A Multi-Center, Randomized, Double-Blind, Multiple Ascending Dose, Placebo-Controlled, Parallel Group 2-Part Study to Assess the Safety, Tolerability, Pharmacokinetics and Pharmacodynamic of the HCV Nucleoside Inhibitor RO5428029 in Healthy Subjects (Part A), and in Chronic Hepatitis C Genotype 1 Infected Patients (Part B).

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Primary1. To evaluate the safety, tolerability and pharmacokineticproperties of RO5428029 in healthy subjects and chronichepatitis C genotype 1 infected patients.2. To evaluate pharmacodynamics (viral load response) ofRO5428029 in chronic hepatitis...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON36081

Source
ToetsingOnline

Brief title
RO5428029 in Chronic Hepatitis C Genotype 1 Infected Patients

Condition

- Viral infectious disorders

Synonym
chronic hepatitis C

Research involving
Human

Sponsors and support

Primary sponsor: Hoffmann-La Roche
Source(s) of monetary or material Support: Industrie

Intervention

Keyword: Chronic Hepatitis C Genotype 1, HCV Nucleoside Inhibitor RO5428029

Outcome measures

Primary outcome

- Safety and tolerability: AEs, 12-lead ECGs, vital signs and laboratory tests

- PK parameters: Cmax, AUC, Tmax and Cmin of RO1080713

- HCV RNA levels

- Resistance emergence

Secondary outcome

- PK: Other pharmacokinetic parameters of RO1080713

- PK: Pharmacokinetic parameters of RO5428029 and/or other metabolites as

needed

Study description

Background summary

The actual recommended treatment for chronic hepatitis C genotype I (PEG-IFN in

combination with ribavirin) has suboptimal results (only 42%-52% of patients achieving virus resistance.
In addition, there are significant safety and tolerability limitations associated with interferon based treatments and presently, there is no treatment for patients who are unable to tolerate or are contraindicated for PEGIFN/RBV therapy. Consequently, there is a substantial need to improve therapeutic
options for patients

Study objective

Primary
1. To evaluate the safety, tolerability and pharmacokinetic properties of RO5428029 in healthy subjects and chronic hepatitis C genotype 1 infected patients.
2. To evaluate pharmacodynamics (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 will be used to:
1. Study the association of biomarkers with efficacy and/ or adverse events associated with medicinal products; and/ or
2. Increase our knowledge and understanding of disease biology; and/or develop biomarker or diagnostic assays;
3. Establish the performance characteristics of these assays.

Study design

Up to 4 additional cohorts may be enrolled to explore alternative BID doses and/or once daily doses depending on the plasma viral load decline observed at Day 7 in Cohort B1. Doses in Part B will not exceed 2000 mg BID

The total duration of the study for each patient will be up to 107 days, comprised of:

Screening

Up to 90 days (Days -90 to -3)

Study Treatment Duration
Up to 7 days (in clinic period starts Day -2 to Day 8)

Safety Follow-Up
7-10 days after the last dose

The total number of confinement days for patients in Part B of the study will be 9 days

Intervention

Proposed dosing schedule:
Cohort B1: 1000 mg BID/ 7 days
Cohort B2: to be decided /7 days
Cohort B3: to be decided /7 days
Cohort B4: to be decided /7days
Cohort B5: to be decided 7days

The doses in this study are adaptive in nature, and only the first dose is fixed (i.e. 500 mg BID in Part A). Subsequent doses will be better defined based on the safety, PK and PD from previous cohorts. The dose selected for each subsequent cohort in each part maybe as specified or lower based upon the results from previous cohorts.
The maximum dose will not exceed 2000 mg BID.

Study burden and risks

- The patient is not allowed to eat and drink from 4 hours before the screening and from 10 pm on the night of the study day.he/she is not allowed to eat..
- hospitalisation
- physical examination (with blood pressure measurement and ECG)
- blood and urine tests
- Sexually active men whose partner can become pregnant or is breastfeeding have to use a double barrier contraceptive method during the study and up to 90 days after the last dose (such as the pill or an intra-uterine device plus condom/cap and spermicidal gel).
- limited use of alcohol/drugs/tabac/medication
- urine has to be collected at home till 2 days after leaving the hospital

In previous studies conducted on healthy volunteers this study medicine was well tolerated and the following side effects were observed: headache, sleepiness and cold.

Contacts

Public
Hoffmann-La Roche

Pharmaceuticals Division, PDR - Grenzacherstrasse 124
4070 Basel
CH
Scientific
Hoffmann-La Roche

Pharmaceuticals Division, PDR - Grenzacherstrasse 124
4070 Basel
CH

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Healthy subjects (Part A) or patients with chronic hepatitis C infection (Part B), 18 to 60 years of age, inclusive
- Body mass index (BMI) between 18 and 32 kg/m2, inclusive, and a minimum weight of 45 kg
- Female subjects/patients must be surgically sterile or post-menopausal
- Male subjects/patients and their partners of childbearing potential must use 2 methods of contraception
- For HCV patients:
- Hepatitis C genotype 1 of >/= 6 months duration at screening
- HCV RNA quantifiable (Roche COBAS TaqMan HCV Test) at screening
- HCV treatment-naïve

- Liver biopsy or non-invasive procedure within the past 2 years showing absence of cirrhosis

Exclusion criteria

- Pregnant or lactating women, and male partners of women who are pregnant or lactating
- Women with reproductive potential
- Positive test for drugs of abuse
- History (within 3 months of screening) of alcohol consumption exceeding 2 standard drinks per day on average (1 standard drink = 10 grams or 1 unit of alcohol
- History or symptoms of any significant disease or disorder
- History of active malignancy within the last 5 years, except for localized or in situ carcinoma (e.g. basal or squamous cell carcinoma of the skin)
- Positive for hepatitis B or HIV infection, and/ or HCV for healthy volunteers (Part A)
- For HCV patients:
- Decompensated liver disease or impaired liver function as defined by any history of ascites, hepatic encephalopathy, hepatocellular carcinoma or bleeding esophageal varices, or prothrombin international normalized ratio (PTINR) >/= 2.0 at screening
- Evidence of cirrhosis and/or incomplete transition to cirrhosis
- Presence or history of non-hepatitis C liver disease

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-09-2011
Enrollment:	50

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	HCV polymerase 9
Generic name:	NVT

Ethics review

Approved WMO Date:	07-07-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	02-08-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	26-09-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	10-11-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-11-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-12-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2011-000640-24-NL
CCMO	NL37121.058.11