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PROPRIETARY DRUG NAME: LC002 “DERMAVIR”

THERAPEUTIC AREA: TREATMENT OF HIV INFECTION

PROTOCOL NO.: GIHU004

PROTOCOL TITLE: A PHASE I STUDY TO EVALUATE THE TOLERABILITY AND SAFETY OF LC002, A DERMAVIR VACCINE, IN HIV-1-INFECTED SUBJECTS CURRENTLY UNDERTREATMENT WITH HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)

STUDY CENTER: St. Laszlo Hospital, Budapest, Hungary

STUDY INITIATION AND COMPLETION DATES: January 12. 2005

PHASE OF DEVELOPMENT: Phase I

STUDY OBJECTIVES:

Primary Objectives

- To evaluate the safety of three doses of DermaVir Patch vaccinations in HIV-infected patients on HAART

Secondary Objectives

- To explore the immunogenicity of DermaVir patch for the treatment of individuals with chronic HIV-1 infection and HAART-induced durable suppression of viral replication
- To evaluate CD4+ and CD8+ T cell counts
- To describe the HIV-specific immune responses
- To explore whether DermaVir Patch treatment augments the magnitude of HIV-1 specific T-cell responses
- To explore whether increasing the dose of DermaVir vaccine has greater efficacy in augmenting HIV specific T-cell responses in HIV-1 infected subjects
- To explore whether there are differences in longitudinal profiles of HIV-specific T-cell levels between treatment arms
- To monitor anti-DNA antibody response after DermaVir immunization
- To explore whether there are differences in the tolerability of DermaVir Patch vaccination with respect to pre-mature treatment discontinuation between treatment arms
- To explore if immunization results in any changes in viral load

METHODS

- Single center, randomized type of trial
- Three treatment arms
- Type of population:

HIV-infected men and women 18 to 50 years of age with a peak plasma HIV-1 RNA level > 1000 copies/mL before initiation of HAART

On a stable HAART regimen without changes or interruptions for at least the 12 weeks prior to study entry

With a plasma HIV-1 RNA level of < 50 copies/mL of plasma HIV-1 RNA at least twice within the 12 weeks prior to study entry

With a CD4+ cell count > 300 cells/mm³ within 12 weeks prior to study entry and a nadir CD4+ cell count > 250 cells/mm³

- Duration of trial and timing of visits.

Subjects will be on study for a total of 4 weeks followed by an additional 48 weeks for safety evaluations

- Information about assessments

Intention to treat population (ITT), who passed the SCREENING and fulfilled all requirements (Inclusion Criteria and avoid Exclusion Criteria)

Evaluable population, who participated in the study

Per Protocol patients, who had completed all the visits, finished the study without any departure from the descriptions of the protocol.

NUMBER OF PATIENTS (PLANNED AND ANALYZED): 9 (3 subjects/cohort)

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION:

- Ability and willingness of subject to give written informed consent
- Documented HIV-1 infection
- On a stable antiretroviral regimen
- Plasma HIV-1 RNA level of less than 50 copies/mL, while on a stable antiretroviral regimen
- Peak plasma HIV-1 RNA level before initiation of HAART > 1000 copies/mL
- CD4 cell count > 300 cells/mm³ within the 12 weeks prior to study entry
- Nadir (lowest) CD4+ cell count > 250 cells/mm³ at any time prior to study entry

STUDY TREATMENT:

- Cohort 1: Three subjects will receive a single low-dose vaccination (0.1 mg DNA/subject, 0.8 mL total DermaVir) at study day 0
- Cohort 2: Three subjects will receive a medium-dose vaccination (0.4 mg DNA/subject, 3.2 mL total DermaVir) at study day 0
- Cohort 3: Three subjects will receive a high-dose vaccination (0.8 mg DNA/subject, 6.4 mL total DermaVir) at study day 0

SAFETY EVALUATIONS:

- Medical History including any previous HIV-related diagnoses and non-HIV-related diagnoses
- Complete HIV treatment history
- ALL concomitant medications during the course of the study
- All prescription medications , including those taken within 30 days prior to study entry

- Nonprescription medications and alternative therapies
- History of drug allergy
- The subject’s prior nadir CD4 cell count
- Complete physical examination
- All confirmed and probable diagnoses and any clinical events
- The vaccination skin-site evaluation

STATISTICAL METHODS:

- Primary endpoint: occurrence of at least one grade 3 or higher adverse event including signs/symptoms, lab toxicities and clinical events that is “possibly, probably” or “definitely” related to study treatment any time from the first day of study treatment until 28 days after DermaVir Patch administration.

RESULTS

- **Subject Disposition and Demography:**

Cohort 1	Gender	Age	Date of Diagnosis	CDC Stage	CD4 Nadir
0001	Female	50	2000.07.11.	A1	530
0002	Male	43	1991.04.03.	A2	261
0003	Male	42	1999.06.03.	A2	350
Cohort 2					
0004	Female	32	2001.12.18.	A2	317
0005	Male	39	1991.08.01.	A2	296
0006	Male	39	1992.05.28.	A2	392
Cohort 3					
0007	Male	46	1990.07.08.	A2	327
0009	Male	29	2003.02.18.	A2	294
0010	Male	32	1998.04.03.	A2	257

- **Safety Results: ongoing**
- **Immunogenicity Results: ongoing**

CONCLUSION(S):ONGOING