjects with stage III and IV melanoma in two cohorts (cohort 1: 12 patients, cohort 2: 28 subjects). All subjects will receive a single injection into a melanoma tumor of adenoviral transduced autologous dendritic cells; within cohort 1, subjects will be divided into four groups each group containing three subjects who will receive a single daily oral dose of Activator Drug (Group A: 0.01 mg/kg, Group B: 0.1 mg/kg, Group C: 1.0 mg/kg or Group D: 10 mg/kg) for 14 consecutive days; with in cohort 2, 28 subjects will receive a single maximum tolerated oral dose of Activator Drug (as determined from cohort 1) for 14 consecutive days. Additional injection(s) of adenovirally transduced autologous dendritic cells in combination with 14 single (once) daily oral doses of Activator Drug may be administered to eligible subjects who meet the criteria for retreatment.