SYNOPSIS OF RESEARCH REPORT [redacted] (PROTOCOL NP25733)

COMPANY: NAME OF FINISHED PRODUCT: NAME OF ACTIVE SUBSTANCE(S):	(FOR NATIONAL AUTHORITY USE ONLY)

TITLE OF THE STUDY / REPORT No. / DATE OF REPORT	A multi-center, randomized, double-blind, multiple ascending dose, placebo-controlled, parallel group 2-part study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of the HCV nucleoside inhibitor RO5428029 in healthy subjects (Part A), and in chronic hepatitis C genotype 1 infected patients (Part B). Report No. [redacted], July 2012. Study data are presented in a synopsis format clinical study report (CSR) as development of RO5428029 was discontinued by the sponsor following lower than expected decreases in viral load in Part B of the study.		
INVESTIGATORS / CENTERS AND COUNTRIES	One center in France enrolled healthy subjects into Part A. Four centers (3 in Poland, one in France screened HCV-infected patients for Part B and 3 centers (in Poland and France) recruited patients into Part B.		
PUBLICATION (REFERENCE)	NA		
PERIOD OF TRIAL	First patient first visit to last patient last visit Part A Jun 28, 2011 to Oct 14, 2011 Part B Nov 08, 2011 to Dec 12, 2011	CLINICAL PHASE	I/II
OBJECTIVES	**Primary** 1. To evaluate the safety, tolerability and pharmacokinetic (PK) properties of RO5428029 in healthy subjects and chronic hepatitis C genotype 1 infected patients. 2. To evaluate pharmacodynamics (PD) (viral load response) of RO5428029 in chronic hepatitis C genotype 1 patients. **Secondary** To monitor the resistance profile of RO5428029 and evaluate potential relationship of baseline susceptibility of the virus with antiviral response in chronic hepatitis C genotype 1 patients.		

	Exploratory Objectives The Roche Clinical Repository (RCR) is a centrally administered facility for the long term storage of human biological specimens including body fluids, solid tissues and derivatives thereof (e.g. DNA, RNA proteins/ peptides). Specimens stored in the RCR may be used to: 1. Study the association of biomarkers with efficacy and/or safety findings associated with medicinal products; and/or 2. Increase our knowledge and understanding of disease biology; and/or 3. Develop biomarker or diagnostic assays; establish the performance characteristics of these assays.
STUDY DESIGN	The NP25733 study was designed to investigate the safety, tolerability and PK properties of RO1080713, the main circulating form of RO5428029 and plasma surrogate marker for the intracellular active metabolite RO1080713-triphosphate. Study Part A was a randomized, double blind, placebo controlled, 14-day, multiple ascending dose (MAD) study of RO5428029 in healthy subjects. Study Part B was a multi-center randomized, double blind, placebo controlled, 7-day, multiple dose study in chronic HCV genotype 1 infected patients (Cohorts B1-B5) to assess the effect of RO5428029 dosing on the HCV viral load in the plasma of treatment-naïve patients.
NUMBER OF SUBJECTS	The total number of subjects and patients planned was up to a maximum of 100; up to 50 healthy subjects in Part A and up to 50 chronic HCV genotype 1 infected patients in Part B.
DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION	**Part A – Healthy Subjects** Healthy male and female subjects, 18 to 60 years of age, inclusive, with a body mass index (BMI) between 18 and 32 kg/m^2, inclusive, and a minimum weight of 45 kg. Female subjects had to be surgically sterile or postmenopausal. **Part B - Chronic Hepatitis C Genotype 1 Infected Patients** Subjects aged 18 to 60 years of age, inclusive with BMI between 18 and 32 kg/m^2, inclusive, and a minimum weight of 45 kg with evidence of chronic hepatitis C virus (HCV) infection greater than or equal to 6 months duration at screening visit (HCV genotype 1 and serum HCV RNA quantifiable at ≥ 1 x 10^5 IU/mL as demonstrated by the Roche COBAS TaqMan HCV Test). Eligible subjects were HCV treatment-naïve. Details of inclusion and exclusion criteria are provided in the study protocol, Section 4.2 (page 584).
TRIAL DRUG / STROKE (BATCH) No.	RO5428029 tablets at the strength of 50 mg, 250 mg and 500 mg were administered to the subjects by investigational staff with approximately 240 ml of still water at the time points specified in the Schedule of Assessments (page 591).

DOSE / ROUTE / REGIMEN / DURATION	The doses in this study were adaptive in nature, and only the first dose was fixed (i.e.500 mg twice daily [bid] in Part A). Subsequent doses were defined based on the safety, pharmacokinetics (PK) and pharmacodynamics (PD) data from previous cohorts. **PART A** Cohort A1: 500 mg bid/14 days (except on Day 14 where only the morning dose was administered). Cohort A2: 1000 mg bid/14 days (except on Day 14 where only the morning dose was administered). Cohort A3: 2000 mg bid/14 days (except on Day 14 where only the morning dose was administered. No further dose levels were administered due to termination of the study. **PART B** Cohort B1: 1000 mg bid/7 days (except on Day 7 where only the morning dose was administered) No further dose levels were administered due to termination of the study.
REFERENCE DRUG / STROKE (BATCH) No.	Matching placebo tablets.
DOSE / ROUTE / REGIMEN / DURATION	Matching placebo tablets were administered as for active medication.
CRITERIA FOR EVALUATION	
SAFETY:	Full detail of all safety assessments and a schedule of study assessments are provided in Section 5 of the study protocol (page 591). Details for the collection and reporting of safety parameters are provided in Section 7 of the study protocol (page 616). A complete or abbreviated physical examination was performed at the time points indicated in the schedule of assessment. BMI was calculated at screening and weight was measured at other time points. A visual acuity and fundoscopic examination was conducted at baseline. Adverse events (AEs) and concomitant medications were monitored throughout the entire study (screening through follow up). Triplicate 12-lead ECG measurements were collected at the time points indicated in the schedule of assessments. The average of the 3 readings was used to determine the ECG intervals assessment (e.g. QT, PR). T-wave information was captured as normal or abnormal. U-wave information was captured as absent/normal or abnormal. All significant post-dose ECG changes from baseline were identified and all QTcF and QTcB values were obtained. Vital signs (body temperature, respiratory rate, blood pressure, pulse rate) were collected at the time points indicated in the schedule of assessments.

	The following safety laboratory assessments were carried out at the time points indicated in the schedule of assessments: • Hemoglobin, hematocrit, erythrocytes (RBC), platelets, leucocytes (WBC), differentials in absolute (counts): neutrophils, eosinophils, lymphocytes, basophils, monocytes. • Prothrombin time-International Normalized Ratio. • Aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, alkaline phosphatase (ALP), albumin, creatinine, urea, total protein, sodium, chloride, calcium, phosphate, potassium, glucose (fasting); TSH, Lipid panel (total cholesterol, triglycerides, HDL and LDL [fasting]) and creatine phosphokinase (CPK) at screening only. A midstream, clean-catch urine specimen was collected for dipstick analysis of protein, blood, glucose, and pH. If there was a clinically significant positive result, urine was to be sent to the laboratory for microscopy and culture. The following laboratory tests were also performed: • Drugs of abuse were measured in urine: e.g., cannabinoids, amphetamines, methamphetamines, opiates, methadone, cocaine, benzodiazepines, and barbiturates. • Serology: HIV-Ab 1& 2, HBsAg and HCVAb. • Alcohol was measured by a breath/urine test. • Urine pregnancy test (β-hCG) was performed in all females. • FSH was measured in all postmenopausal females.
PHARMACOKINETICS:	Blood and urine samples for the analysis of RO1080713 (the major metabolite of the pro-drug RO5428029) were collected at the time points in the schedule of assessments. Details are provided in the study protocol (page 607). Plasma and urine samples were analyzed using a specific LC/MS/MS method. The primary plasma PK parameters were C_{max}, $T_{max,}$ AUC_{tau} on Day 1 and last day of dosing. The secondary PK parameters were $T_{½}$, CL/F and V_d/F, $AUC_{0\text{-}inf}$, C_{trough}, and accumulation index after the last day of dosing (Day 7 (patients)/Day 14 (healthy subjects). Urine PK parameters included renal clearance (CL_R) and cumulative amount and percentage of drug excreted in the urine (Ae).
PHARMACODYNAMICS:	Blood samples were collected to evaluate PD parameters in Part B only, as specified in the schedule of assessments. Full details are provided in the study protocol (page 607). **HCV Viral Load** HCV RNA (5 mL per time point) was measured using Roche COBAS Taqman HCV Test. Serum samples were collected throughout the study for HCV RNA viral load quantification and for viral resistance monitoring (sequence and/or phenotypic analyses).

	HCV Viral Resistance Monitoring Blood samples (5 mL per time point) were collected to monitor for the development of viral resistance in patients (viral breakthrough, non-response or partial response). These results were not available at the time of this report and will be provided on request.
STATISTICAL METHODS	**Healthy Subjects** The primary variables following multiple doses of RO5428029 in healthy subjects were: • Safety and tolerability: AEs, 12-lead ECGs, vital signs and laboratory tests. • PK parameters: C_{max}, AUC_{tau}, T_{max} and C_{min} of RO1080713. The secondary variables were: • Other PK parameters of RO1080713. • PK parameters of RO5428029 and/or other metabolites as needed **HCV Patients** The primary variables following multiple doses of RO5428029 in HCV patients were: • Safety and tolerability: AEs, 12-lead ECGs, vital signs and laboratory tests • PK parameters: C_{max}, AUC_{tau}, T_{max} and C_{min} of RO1080713. • HCV RNA levels. • Resistance emergence. The secondary variables were: • Other PK parameters of RO1080713. • PK parameters of RO5428029 and/or other metabolites as needed. **Safety** For safety and tolerability assessments, listings, summary tables, and graphs (individual plots and/or mean plots) by cohort and treatment group, of AEs, 12-lead ECGs, vital signs and laboratory tests were produced. **Pharmacokinetic Analysis** Parts A and B: Individual and mean plasma concentrations and urine concentrations at each sampling time point for RO1080713, the major plasma circulating form of RO5428029 which is reflective of activity, and other metabolites of RO5428029 as appropriate are presented by listings and descriptive summary statistics including means, geometric means, ranges, standard deviations and coefficients of variation. Individual and mean concentration versus time will be plotted on semi-logarithmic scales. Plasma PK parameters were estimated using non-compartmental methods. Dose-proportionality, drug accumulation and achievement of steady state assessment are presented.

All PK parameters are presented by individual listings and summary statistics including means, geometric means, medians, ranges, standard deviations and coefficients of variation.

Pharmacodynamic Analysis (Part B only)

HCV ribonucleic acid (RNA) (log_{10} IU/mL) concentrations over time from baseline (pre-dose) and change in HCV RNA (log_{10} IU/mL) concentrations are presented by listings. Summaries of HCV RNA measurements (absolute and change from baseline) at each nominal time point are provided by treatment group (i.e. active drug and placebo).

Exploratory analysis was carried out on the relationship of PK of RO1080713 and/or its metabolite(s) and HCV RNA levels and other factors that may be associated with response.

Full details of the statistical considerations and analysis plan are provided in the Section 8 of the study protocol (page 620).

METHODOLOGY

Screening and baseline procedures for Part A included a complete pre-treatment medical history, physical examination, vital signs, pregnancy test, eye examination, triplicate ECG assessments, laboratory assessments (including FSH test, drugs of abuse, serology, biochemistry, hematology with differential, and urinalysis). In addition, CHC-infected patients participating in Part B required a liver biopsy or non-invasive (e.g. Fibroscan) evaluation ≤ 24 calendar months prior to study treatment. Patients with cirrhosis or incomplete / transition to cirrhosis were excluded. HCV genotyping and HCV RNA levels were also assessed.

Procedures during the study treatment included triplicate ECG assessments, safety monitoring including serious and non-serious AEs, vital signs, laboratory assessments, including biochemistry, hematology with differential, PT-INR, urinalysis, HCV RNA viral load (Part B), PK, drug resistance monitoring (Part B), and biomarker analysis (RCR). For Part B, a sample was drawn for IL28B genotyping on Day -1.

All medications (prescription and over-the-counter taken within 30 days of study screening were recorded on the appropriate or section of the electronic case report form (page 687)), Details of study requirements regarding concomitant medication and treatment are provided in the study protocol on page 588.

The total blood draw to assess clinical laboratory measurements, RCR sampling and determine plasma concentrations was approximately 262 mL in Part A and approximately 395 mL in Part B.

The end of the study was defined as last patient/subject last visit (LPLV) or observation (LSLO) whichever was the later date.

RESULTS: STUDY POPULATION

Patient Disposition

A total of 30 healthy subjects were recruited from one center for Part A and a further 10 HCV-infected patients were recruited from 3 centers for Part B. In Part A, 8 subjects were recruited to each of the cohorts of RO5428029 500 mg bid, 1000 mg bid and 2000 mg bid, and 2 subjects were recruited to the placebo group in each cohort. In Part B, 8 patients with HCV were recruited to the RO5428029 1000 mg bid group and 2 patients were recruited to the placebo group.

Overall, 5 subjects were discontinued from study treatment due to adverse events (AEs) (page 134): 3 subjects in the RO5428029 placebo group, 1 subject in the RO5428029 500 mg group and 1 subject in the RO5428029 1000 mg group. All AEs leading to withdrawal were in the Cardiac Disorders system organ class (SOC).

Demographic Data and Baseline Characteristics

Demographic data are summarized on page 18 . All study participants were male, apart from 2 female subjects recruited to the RO5428029 500 mg group in Part A and one female patient recruited to the placebo group in Part B. Mean age ranged from 31.8 to 51.5 years and mean body mass index (BMI) ranged from 23.91 to 27.29 kg/m^2.

PHARMACOKINETIC RESULTS

Plasma levels of RO1080713 (parent compound) were measured up to 12 h following a single dose on Day 1 in all subjects and up to 72 h following multiple doses of the RO5428029 on Day 7 and Day 14 in HCV patients and healthy subjects, respectively. Additional PK samples were taken throughout the study to characterize achievement of the steady state in all subjects. Urine levels of RO1080713 were measured up to 48 h on the last dosing day in all subjects dosed with RO5428029 to characterize the renal excretion of the parent drug (RO1080713). Since it had been established in previous studies that levels of the prodrug are insignificant only the PK of the parent drug has been characterized.

Blood samples were collected at pre-dose, and 30 minutes, 1, 2, 3, 4, 5, 6, 8, 10, 12 h on Day 1 and additionally at 16, 24, 48 and 72 hours after dosing on the last dosing day. Actual sampling times were generally adhered to this schedule and were documented for each subject. Plasma concentrations of RO1080713 were determined by LC/MS/MS methods, and the mean RO1080713 plasma concentrations by dose level are shown on page 521. The computed plasma PK parameters for each subject are provided on page 535. A summary of computed PK parameters by dose level is provided in Table 1 and Table 2 below.

RO1080713 was rapidly absorbed, with C_{max} attained within 1 to 5 hours. Both C_{max} and $AUC_{0\text{-}12h}$ (AUC_{tau}) increased with dose, except that the mean dose normalized C_{max} decreased slightly from 500 to 2000 mg. Since accumulation for both C_{max} and $AUC_{0\text{-}inf}$ were lower than anticipated based on the terminal half-life of the drug and the dosing frequency, half-life after the last dose was estimated using the following formula: accumulation ratio = 1/ 1-e^(-$k_e$tau) and $T_{1/2}$ = ln 2/k_e, where k_e is the elimination rate and tau is the dosing frequency, instead of using the terminal part of the plasma concentration profile. This computation resulted in an effective half-life of 4-6 hours in all subjects relative to a 12 hour half-life as determined from the terminal part of the curve.

Table 1 Single-Dose PK Parameters (Mean and CV%) of RO1080713 after Dosing with RO5428029 on Day 1

PK Parameter	*500 mg HV*	*1000 mg HV*	*1000 mg HCV*	*2000 mg HV*
*T_{max} (h)	2.0 (2.0-4.0)	3.0 (2.0-5.0)	3.0 (2.0-5.0)	2.0 (2.0-4.0)
C_{max} (µg/mL)	4.67 (21.4)	8.02 (15.2)	9.22 (18.5)	14.7 (20.9)
$AUC_{0\text{-}12h}$ (µg*h/mL)	28.2 (21.3)	49.5 (13.6)	55.7 (17.9)	96.2 (21.2)

* median (range)

HV=healthy volunteer; HCV=HCV-infected patient

PK analysis from the healthy volunteers showed dose proportional increase in $AUC_{0\text{-}12h}$ among the 3 doses tested and slightly less than proportional increase in C_{max}. After the highest dose of 2000 mg BID on the last day (Day 14) of dosing in healthy subjects, the peak plasma concentration (C_{max}) was 19.0 µg/mL, area under the curve ($AUC_{0\text{-}12h}$) was 121 µg*h/mL and the trough plasma concentration (C_{min}) was 3.36 µg/mL. Exposures in HCV patients after 7 days of BID dosing with 1000 mg of RO5428029 were as follows: C_{max} of 10.6 µg/mL, $AUC_{0\text{-}12h}$ of 67.8 µg*h/mL and C_{min} of 2.00 µg/mL.

Table 2 Steady-State PK Parameters (Mean and CV%) of RO1080713 after Multiple Dosing with RO5428029 on Day 7 (HCV Patients, HCV) and Day 14 (Healthy Volunteers, HV).

PK Parameter	500 mg HV	1000 mg HV	1000 mg HCV	2000 mg HV
*T_{max} (h)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	3.0 (2.0-5.0)	2.0 (2.0-4.0)
C_{max} (µg/mL)	5.76 (18.1)	9.78 (19.0)	10.6 (16.4)	19.0 (19.4)
C_{12h} (µg/mL)	1.02 (25.2)	1.53 (15.1)	2.00 (25.4)	3.36 (29.8)
AUC_{0-12h} (µg*h/mL)	33.2 (18.5)	58.0 (14.5)	67.8 (19.4)	121 (20.0)
effective $T_{1/2}$ (h)	4.28 (34)	3.96 (15)	4.02 (12)	6.09 (39)
Accumulation Index	1.14 (11.2)	1.13 (4.48)	1.29 (19.9)	1.15 (3.5)

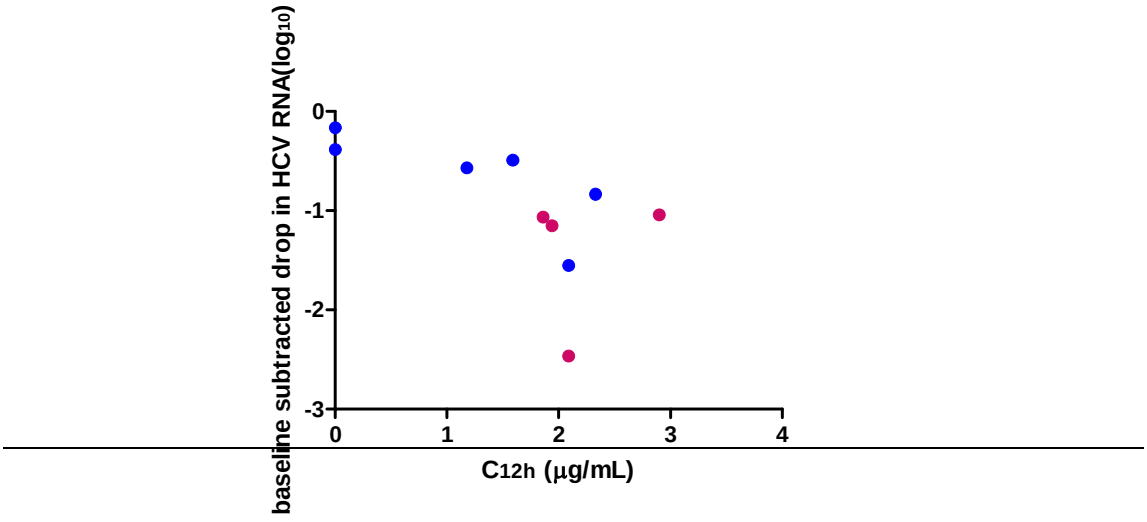
* median (range) HV=healthy volunteer; HCV=HCV-infected patient

The mean renal clearance of RO1080713 ranged from 106 to133 ml/min which accounted for 53.3% to 68.7% of the total dose of the prodrug (RO5428029) indicating renal excretion is a major contributor of the clearance mechanism of the parent drug page 531.

PHARMACODYNAMIC RESULTS

Absolute values of log_{10} HCV RNA levels are summarized for the 10 HCV patients on page 111. Changes from baseline are summarized on page 113. Individual viral load data are listed on page 430. The viral load drop in the treated group ranged from -0.49 to -2.46 log_{10} IU/mL with a median of -1.05 log_{10} IU/mL versus the control group of -0.27 log_{10} IU/mL.

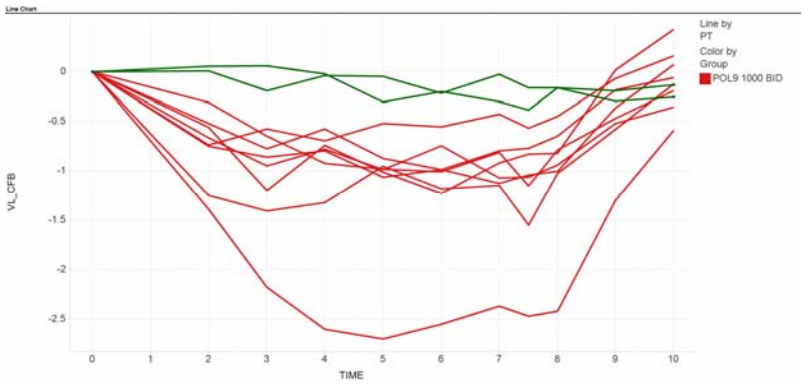
Figure 1 PK PD Correlation of Trough Concentrations on Day 7 (12 h Post-Dose) vs Change in HCV RNA Levels in Individual Subjects.



Blue dots indicate subjects with genotype 1B variation and red dots indicate patients with genotype 1A variation. Dots on the Y-axis indicate placebo subjects.

As seen in Figure 1 there was a decrease in the HCV RNA levels in each patient dosed with the drug compared to the placebo. There was no apparent effect of the sub genotype (1A or 1B) on the decrease in HCV RNA levels. A similar analysis was performed to examine the impact of the IL28B status and again no impact of this is noted on HCV RNA levels. Figure 2 shows the daily decrease in HCV RNA levels upon bid dosing with the drug and the impact of drug withdrawal on the HCV RNA levels. As can been in the figure there was an initial rapid decline in the HCV RNA level in the first 24 hours; subsequently the effect appeared to reach a plateau with a mean decrease of about 1 log unit. Withdrawal of the drug on Day 7 resulted in rapid increase of HCV RNA levels indicating that it is likely that the drug has a direct PD effect.

Figure 2 Individual Change in HCV RNA Levels over 7 Days of Dosing with RO5428029 1000 mg bid



Lines in green indicate data for placebo subjects

SAFETY RESULTS

Extent of Exposure to Study Treatment

Details of study drug administration for each subject/patient are listed on page 326. Maximum cumulative doses of RO5428029/placebo were 13,500 mg, 27,000 mg and 54,000 mg in the 500 mg, 1000 mg and 2000 mg groups respectively.

Adverse Events

Adverse events are summarized by treatment group and preferred term on page 15 and listed for each patient on page 121. A total of 54 AEs were reported by 25 subjects and 8 AEs were reported by 6 HCV patients. The most frequently reported AE was headache (13 events in healthy subjects and 5 events in HCV patients with no relevant differences between the treatment groups). In the Cardiac Disorders system organ class (SOC), 3 subjects in the placebo group reported events of extrasystoles. Two subjects in the 500 mg group and one subject in the 1000 mg group reported events of palpitations and one subject in each of these groups reported an event of sinus tachycardia. No other events were reported by more than one subject in any treatment group.

Most AEs reported were mild. The only 2 AEs that were considered of 'severe' intensity occurred in healthy volunteers and both were reports of palpitations (one subject in the 500 mg group, and the other in the 1000 mg group), both events resolved with no treatment upon study drug discontinuation. The only AE that was reported as "unresolved" was extrasystoles documented in a healthy volunteer dosed with placebo, who persisted with premature ventricular contractions in 24-hour ECG-Holter recordings after a washout period, this event was considered as "non-clinically significant" by a cardiologist; all other AEs were considered 'resolved with no sequelae' at the end of the study. No serious adverse events were reported during the study.

Five subjects were discontinued due to AEs. In the 500 mg group subject [redacted] withdrew on Day 3 following palpitations considered severe and an episode of tachycardia of moderate intensity. Subject [redacted] (placebo) was discontinued on Day 1 following an event of extrasystoles of moderate intensity. Subject [redacted] (1000 mg) withdrew on Day 1 of treatment following a severe event of palpitations. Treatment had been previously interrupted due to sinus tachycardia of mild intensity. Subject [redacted] (placebo) was discontinued on Day 7 following an event of extrasystoles of moderate intensity. These events were all considered by the investigator to be probably related to treatment and resolved without sequelae. Subject [redacted] (placebo) was discontinued on Day 7 after a mild event of extrasystoles. This event was considered by the investigator to have a remote likelihood of being related to treatment and was unresolved at the end of the study.

Laboratory Parameters

In general, mean values for the various laboratory parameters remained within normal limits over the course of the study, with no clinically significant or dose-related safety signals for hematology, liver function, renal function, and other clinical chemistry evaluations. Laboratory parameters are listed for each patient on page 137. Lymphocyte counts (absolute values and changes from baseline) are listed on page 307. Marked laboratory abnormalities are listed on page 323. Subject [redacted] had a low calcium level on Day 12 and a low neutrophil count on Day 22. Subject [redacted] had 2 reports of elevated alanine aminotransferase (ALAT) on Day 16 and Day 17. Subject [redacted] had an elevated ALAT on Day 8. Subject [redacted] had 2 reports of a high neutrophil count on Day 8 and Day 14. Shift tables of changes in grade of laboratory parameters are provided on page 22 . There were 3 occurrences of white blood cell count shifting from grade 0 to grade 1 and 5 occurrences of ALAT levels shifting from grade 0 to grade 1.

Electrocardiograms

There were no clinically significant or dose-dependent changes from baseline in ECG parameters. Electrocardiogram data (absolute values and changes from baseline) are summarized by treatment group on page 55 and listed for each patient on page 350.

Maximum post-baseline QTcF and QTcB intervals are summarized on page 49 and page 47 respectively. Intervals were all ≤450 ms except for one subject in the 500 mg group with a QTcF interval of >450≤480 ms and one subject in the 1000 mg group with a QTcB interval of >450≤480 ms. Two subjects in the 500 mg group, one subject in the 1000 mg group and 4 subjects in the 2000 mg group had a change in QTcB interval from baseline of >30-60 ms (page 51). All subjects had a change in QTcF interval from baseline of ≤30 ms (page 53). QTcB and QTcF data are listed per patient on page 435 and page 478, respectively.

Vital Signs

There was no apparent pattern of clinically significant changes in vital signs. Vital signs (diastolic and systolic blood pressure and heart rate) are summarized on page 115. No abnormal values were reported.

CONCLUSIONS

- PK data analysis showed that the concentration at trough (C12h) achieved with a dose of 1000 mg BID (1.79-1.99 mcg/mL) was in the range of the target concentration (0.5-2 μg/mL) and that the effective half-life of the drug (~ 4 h) would require a BID regimen.
- Lower than expected decreases in viral load were seen in Part B of the study leading to study termination by the sponsor.
- Safety results indicated that RO5428029 dosed up to 2000 mg BID for up to 14 days was well tolerated. Clinical safety information collected raised no safety concerns, and there was no evidence to suggest a clinical safety signal of drug-induced AEs or laboratory test abnormalities.