A Safety and Efficacy Study of SCH 503034 in Previously Untreated Subjects With Chronic Hepatitis C (CHC) Infected With Genotype 1

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The primary objective of this study is to evaluate the efficacy of SCH 503034800 mg TID PO in combination with PegIntron 1.5 *g/kg QW SC plus ribavirin (800 - 1400 mg/day) in previously untreated adult chronic hepatitis C (CHC) subjects infected...

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

Summary

ID

NL-OMON30320

Source
ToetsingOnline

Brief title
n.a.

Condition

- Viral infectious disorders

Synonym
Chronic Hepatitis C, Hepatitis C virus infection

Research involving
Human

Sponsors and support

Primary sponsor: Schering-Plough

Source(s) of monetary or material Support: Industrie: Schering Plough BV

Intervention

Keyword: CHC, genotype 1, SCH 503034, untreated

Outcome measures

Primary outcome

Primary Efficacy Endpoint: The primary efficacy endpoint is the achievement of SVR, defined as plasma HCVRNA levels below the lower limit of detection at follow-up week 24 (FW 24). Subjects will be declared treatment failures in one of the following ways:

* Subjects in any of the 5 treatment arms who are HCV-RNA positive at FW 24.

* Subjects in any of the 5 treatment arms who are missing their HCV-RNA level at FW 24 and are not HCV-RNA negative at FW 12.

Secondary outcome

Key Secondary Efficacy Endpoint(s): The secondary endpoints in this study are:

* The proportion of subjects with HCV-RNA levels below the limit of detection at FW 12.

* The proportion of subjects with HCV-RNA levels below the limit of detection at 72 weeks post randomization.

* The relationship between early virologic response (EVR) and SVR.

* The relationship between virologic response at FW 12, FW 24 (SVR), and 72 weeks post randomization.

Study description

Background summary

Combination therapy with peginterferon and weight-based ribavirin is the standard of care for the treatment of chronic hepatitis C patients infected with HCV genotype 1; however, only approximately 50% of these patients achieve sustained virologic response (SVR). SCH 503034 blocks the HCV NS3 protease, thereby preventing viral replication, a new mechanism of action compared to both interferon alfa and ribavirin. SCH 503034 may improve virologic response and shorten treatment duration when added to the current standard of care regimen of peginterferon alfa-2b plus ribavirin.

Study objective

The primary objective of this study is to evaluate the efficacy of SCH 503034 800 mg TID PO in combination with PegIntron 1.5 *g/kg QW SC plus ribavirin (800 - 1400 mg/day) in previously untreated adult chronic hepatitis C (CHC) subjects infected with genotype 1.

Secondary Objectives
The secondary objectives of this study are as follows:
* To evaluate the safety of SCH 503034 when used in combination with PegIntron 1.5 *g/kg QW SC plus ribavirin (800 to 1400 mg/day PO).
* To assess the relationship of early virologic response (EVR) and time to HCV-RNA negative, to SVR.
* To assess the effect of the 4 week lead in with PegIntron and ribavirin on SVR (FW 24).
* To assess the effect of duration of treatment with SCH 503034 on SVR.
* To assess the proportion of subjects with HCV-RNA levels below the limit of detection at FW 12.
* To assess the proportion of subjects with HCV-RNA levels below the limit of detection at 72 weeks post randomization.
* To explore the relationship between virologic response at FW 12, FW 24 (SVR), and 72 weeks post randomization.

Study design

Randomized, 5-arm, comparative, open-label trial to be conducted in conformance with Good Clinical Practice. The 5 arms of the study will compare: PegIntron and ribavirin for 4 weeks followed by PegIntron, ribavirin and SCH 503034 for 44 weeks (Arm 5) versus PegIntron, ribavirin and SCH 503034 for 48 weeks (Arm 4) versus PegIntron and ribavirin for 4 weeks followed by PegIntron, ribavirin and SCH 503034 for 24 weeks (Arm 3) versus PegIntron, ribavirin, and SCH 503034 for 28 weeks (Arm 2) versus PegIntron and ribavirin for 48 weeks (control, Arm 1).

Type of Blinding: Open-label.
Randomization: 1:1:1:1:1
Stratification: Black vs non-Black and cirrhosis vs no cirrhosis.

Intervention

The 5 arms of the study will compare: PegIntron and ribavirin for 4 weeks followed by PegIntron, ribavirin and SCH 503034 for 44 weeks (Arm 5) versus PegIntron, ribavirin and SCH 503034 for 48 weeks (Arm 4) versus PegIntron and ribavirin for 4 weeks followed by PegIntron, ribavirin and SCH 503034 for 24 weeks (Arm 3) versus PegIntron, ribavirin, and SCH 503034 for 28 weeks (Arm 2) versus PegIntron and ribavirin for 48 weeks (control, Arm 1).

*PegIntron by injection (under the skin) once a week. The dose of PegIntron will be based on the weight on Day 1 of visit 1.
*Rebetol capsules twice daily with food (morning and evening). The dose of Rebetol (800-1400 mg/day) will be based on the weight on Day 1 of visit 1.
*SCH 503034 capsules 3 times each day (optimally every 8 hours (7 to 9 hours)) with food.

Study burden and risks

Burden: # visits and Blood drawings

blood drawings: approximately 15-20 max 30 ml blood per visit.

If we take 30 ml perv isit:
Arm 1 14 visits in 48 weken (HCV neg.) and 20 visits in 48 weeks (HCV pos.); max 520ml/48 weeks en max 600ml/48 weeks,
Arm 2 11 visits in 28 weeks; max 330ml/28 weeks
Arm 3 11 visits in 28 weeks max 330ml/28 weeks
Arm 4 14 visits in 48 weeks max 420ml/48 weeks
Arm 5 14 visits in 48 weeks max 420ml/48 weeks

Arm 1,4 en 5: 3 visits in 24 weeeks follow-up period.
Arm 2 and 3: 5 visits in 44 weeks follow up

Risk:
Research studies often involve some risks, not all of which may be currently known. SCH 503034, PegIntron and Rebetol are associated with side effects, as described in the protocol and patient information form.
Drawing blood may cause discomfort or bruising from the insertion of the needle, fainting (infrequent) and infection at the needle stick site (rare).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Subject must be between 18 and 60 years of age; 2. Subject*s body weight must be between 45 and 125 kg; 3. Subject must have documented chronic hepatitis C genotype 1 with most recent (within 6 months of Day 1) quantitative HCV-RNA result greater than or equal to 10,000 IU/mL; 4. Subject must have a liver biopsy within 5 years of Day 1 with histology consistent with chronic hepatitis and no other etiology for chronic liver disease. A copy of the local pathology report must be available in the site*s file; 5. Subject and subject's partner(s) must each agree to use acceptable methods of contraception 2 weeks prior to Day 1 and at least 6 months or longer if dictated by local regulations after last dose of study drug (see Section 7.6.1). 6. Subjects must be willing to give written informed consent

Exclusion criteria

1. Subjects who received prior treatment for hepatitis C
2. Subjects known to be co-infected with HIV or hepatitis B virus (HBsAg positive)
3. Evidence of decompensated liver disease as specified in the protocol
4. Diabetic and hypertensive subjects with clinically significant ocular exam findings
5. Pre-existing psychiatric condition as specified in the protocol
6. Clinical diagnosis of substance abuse of drugs, see for details protocol.
7. Evidence of active or suspected malignancy, or a history of malignancy, within the last 5 years (except adequately treated basal cell carcinoma of the skin)
8. Subjects who are pregnant or nursing. Subjects who intend to become pregnant during the study period. Male subjects with partners who are, or intend to become, pregnant during the study period
9. Participation in any other clinical trial within 30 days of the screening visit or intention to participate in another clinical trial during participation in this study. Treatment with any investigation drug within 30 days of screening visit in this study.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2007
Enrollment:	5
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	nog geen naam
Generic name:	nog geen naam
Product type:	Medicine
Brand name:	Pegintron
Generic name:	Peginterferon alfa-2b (gepegyleerd inerferon)
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Rebetol
Generic name:	Ribavirin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	21-11-2006
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-01-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-03-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-05-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-07-2007
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-01-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-08-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2006-002543-92-NL
CCMO	NL14950.018.06