This report may include approved and non-approved uses, formulations, or treatment regimens. The results reported may not reflect the overall profile of a product. Before prescribing any product mentioned in this report, healthcare professionals should consult local prescribing information for the product approved in their country.

2.0 SYNOPSIS

MERCK SHARP & DOHME CORP., A SUBSIDIARY OF MERCK & CO., INC SCH 417690 / MK-7690 Vicriviroc, non-interventional HIV	**CLINICAL STUDY REPORT SYNOPSIS**

PROTOCOL TITLE/NO.: COVER-Continuing Observation after Vicriviroc (VCV) Exposure Registry — P04999

PROTECTION OF HUMAN SUBJECTS: This study was conducted in conformance with applicable country or local requirements regarding ethical committee review, informed consent, and other statutes or regulations regarding the protection of the rights and welfare of human subjects participating in biomedical research.

INVESTIGATOR(S)/STUDY CENTER(S): Multicenter. Subjects were enrolled at centers in North and South America, Europe, and South Africa.

PUBLICATION(S): None

PRIMARY STUDY PERIOD: 27 AUG 2007 – 03 SEP 2010 **CLINICAL PHASE:** 3

DURATION OF TREATMENT: No study treatment was administered in this observational study.

OBJECTIVE(S):

Primary Objective: To assess certain long-term clinical outcomes, namely development of malignancies, AIDS-defining events, and death in subjects who had discontinued from clinical trials with VCV.

Secondary Objective: To assess evolution of viral tropism in subjects after VCV discontinuation relative to subjects with no history of VCV exposure.

STUDY STATUS: The study was terminated early, after the Sponsor discontinued the development of vicriviroc for the treatment of HIV in June 2010.

STUDY DESIGN: This was a nonrandomized, prospective, observational, multisite registry for subjects with HIV who participated in Phase 2 and 3 VCV studies. The number of subjects to be enrolled in the registry was not predetermined. All subjects with HIV who had participated in a Phase 2 or 3 clinical trial of VCV and were no longer receiving study drug (VCV or placebo) were eligible for registry enrollment, regardless of duration of study treatment. Subjects from the Aids Clinical Trial Group (ACTG) A5211 study (and its rollover P04100) did not participate in this registry because they were followed by the ACTG.

Subjects enrolled in the registry were to be followed at study visits once every 6 months for up to 5 years. Assessments of long-term safety included the incidence of malignancies and AIDS-defining events, evolution of viral tropism, and HIV RNA and CD4+ counts, when available. Results of viral tropism assays (performed in a central laboratory) were to be collected prospectively at each 6-month visit. HIV RNA and CD4+ counts for the period between visits were to be obtained as available, with the expectation that these tests would be performed regularly per standard of care.

SUBJECT/PATIENT DISPOSITION: A total of 179 subjects participated in the registry, including 156 subjects who had received VCV and 23 subjects who had received placebo in a previous VCV trial. Three subjects discontinued participation in the registry: two withdrew consent and one was lost to follow-up. The remaining subjects were discontinued when the registry was terminated by the Sponsor.

DOSAGE/FORMULATION NOS.: No study medication was provided in this program. The protocol did not recommend the use of specific medication. Antiretroviral treatments were selected and prescribed by each subject's primary HIV physician.

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DIAGNOSIS/INCLUSION CRITERIA:

Subject Inclusion Criteria

The subject must have met all of the criteria listed below to be enrolled in the registry:

- Subjects must have participated in a Phase 2 or 3 study with VCV and must no longer receive study drug, regardless of VCV exposure (ie, placebo recipients with no VCV exposure during the study are also eligible).

Subject Exclusion Criteria

The subject was to have been excluded if any of the criteria listed below were met:

- Subject was unwilling to participate in the registry or to give informed consent.

EVALUATION CRITERIA: Assessment of the long-term safety of VCV-treated subjects who were enrolled in clinical trials, included the following data when available:

- The incidence of malignancies and AIDS-defining events,
- Evolution of viral tropism, and
- HIV RNA and CD4+ counts.

No serious adverse events were to be documented on the case report form except those judged to be related to the venipuncture for the tropism viral assay, if applicable.

STATISTICAL PLANNING AND ANALYSIS: The primary endpoints for the registry were the incidence of malignancies, the incidence of AIDS-defining events, and the death rate. The key secondary endpoints were the incidence of change in plasma viral tropism, time to change in plasma viral tropism and, depending on data available, change in HIV RNA and CD4+ counts. Descriptive statistics were to be provided for registry endpoints. This was not a randomized study; therefore, no inferential analysis of data was planned. The incidence rate of malignancy, AIDS-defining events, emergence of CXCR4-tropic virus, and persistence of CXCR4-tropic virus were to be summarized without regard to prior treatment group as follows:

- Incidence proportion = (number of subjects with events/total number of subjects)*100
- Incidence rate = number of subjects/person-months of follow-up.

As a result of early study termination by the Sponsor and low enrollment in the registry, the following planned analyses were not performed: incidence rates based on subjects' time on study, changes from baseline in CD4 count and HIV RNA, and changes in viral tropism. Subject data listings were prepared.

RESULTS:

The registry enrolled 127 men and 52 women who previously had participated in a Phase 2 or 3 VCV trial (P03672, P04405, P04875, P04889, or P05057). Subjects with prior VCV exposure and those with no VCV exposure were well matched, with 71% and 74% male subjects, respectively, and median ages of 46 years and 45 years, respectively. In both groups, 61% of subjects were white.

Summary of Primary Endpoints in P04999

Subjects (Number, %)	VCV Exposure (N=156)	No VCV Exposure (n=23)
Malignancies	0	0
AIDS-defining events	0	0
Deaths	0	0

No new malignancies were found in either group. AIDS-defining events were common at Baseline, but no new events were reported on study. There were no reports of death or serious adverse events (limited to events associated with venipuncture for the tropism viral assay).

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CONCLUSIONS: No new malignancies, AIDS-defining events, or deaths were reported in this registry of subjects who previously participated in a clinical trial of vicriviroc. Conclusions regarding the impact of vicriviroc exposure on subsequent health cannot be drawn from the results of this registry because the program was terminated early and enrollment was low.