A Phase Ib, double-blind, randomized, placebo-controlled trial in genotype 1 HCV-infected patients to determine the safety, tolerability, pharmacokinetics and antiviral activity of repeated doses of TMC649128 given as monotherapy and given in combination with pegylated interferon + ribavirin

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1. To determine the safety and tolerability of TMC649128/TMC619688 during multiple dosing in treatmentnaïve and treatment-experienced genotype 1 HCV-infected subjects at different dose regimens as 10-days and 14-days monotherapy.2. To determine the...

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

Summary

ID

NL-OMON35874

Source
ToetsingOnline

Brief title
TMC649128/interferon/ribavirin in HCV patients

Condition

- Viral infectious disorders

Synonym
hepatitis C, liver disease

Research involving
Human

Sponsors and support

Primary sponsor: PRA International EDS
Source(s) of monetary or material Support: Tibotec BVBA;Beerse;Belgium

Intervention

Keyword: HCV patients, interferon, ribavirin

Outcome measures

Primary outcome

Pharmacodynamics:

HCV RNA levels, intracellular triphosphate (TMC652337) in PMBC*s, safety

parameters

Pharmacokinetics:

plasma and derived urine TMC649128, TMC619688 and TMC649129 concentrations,

whole blood concentration of TMC649128, plasma concentrations of RBV, derived

plasma and whole blood pharmacokinetic parameters

Safety:

adverse events, vital signs, ECG-parameters, laboratory parameters, physical

examination

Anti-viral activity:

HCV RNA levels

Secondary outcome

NA

Study description

Background summary

A Phase Ib, double-blind, randomized, placebo-controlled trial in genotype 1 HCV-infected patients to determine the safety, tolerability, pharmacokinetics and antiviral activity of repeated doses of TMC649128 given as monotherapy and given in combination with pegylated interferon + ribavirin

Study objective

1. To determine the safety and tolerability of TMC649128/TMC619688 during multiple dosing in treatmentnaïve and treatment-experienced genotype 1 HCV-infected subjects at different dose regimens as 10-days and 14-days monotherapy.
2. To determine the pharmacokinetic profile of TMC649128, TMC619688 and TMC649129 during multiple dosing in treatment-naïve and treatment-experienced genotype 1 HCV-infected subjects at different dose regimens as 10-days and 14-days monotherapy.
3. To determine the dose dependency of the antiviral effect of TMC649128/TMC619688 during multiple dosing in treatment-naïve and treatment-experienced genotype 1 HCV-infected subjects at different dose regimens as 10-days and 14-days monotherapy.
4. To assess the pharmacokinetic/pharmacodynamic (PK/PD) relationship for antiviral activity, intracellular triphosphate (TMC652337) and safety of TMC649128, TMC619688 and TMC649129.
5. To determine the short term safety and tolerability of the co-administration of TMC649128 and PegIFN *-2a/RBV during multiple dosing for 14 days in treatment-naïve genotype 1 HCV-infected subjects.
6. To explore the drug-drug interaction between TMC649128/TMC619688 or TMC649129 and PegIFN *-2a/RBV during multiple dosing for 14 days in treatment-naïve genotype 1 HCV-infected subjects.
7. To assess in a preliminary way the short term antiviral effect of the combination of TMC649128/TMC619688 with PegIFN *-2a/RBV during a 14-day dosing period in treatment-naïve genotype 1 HCV-infected subjects.

Study design

This study is divided in 2 parts. In the first part of the study, the study medication will be given as monotherapy. In the second part, the study medication will be given in combination with other medication.

The monotherapy part of this study will be performed in 30 genotype 1 HCV-infected patients, subdivided over 3 panels of 10 patients each. In each panel patients will receive the study medication during 10 or 14 days.

The combination therapy part of this study will be performed in 20 genotype 1 HCV-infected patients in 1 panel.

Intervention

Monotherapy phase
Panel 1: TMC649128 at 1000 mg q24h (n=8) or placebo (n=2) q24h on Days 1-10 under fed conditions
Panel 2: TMC649128 at 1600 mg (n=8) or placebo (n=2) q12h on Days 1-14 under fed conditions
Panel 3: TMC649128 at a selected dose (n=8) or placebo (n=2) q12h OR q24h on Days 1-14 under fed conditions

Combination therapy phase
Panel 4, Arm 1: placebo (q12h OR q24h, dosing regimen matched to Arm 2 of Panel 4) + PegIFN *-2a/RBV (n=10) on Days 1-14 under fed conditions
Panel 4, Arm 2: TMC649128 at a selected dose (q12h OR q24h) + PegIFN *-2a/RBV (n=10) on Days 1-14 under fed conditions.

Study burden and risks

Procedures: pain, light bleeding, haematoma and possibly an infection

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Hepatitis C infected patients
Genotype 1
18-65 year
BMI 18.0 - 35.0 kg/m2

Exclusion criteria

positive for Hepatitis B or HIV
except from hepatitis C infection diagnosed as not-healthy

Study design

Design

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):	01-07-2011
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pegasys
Generic name:	pegylated interferon

Ethics review

Approved WMO Date:	12-05-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-05-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-09-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-09-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2011-001305-27-NL
CCMO	NL36561.056.11