A PHASE 1, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, ASCENDING DOSE STUDY EVALUATING THE SAFETY, TOLERABILITY AND PHARMACOKINETICS AND ANTIVIRAL ACTIVITY OF JTK-652 ADMINISTERED FOR FOUR WEEKS IN SUBJECTS WITH CHRONIC HEPATITIS C INFECTION

Published: 24-09-2007
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Primary : to investigate the safety, tolerability and antiviral activity of multiple oral doses of JTK-652 administered for 4 weeks in subjects with chronic hepatitis C infection (genotype 1a, 1b)Secondary : to investigate the pharmacokinetics of...

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

Summary

ID

NL-OMON31911

Source
ToetsingOnline

Brief title
JTK-652 proof of concept study

Condition

- Viral infectious disorders

Synonym
hepatitis c

Research involving
Human

Sponsors and support

Primary sponsor: Japan Tobacco Inc.
Source(s) of monetary or material Support: 4e geldstroom;industrie

Intervention

Keyword: entry inhibitor, Hepatitis C, JTK-652

Outcome measures

Primary outcome

Safety : AEs, clinical laboratory parameters, vital signs, ECG and physical

examination

Pharmacokinetics : plasma JTK-652 concentrations, pharmacokinetic parameters

(Cmax, Ctrough, tmax, AUC0-*, Rac

Secondary outcome

Efficacy : HCV RNA reduction (log10 copies/mL) from baseline at Week 4 and

percent change and change from baseline in ALAT reduction (IU/L) at Week 4

Study description

Background summary

Hepatitis C results from infection with the hepatitis C virus (HCV) through exposure to infected blood. When infected with HCV, the disease usually progresses asymptomatically, although malaise followed by anorexia, nausea,

vomiting or jaundice may develop in some cases. Fifty-five to 85% of HCV-infected patients become persistent HCV-infected patients (HCV carriers), and chronic hepatitis develops in 65% to 70% of the HCV carriers. The most important sequelae of chronic HCV infection are progressive liver fibrosis leading to cirrhosis and hepatocellular carcinoma. If HCV carrier individuals aged 40 years remain untreated until 70 years old, it is expected that 20 to 25% of them will develop hepatocellular carcinoma. The number of HCV carriers is estimated to be 170 million worldwide and 2 million in Japan1, and that of newly infected patients is estimated to be 3 to 4 million worldwide per year.2
In the treatment of hepatitis C, the standard therapy is the treatment with interferon (IFN), either alone or in combination with ribavirin (RBV). IFNs used for the treatment include standard IFN and IFN modified with polyethylene glycol (pegylated-IFN; PEG-IFN), which is used in a once-a week dosing regimen due to prolonged half-life in blood. At present, the first-line drug is PEG IFN because of lower frequency of dosing and better safety and efficacy. The most effective treatment is a combination with PEG-IFN and RBV. Basically, all patients with chronic hepatitis C are subject to the treatment, however, the aggressive treatment is recommended particularly for patients with an increased risk of developing liver cirrhosis.

JTK-652 shows potent inhibitory activity against the HCV pseudo typed virus infection. Thus, an anti-HCV effect is expected when JTK-652 is administered alone or in combination with IFN. The mechanism of action of JTK-652 is quite different from that of the NS3 protease inhibitor or the NS5B RNA polymerase inhibitor that have been intensively developed by the other pharmaceutical companies. Therefore, additive or synergy anti-HCV effect is also expected when JTK-652 is administered in combination with these inhibitors. In addition, it is expected that JTK-652 will exert anti-HCV activity against drug-resistant viruses.

Study objective

Primary : to investigate the safety, tolerability and antiviral activity of multiple oral doses of JTK-652 administered for 4 weeks in subjects with chronic hepatitis C infection (genotype 1a, 1b)
Secondary : to investigate the pharmacokinetics of multiple oral doses of JTK-652 in subjects with chronic hepatitis C infection (genotype 1a, 1b)

Study design

a randomized, double-blind, placebo-controlled study in subjects with chronic hepatitis C infection enrolled into two multiple dose cohorts (JTK-652 400 mg and 800 mg). In each cohort, ten subjects (8 active and 2 placebo) will be randomized to receive JTK-652 or placebo every 8 hours for 4 weeks.

Intervention

JTK-652

Study burden and risks

JTK-652:
As JTK-652 is currently administered to man for the first time in studies with healthy volunteers, adverse effects in man have not been reported by date of this report. In previous studies with rats and dogs in which JTK-652 was administered daily in (very) high doses over a period of 1 month, the following adverse effects were observed: vomiting, abnormal faeces (whitish and soft stool, or diarrhoea), slightly increased liver enzymes and fat change in specific liver cells, hypertrophy of sinusoidal cells in liver (increase in size of a specific type of liver cells not associated with changes in liver enzyme function), slight prolonged blood coagulation time not associated with changes in bleeding, mild increase in thyroid weight and increase in size of typical cells in the thyroid gland. At very high doses sensitivity for sun light was found.

Procedures:
pain, a bruise from the canula. Light bleeding and possibly an infection from blood collection

Contacts

Public
Japan Tobacco Inc.

JT BLdg. 2-1, Toranomon 2-chrome
Minato-ky, Tokyo, 105-8422
Japan
Scientific
Japan Tobacco Inc.

JT BLdg. 2-1, Toranomon 2-chrome
Minato-ky, Tokyo, 105-8422
Japan

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Age : 18-65 yr, inclusive
BMI : 18.5-32 kg/m2, inclusive
Subjects : males and postmenopausal females with
- chronic hepatitis C infection (genotype 1a or 1b, or mixed 1a/1b)
- HCV-RNA * 100 KIU/mL
- ALAT * 5 times of upper limit of normal (ULN

Exclusion criteria

1. Evidence of human immunodeficiency virus (HIV) infection (enzyme immunoassay confirmed by Western blot)
2. Evidence of chronic hepatitis B virus (HBV) infection (HB surface antigen [HBsAg])
3. Evidence of acute hepatitis A infection (hepatitis A IgM+)
4. Antiviral therapy for HCV within preceding 6 months (including all types of interferon, ie, standard, pegylated)
5. Systemic antiviral, cytotoxic, hepatotoxic, or immunomodulatory therapy within 3 months prior to first dose
6. Recent (* 3 months prior to screening) history of alcohol or drug abuse
7. Evidence of Child-Pugh B or C liver disease (for Child-Pugh classification see Appendix 9.7)

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):	20-01-2008
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	JTK-652
Generic name:	JTK-652

Ethics review

Approved WMO Date:	24-09-2007
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-12-2007
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-12-2007
Application type:	First submission
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	EUCTR2007-005093-31-NL
CCMO	NL19812.056.07