

PROTOCOL NO.: ACTG 5176

THERAPEUTIC AREA: TREATMENT OF HIV INFECTION

PROTOCOL TITLE: A Phase I/II, Randomized, Double-Blind Study to Evaluate the Safety, Tolerability, and Immunogenicity of LC002, a DermaVir Vaccine, in HIV-1-Infected Subjects Currently Under Treatment with Highly Active Antiretroviral Therapy (HAART)

STUDY HYPOTHESIS AND OBJECTIVES

Vaccination with DermaVir is hypothesized to be safe and tolerable.

Primary Objective

To evaluate the safety and tolerability (i.e., to select a dosing regimen) of DermaVir, a candidate topical therapeutic DNA vaccine.

Secondary Objectives

To explore the immunogenicity of DermaVir for the treatment of individuals with chronic HIV-1 infection and highly active antiretroviral therapy (HAART)-induced durable suppression of viral replication.

STUDY TEAM:

Protocol Chair

Richard Pollard, M.D.
Division of Infectious Diseases
University of California,
Davis Medical Center

Protocol Vice Chair

David Asmuth, M.D.
Division of Infectious and Immunologic Diseases
Department of Internal Medicine
University of California,
Davis Medical Center

DAIDS Clinical Representative

Elizabeth Adams, M.D.
HIVRB, TRP, DAIDS, NIAID, NIH

Clinical Trials Specialist

Catherine A. Battaglia, M.P.H.
Social & Scientific Systems, Inc.
ACTG Operations Center

Statisticians

John Spritzler, Sc.D.
Immunology RAC, Adult Division
Statistical & Data Analysis Center
Harvard School of Public Health

Roy Matining, M.S.
Statistical & Data Analysis Center
Harvard School of Public Health
Center for Biostatistics in AIDS Research

Minya Pu, M.A.
Statistical & Data Analysis Center
Harvard School of Public Health
Center for Biostatistics in AIDS Research

Data Manager

Julie Dudeck, M.P.H.
Frontier Science and Technology Research Foundation

DAIDS Pharmacist

Ana Martinez, R.Ph.
Pharmaceutical Affairs Branch
DAIDS, NIAID, NIH

Immunologist

Xiao-Dong Li, Ph.D.
Virology and Immunology Research Laboratory
Division of Infectious Diseases
University of California,
Davis Medical Center

Investigators

Nancy Connolly, M.D.
Department of Medicine
Division of Infectious Disease
University of Pittsburgh Medical Center

Jeffrey M. Jacobson, M.D.
Beth Israel Medical Center

Benigno Rodriguez, M.D.
Division of Infectious Diseases ACTU
University Hospital of Cleveland

Albert W. Wu, M.D., M.P.H.
The Johns Hopkins University
Bloomberg School of Hygiene Public Health
Health Policy and Management
Department of Epidemiology and Medicine

Field Representative

Kim Whitely, R.N.
Metro Health Medical Center

Laboratory Technologist

Kathleen A. Medvik, B.S., M.T. (A.S.C.P.)
Case Western Reserve University

CCG Representative

Joseph B. Robinson
University of California at Davis

Industry Representatives

Julianna Lisiewicz, Ph.D.
Genetic Immunity

Franco Lori, M.D.
Research Institute for Genetic and Human Therapy (RIGHT)

Laboratory Data Coordinator

Amanda Zadzilka, B.S.
Frontier Science & Technology Research Foundation

STUDY INITIATION AND COMPLETION DATES: January 2005 -

PHASE OF DEVELOPMENT: Phase I/II

DESIGN: A5176 is a phase I/II, randomized, double-blind trial designed to evaluate the safety, tolerability, and immunogenicity of a candidate topical therapeutic DNA vaccine, DermaVir, for the treatment of individuals with chronic HIV-1 infection who have highly active antiretroviral therapy (HAART)-induced durable suppression of viral replication. Subjects will be sequentially enrolled into one of three cohorts and randomized to receive either DermaVir (six subjects per cohort) or DermaVir placebo (two subjects per cohort). Enrollment of subjects into the higher dose Cohorts 2 and 3 will occur if at least six of the eight subjects were on study until at least 14 days after receiving their second study vaccination and no subject in the current or lower dose cohort experienced a primary safety endpoint.

DURATION: Subjects will be on study for a total of 61 weeks. Each cohort's immunization schedule will be administered over a 13-week period, with an additional 48 weeks of follow-up for safety evaluations.

SCHEMA (Cont.)

- SAMPLE SIZE: A total of 24 subjects (eight subjects/cohort) will be enrolled and randomized to receive DermaVir or DermaVir placebo.
- POPULATION: HIV-infected men and women 18-50 years of age who are on a stable HAART regimen within the 12 weeks prior to study entry.
- REGIMEN: Cohorts will be sequentially enrolled:
- Cohort 1:
 - Arm A: Six subjects will receive three separate low-dose vaccinations (0.1 mg DNA/subject, 0.8 mL total, administered over two skin sites of 80 cm² each, 0.4 mL/site) on study days 7, 49, and 91 (weeks 1, 7, and 13).
 - Arm B: Two subjects will receive three separate placebo vaccinations (0.8 mL total, administered over two skin sites of 80 cm² each, 0.4 mL/site) on study days 7, 49, and 91 (weeks 1, 7, and 13).
 - Cohort 2:
 - Arm C: Six subjects will receive three separate high-dose vaccinations (0.4 mg DNA/subject, 3.2 mL total, administered over four skin sites of 80 cm² each, 0.8 mL/site) on study days 7, 49, and 91 (weeks 1, 7, and 13).
 - Arm D: Two subjects will receive three separate placebo vaccinations (3.2 mL total, administered over four skin sites of 80 cm² each, 0.8 mL/site) on study days 7, 49, and 91 (weeks 1, 7, and 13).
 - Cohort 3:
 - Arm E: Six subjects will receive six separate high-dose vaccinations (0.4 mg DNA/subject, 3.2 mL total, administered over four skin sites of 80 cm² each, 0.8 mL/site) on study days 0, 7, 42, 49, 84, and 91 (weeks 0, 1, 6, 7, 12, and 13).
 - Arm F: Two subjects will receive six separate placebo vaccinations (3.2 mL total, administered over four skin sites of 80 cm² each, 0.8 mL/site) on study days 0, 7, 42, 49, 84, and 91 (weeks 0, 1, 6, 7, 12, and 13)