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

Title of Study: Vicriviroc (SCH 417690) in Combination Treatment With an Optimized ART Regimen in HIV-Infected Treatment-Experienced Subjects (VICTOR-E4) Final Analysis (Protocol No. P04889)	
Investigators: Multicenter, multinational	
Study Centers: 99 sites in North America, Europe, Latin America, and South Africa	
Publication: Gathe J, Diaz R, Fätkenheuer G, Zeinecker J, Mak C, Vilchez R, Greaves W, Kumar S, Onyebuchi C, and Dunkle L. Phase 3 trials of vicriviroc in treatment-experienced subjects demonstrate safety but not significantly superior efficacy over potent background regimens alone. Presented at the 17th Conference on Retroviruses and Opportunistic Infections; 2010 Feb 16-19; San Francisco (CA).	
Studied Period: 31 JUL 2007 to 26 OCT 2010	**Clinical Phase:** 3

Objectives

Primary: To confirm the hypothesis that vicriviroc (VCV) 30 mg once daily (QD) provided added benefit in plasma human immunodeficiency virus (HIV) ribonucleic acid (RNA) reduction when added to an optimized background therapy (OBT).

Secondary: To evaluate the safety and tolerability of VCV compared to placebo, each in combination with OBT.

Methodology: This was one of two identically designed, randomized, double-blind, placebo-controlled, parallel-group, multicenter studies of VCV which was conducted in conformance with Good Clinical Practices (GCP) in treatment-experienced subjects infected with solely CCR5-tropic HIV virus. Screening occurred up to 60 days before randomization. Eligible subjects were randomized in a 2:1 ratio to 48 weeks of treatment with VCV 30 mg QD or placebo, each in addition to an open-label OBT containing at least two fully active antiretroviral agents and a ritonavir-boosted protease inhibitor (PI/r). The OBT was selected by investigators based on viral susceptibility testing performed during Screening, subject's history of prior antiretroviral drug use, and toxicity. Subjects returned at Weeks 1, 2, 4, 8, 12, 16, 20, 24, 32, 40, and 48 for assessments related to antiviral efficacy, safety, and pharmacokinetics (PK).

The Trofile™ assay (Monogram Biosciences, Inc) was used throughout the study to determine viral tropism. A retrospective reanalysis of viral tropism for all subjects determined to have CCR5-tropic virus at Baseline was carried out prior to the locking and unblinding of the Week 48 final analysis. Only subjects who had virus that was assayed to be CCR5-tropic by the Trofile assay and the Trofile Enhanced Sensitivity (Trofile ES) assay were included in the primary evaluation of efficacy (modified intent-to-treat [MITT] population). Subjects who were determined to have dual/mixed CCR5/CXCR4-tropic virus by the Trofile ES assay were included in the Full Analysis Set (FAS) population, in addition to all of the MITT subjects. Efficacy analyses based on the FAS population were also done as supportive analyses.

Efficacy was evaluated primarily by measurements of HIV RNA, which were scheduled at all visits. Other assessments included measurements of CD4 cells, monitoring coreceptor tropism of HIV isolates and susceptibility to VCV and components of OBT. The evaluation of safety included physical examinations, vital signs assessments, electrocardiograms (ECGs), clinical laboratory tests, and emergence of complicating medical conditions. Subjects were observed and questioned for occurrence of possible adverse events (AEs) and acquired immunodeficiency syndrome (AIDS)-defining events (ADEs). Prior and concomitant medications were recorded.

An independent, external Data Safety Monitoring Board (DSMB) was constituted to review data on a periodic basis, including formal reviews at the Week 24 and Week 48 time points. An Adjudication Committee reviewed all ADEs.

Number of Subjects: With a planned sample size of 375 subjects (250 subjects in the VCV arm and 125 subjects in the control arm), the study had >95% power to demonstrate superiority of VCV over placebo, each in combination with OBT, when the true response with 40% on VCV and 20% on placebo, assuming the nontreatment-related discontinuation rate was 10% (based on a two-sided test at alpha = 0.05). The enrolled population was 400 subjects (267 subjects in the VCV arm and 133 subjects in the control arm).

Diagnosis and Criteria for Inclusion: Subjects eligible for the study were: adults (≥16 years of age or the minimum age that defined an adult as determined by local regulatory agencies) with documented CCR5-tropic HIV infection only; plasma HIV RNA >1,000 copies/mL either on a stable regimen of three or more antiretroviral drugs for at least 4 weeks at the time of Screening or on no antiretroviral agents for at least 4 weeks prior to

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Screening; antiretroviral therapy (ART)-experienced with documented resistance to at least two of the following three drug classes: nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), or protease inhibitors (PIs) or, alternatively, ≥6 months of antiretroviral class experience with at least two of the following: one NRTI, one NNRTI or two PIs (excluding low-dose ritonavir); no history of previous malignancy (with the exceptions of cutaneous Kaposi's sarcoma without visceral or mucosal involvement that resolved with highly active antiretroviral therapy [HAART] but without systemic anti-cancer treatment, and basal-cell carcinoma of skin surgically resected with disease-free margins on pathology exam); no history of prior receipt of cytotoxic cancer chemotherapy that may have increased the risk of malignancy; no history of recurrent seizures, or central nervous system (CNS) condition or drug use judged to predispose to seizure; no active untreated AIDS-defining opportunistic infection; and acceptable hematologic, renal, and hepatic laboratory parameters.

Test Product, Dose, Mode of Administration, Batch Nos: Vicriviroc (VCV) tablet, 30 mg administered orally (PO) QD (Batch Nos. [redacted]

Duration of Treatment: Subjects were treated for 48 weeks. After Week 48, subjects (except for those enrolled in UK sites) were offered open-label VCV 30 mg QD. Additionally, subjects who discontinued prior to Week 48 may have been eligible for the open-label segment of the study. Including the open-label extension period, the maximum duration of subject participation in this study was 3.25 years.

Reference Therapy, Dose, Mode of Administration, Batch No: Batch numbers for placebo matching tablets were [redacted] and [redacted]

Criteria for Evaluation

Primary Efficacy Endpoint

- The proportion of subjects with undetectable plasma HIV RNA (<50 copies/mL) at Week 48 when all subjects had either completed 48 weeks of treatment or had discontinued from the study.

Key Secondary Efficacy Endpoints

- Mean change from Baseline in plasma HIV RNA (log_{10} copies/mL) at 48 weeks.
- Proportion of subjects with <400 copies/mL of plasma HIV RNA at 48 weeks.
- Proportion of subjects with ≥2 log_{10} reduction from Baseline in plasma HIV RNA at 48 weeks.

Other Secondary Efficacy Endpoints

- Time to Loss of Virologic Response (TLOVR).
- Mean change from baseline CD4 count at 48 weeks.

Virologic Endpoints:

- Frequency of emergence of viral resistance to VCV or other regimen components.
- Frequency of detection of CXCR4-tropic or dual/mixed CCR5/CXCR4-tropic virus.
- Frequency of detection of CXCR4-tropic or dual/mixed CCR5/X4-tropic virus accompanied by a significant decrease in CD4 cell count below the baseline value.

Clinical Safety Endpoints:

- Proportions of subjects with clinical adverse experiences as follows:
  - Proportion of subjects with at least one adverse event (AE).
  - Proportion of subjects with at least one serious AE (SAE; including seizures and malignancies).
  - Proportion of subjects with discontinuation for an AE.
  - Proportion of subjects with Grade 3/4 AEs.

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- Proportion of subjects with clinically significant laboratory abnormalities (ie, abnormalities requiring medical intervention). A clinically significant laboratory abnormality was one that met one or both of the following criteria:
    1. Required intervention/additional therapy.
    2. Was associated with a clinical manifestation.
    - ADEs (per Adjudication Committee)
    - Clinical AEs of interest in the following categories: malignancies, hepatoxicities, ischemic cardiovascular events, herpes simplex virus (HSV) infections, upper respiratory tract infections (URIs), hyperlipidaemia, seizure.
    - AEs leading to deaths.

Interim at Wk 24 Analysis: A planned interim analysis was conducted when all subjects had completed 24 weeks of treatment or had dropped out.

- A complete evaluation of the efficacy and safety profile was carried out at alpha level of 0.05. Data for the primary and secondary efficacy variables as well as all safety endpoints was evaluated at the 24 weeks time point.
- The unblinded interim analysis was reviewed by the DSMB.
- A limited number of sponsor representatives were unblinded for the 24-week analysis, while the investigator, patient and all personnel directly responsible for conduct of study remained blinded until the end of the 48-week treatment period.

Statistical Methods

Efficacy: The efficacy evaluation was based on the MITT population, which was the subset of all randomized and treated subjects (FAS) who had CCR5-tropic virus at Baseline as determined by both the Trofile and Trofile ES assays. Efficacy evaluations based on the FAS population, which included all randomized and treated subjects, were also performed to assess the robustness of the results. The primary efficacy analyses were performed when all subjects either completed 48 weeks of treatment or had discontinued from the study. The primary efficacy endpoint was the proportion of subjects with plasma HIV RNA <50 copies/mL at Week 48. It was analyzed in a logistic regression with treatment (VCV + OBT/Placebo + OBT), use of enfuvirtide in baseline OBT (yes/no), and baseline HIV RNA count (≤100,000/>100,000 copies/mL) as covariates. Study randomization was stratified by intended use of enfuvirtide in OBT and screening HIV RNA. However, the actual use of enfuvirtide at Baseline and baseline HIV RNA were incorporated in the analysis model. The primary hypothesis was that VCV in combination with OBT would produce superior HIV viral suppression in comparison to OBT alone among CCR5-tropic virus infected subjects.

Missing data in the primary endpoint was handled in the primary analysis using the “Non-Completer=Failure” (NC=F) algorithm.

Success or failure of the primary efficacy endpoint was determined by whether the HIV RNA viral count (measured or imputed as described in **Section 9.7** [Statistical Methods]) was $<$ or $\geq$50 copies/mL.

The following parameters were analyzed as key secondary efficacy endpoints:

- Mean change from Baseline in plasma HIV RNA ($\log_{10}$ copies/mL) at 48 weeks.
- Proportion of subjects with $<$400 copies/mL of plasma HIV RNA at 48 weeks.
- Proportion of subjects with a $\geq$2 $\log_{10}$ reduction from Baseline in plasma HIV RNA at 48 weeks.

The following parameters were analyzed as additional secondary efficacy endpoints:

- Time to loss of virologic response (TLOVR) at Week 48.

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- Mean change from Baseline CD4 cell count at Week 48.

The proportion of subjects with <400 copies/mL HIV RNA, was analyzed by an analogous logistic regression as the primary efficacy endpoint. Mean change from baseline $\log_{10}$ HIV RNA copies/mL and mean change from baseline CD4 cell count were analyzed in an analysis of variance (ANOVA) model using the same covariates.

Missing data were handled based on the NC=F algorithm as for the primary efficacy analysis.

The durability of effective treatment was measured by the TLOVR. The difference in TLOVR was analyzed by log-rank test. In addition, Kaplan-Meier plots were presented by treatment.

The primary efficacy analysis was controlled at alpha level of 5%. If the primary analysis was significant, analysis of the key secondary variables were carried out with a Hochberg's procedure to control the overall false discovery rate at <5%. Analyses of the additional secondary endpoints that were not designated as "key" were intended for supportive purposes, and were not corrected for multiplicity.

Data for the primary and secondary variables were summarized by treatment at all time points. Results from statistical modeling, including point estimates, confidence intervals, and p values, were also presented.

Safety: The safety evaluation was based on all randomized and treated subjects (Safety Population). Subject data were tabulated and analyzed according to the actual treatment received by the subject, regardless of the treatment groups for which they were randomized.

The virologic and clinical safety endpoints defined earlier were summarized by treatment arm. Incidence of AEs, rates adjusted for duration of exposure and development of HIV resistance to VCV and other regimen components were tabulated. The relationship between coreceptor tropism and detection of dual/mixed CCR5/CXCR4-tropic virus on treatment and at study discontinuation or virologic failure was also analyzed on a post hoc basis. Laboratory data were listed, and values outside the normal ranges were flagged. Mean change in lab values over time were summarized. Evolution of laboratory abnormalities were evaluated by tabulation of worst on-study values by normal or abnormal baseline values.

Other Analyses of Clinical Interest: Incidence of ADEs was tabulated and the effect of baseline characteristics was evaluated.

Interim Analysis: There was one planned interim analysis at Week 24, when all subjects had either completed 24 weeks of treatment or had discontinued from the study. A complete evaluation of the efficacy and safety profile was carried out.

SUMMARY-CONCLUSIONS

RESULTS: Of the 400 randomized subjects, 397 subjects received at least one dose of study drug. Two subjects were randomized to the VCV treatment group, but never received VCV and one subject was randomized to placebo but not treated. The proportion of treated subjects that completed 48 weeks of blinded treatment was similar in both treatment groups; 203 (76%) of 267 subjects randomized to VCV and 100 (75%) of 133 subjects randomized to control. Treatment failure, as determined by investigator judgment, was the most common reason for discontinuation during the double-blind segment of the protocol. The mean duration of treatment was 41 weeks for both treatment groups. Investigators listed treatment failure in 9% (23/267) of VCV and 9% (12/133) of control subjects as the reason for discontinuation. Adjusting for duration of exposure in each treatment provided a rate-based assessment of AEs that accounts for exposure.

The MITT population consisted of 234 VCV subjects and 112 control subjects. The proportion of MITT subjects that completed 48 weeks of blinded treatment was similar in both treatment groups; 178 (76%) of 234 VCV subjects and 85 (76%) of 112 control subjects. Treatment failure, as determined by investigators, was the most common reason for discontinuation during the double-blind segment of the protocol, and this occurred with similar frequencies in both treatment groups. Investigators listed treatment failure in 8% (19/234) of VCV and 9% (10/112) of control subjects in the MITT population. No significant difference was observed in the time to discontinuation for any reason between the VCV and control groups.

Note that not all subjects who met the criteria for protocol defined virologic failure (PDVF) were considered treatment failures or vice versa. On the VCV arm (MITT population), 31 subjects met the criteria for PDVF. Of these, 18 subjects discontinued for reason of "treatment failure", two discontinued for adverse event(s) and one was lost to follow-up. Note that 10 subjects who were considered PDVFs were kept on study by investigators

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and completed the study. On the control arm (MITT population), there were 16 subjects who met the criteria for PDVF. Of these, 8 subjects discontinued for "treatment failure", one discontinued for noncompliance, and one was lost to follow-up, while 6 subjects were kept on study.

Efficacy

Summary of Demographics and Selected Baseline Characteristics (MITT Population): All subjects had CCR5-tropic virus at Baseline. The mean age of subjects was 43.3 years (range 18 to 73 years). Twenty-five percent of subjects were female. Approximately half of subjects identified themselves as other than White. Slightly over 60% of subjects were from North America and Europe and the remainder from Latin America (16%) and South Africa (22%). Similar characteristics were observed in the FAS population.

The VCV and control arms were generally well balanced with respect to the demographic and baseline characteristics of the subjects. However, there was a slight difference in mean (SD) baseline CD4 count between the two groups, the mean count was 273 (172) in the VCV group and 287 (191) in the control group. Co-infection with HIV and HCV was documented in 9% (21/234) of VCV and 9% (10/112) of control subjects and co-infection with HIV and HBV was documented in <1% (1/234) of VCV and 1% (1/112) of control subjects. A history of one or more ADEs was reported in 36% (85/234) of VCV and 32% (36/112) of control subjects.

There were no major differences in the use of prior antiretroviral drug classes between the two groups. Substantial numbers of subjects in the VCV and control groups had an overall sensitivity score (OSS) of ≥3 (65% [152/234] and 70% [78/112], respectively). A similar proportion of subjects in the VCV and control groups had ≥2 active antiretroviral drug classes in their OBT, 88% (205/234) and 92% (103/112), respectively. The composition of antiretroviral drugs used by subjects in their baseline OBT was similar between the two groups; enfuvirtide (2% [5/234] VCV; 4% [5/112] control), darunavir (38% [90/234] VCV; 41% [46/112] control), raltegravir (25% [59/234] VCV; 28% [31/112] control), darunavir and raltegravir (19% [45/234] VCV; 24% [27/112] control), and enfuvirtide, darunavir, and raltegravir (<1% [1/234] VCV; 2% [2/112] control).

Efficacy Analyses: No significant difference was observed in the proportion of subjects with HIV RNA <50 copies/mL between the VCV and control groups (64% [150/234] VCV versus 61% [68/112] control; p=0.55) at 48 weeks. Analyses of the primary efficacy variable were further conducted in subpopulations defined by relevant baseline characteristics including gender, race, baseline HIV RNA, baseline CD4 count, OSS, GSS, PSS, use of T20, use of darunavir, and use of raltegravir and their combinations. The results from the subgroup analyses showed similar results as the primary endpoint; no significant differences were observed between the VCV and control groups at 48 weeks. Consistent with the results for the primary endpoint, no significant differences were observed between the VCV and control groups in any of the secondary endpoints at 48 weeks.

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Summary of Results at Week 48 (Non-Completer-Equals-Failure Analysis in the Modified Intent-to-Treat Population)

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Response Criteria	**VCV 30 mg (n=234)**	**Control (n=112)**	**p-Value VCV vs Control**
Mean (SD) Change from Baseline in Log_{10} HIV RNA[a,b]	-1.93 (1.46)	-1.97 (1.45)	0.98
Mean (SD) Change from Baseline in CD4 Count[b,c]	+137 (156)	+125 (151)	0.45
No. (%) of Virologic Responders at Week 48			
Primary Response Criteria	**VCV 30 mg (n=234)**	**Control (n=112)**	**p-Value VCV vs Control**
HIV RNA <400 copies/mL[a,d]	165 (71)	79 (71)	>0.99
≥2.0 log_{10} Drop in HIV RNA from Baseline[a,d]	160 (68)	75 (67)	0.80
No. (%) of Subjects at Week 48			
Criterion	**VCV 30 mg (n=234)**	**Control (n=112)**	
Protocol-Defined Virologic Failure, n (%)[e]	31 (13)	16 (14)	

Control=placebo QD + OBT; HIV=human immunodeficiency virus type 1; HIV RNA=HIV-1 RNA; OBT=optimized background therapy; QD=once daily; RNA=ribonucleic acid; T20= enfuvirtide; VCV=vicriviroc 30 mg QD + OBT.

[a] Key secondary efficacy endpoint.

[b] ANOVA model with treatment, the use of T20 in baseline OBT (Y,N), and the baseline HIV RNA in copies/mL (≤100,000, >100,000) as covariates.

[c] Other (not key) secondary efficacy endpoint.

[d] Logistic regression with treatment, the use of T20 in baseline OBT (Y,N), and the baseline HIV RNA in copies/mL (≤100,000, >100,000) as covariates.

[e] Protocol-defined virologic failure was not a pre-specified endpoint.

Among the MITT population, detection of dual/mixed CCR5/CXCR4-tropic virus and/or CXCR4-tropic virus at any time on study occurred in only 3% (8/234) of subjects treated with VCV and 1% (1/112) of subjects in the control group as detected by the standard Trofile assay. However, in the VCV group only 8 of 243 (3%) had detectable dual/mixed CCR5/CXCR4-tropic virus at the last available result. There were no subjects with dual/mixed CCR5/CXCR4-tropic virus and/or CXCR4-tropic virus detected who had more than a 50% decline in CD4 cell count below the baseline value.

The association of baseline OBT with detection of dual/mixed CCR5/CXCR4-tropic virus and/or CXCR4-tropic virus and PDVF was also assessed. The majority of subjects with PDVF in both the VCV (81% [25/31]) and control (63% [10/16]) arms had 3 or more fully active drugs in their OBT at Baseline.

VCV susceptibility testing was performed at specified intervals during treatment using the PhenoSense Entry assay. Subjects with virus that had relative maximal percent inhibition (R-MPI) values of <0.95 on study were considered to have emergent VCV resistance. One subject in the VCV group (1 of 234 subjects, MITT population) and no subjects in the control group showed emergent VCV resistance. This subject had DM/X4-tropic virus detected at Weeks 12 and 20, but R5-tropic virus detected at Week 48. Although a protocol-defined virologic failure by Week 40, the subject completed the study. These findings suggest that VCV resistance was not a primary cause of virologic failure in this study and was uncommon among subjects with PDVF.

Safety: The majority of the subjects (86% [228/265] VCV; 86% [113/132] control) experienced at least one

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treatment-emergent AE (TEAE), and the frequency was similar in both groups. Most AEs were mild (22% VCV; 27% control) or moderate (49% VCV; 41% control) in severity (Grade 1 or 2). Approximately one-third of the TEAEs were judged by investigators to be related to treatment in both groups. The cumulative exposure-adjusted rate of TEAEs was similar in both groups (109 per 100 person-years VCV; 110 per 100 person-years control). The most commonly reported TEAEs were diarrhea, nausea, and headache. The most commonly reported AE, diarrhea, was reported by 25% of VCV subjects and 20% of control subjects. Nausea was reported more frequently in the VCV group (18%) compared to the control group (10%). Headache was reported by 14% of VCV subjects and 19% of control subjects. The TEAEs judged to be treatment related that were reported with the greatest frequency and highest rates fell into the category of Gastrointestinal Disorders. Nausea was reported with the same frequency in the VCV group (8%) and the control group (8%). Diarrhea was reported with similar frequencies in both groups (7% VCV; 5% control).

The proportion of subjects with Grade 3/4 AEs was similar in the two groups (16% VCV; 17% control). In the VCV and control groups, the proportion of subjects that had Grade 3/4 AEs judged to be treatment related by the investigators occurred with similar frequencies in both groups (3% VCV; 5% control).

SAEs were reported with the same frequency between the VCV (13%) and control (13%) groups. The most commonly reported SAEs were pneumonia (3/265, 1%, VCV and 1/132, 1% control), and urinary tract infection (UTI) (3/265, 1%, VCV subjects and 0 control subjects). The following SAEs were reported in no more than 2 subjects in each group: diarrhea (2/265, 1%, VCV; 1/132, 1%, control), pyrexia (1/265, <1% VCV; 2/132, 2%, control), cholecystitis (2/265, 1%, VCV and 0 control subjects), lower respiratory tract infection (0 VCV subjects and 2/132, 2%, control subjects), alanine aminotransferase (ALT) increased (2/265, 1%, VCV and 0 control subjects), aspartate aminotransferase (AST) increased (2/265, 1%, VCV and 1/132, 1%, control), and depression (2/265, 1%, VCV and 2/132, 2%, control).

In the VCV group 5% of subjects discontinued the study because of AEs and in the control group 2% of subjects discontinued because of AEs.

No TEAE leading to study discontinuation was reported in more than one subject. One death was reported in the VCV group, none in the control group. The relationship of the non-Hodgkin's lymphoma that was the immediate cause of death to study treatment was considered possible by the investigator. The non-Hodgkin's lymphoma (plasmablastic lymphoma) met the criteria for an ADE as proposed by the Centers for Disease Control (CDC).

Seizure, malignancy, premalignancy, hepatocellular injury, dyslipidemia, cardiovascular (ischemic events), herpes simplex virus (HSV) infection, and upper respiratory tract infection (URI) were monitored carefully as events of interest. The rate of subjects reporting any AE of interest was 49 per 100 person-years in the VCV group versus 46 per 100 person-years in the control group. There were no seizures reported in the VCV group and one reported in the control group (<1 per 100 person-years).

The overall rates of malignancies reported were higher in the VCV group (2.40 per 100 person-years) than in the control group (0.97 per 100 person-years). Five malignancies were reported in five subjects exposed to VCV in this study during the 48-week double-blind treatment period. One subject in the control group had a squamous cell carcinoma. [redacted] The overall rates for TEAEs associated with hepatocellular disorders were 14.85 in the VCV group and 10.71 in the control group. The most commonly reported hepatocellular TEAEs were ALT increased, AST increased, blood bilirubin increased, and hyperbilirubinemia. The numbers of TEAEs associated with disorders of lipid metabolism (dyslipidemias) were small and the overall rates between the treatment groups were similar. Two ischemic cardiovascular TEAEs were reported in this study: myocardial infraction (n=1) and angina pectoris (n=1). Both were reported in control group subjects.

HSV infections were reported as AEs in both treatment arms. The rates of HSV infections were similar in the two groups (VCV 6 per 100 person-years, control 8 per 100 person-years). The rate of URIs (including nasopharyngitis, pharyngitis, and sinusitis) was 29 per 100 person-years in the VCV group versus 25 per 100-person years in the control group.

During the open-label extension period, four subjects experienced cardiovascular SAEs of myocardial infarction, all of which were severe or life-threatening and required hospitalization.

CONCLUSIONS:

- VCV did not meet the primary efficacy endpoint in this trial.

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- Resistance to VCV or components of the OBT was infrequent.
- Overall, VCV was well tolerated and safe in this treatment-experienced population.
- A small proportion of subjects discontinued for AEs.
- Discontinuations were more frequent for VCV recipients, but there was no pattern to the AEs leading to the discontinuation.
- GI AEs, particularly nausea, were more frequent with VCV
- An imbalance in the number of malignancies between treatment groups was reported, but there was no specific pattern to the malignancies.
- The rate of malignancies in the VCV group was similar to rates observed for maraviroc.

Date of the Report: 09 AUG 2011