



Clinical trial results:

High-dose intravenous silibinin infusions during 10 days as add-on treatment to triple therapy (telaprevir, peginterferon alpha and ribavirin) in cirrhotic GT 1 hepatitis C virus infected patients being null responders to prior dual therapy with peginterferon alpha and ribavirin – a proof-of-concept trial on antiviral efficacy and safety

Summary

EudraCT number	2012-004442-15
Trial protocol	DE
Global end of trial date	03 March 2014

Results information

Result version number	v1 (current)
This version publication date	30 August 2020
First version publication date	30 August 2020
Summary attachment (see zip file)	HISTORY (2014-12-03_HISTORY_Ergebnisbericht_in_Arzneimittelpruefungen_final1.0.pdf)

Trial information

Trial identification

Sponsor protocol code	HISTORY
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	DRKS: DRKS00005455

Notes:

Sponsors

Sponsor organisation name	Universität Leipzig
Sponsor organisation address	Ritterstr. 26, Leipzig, Germany,
Public contact	Prof. Dr. Thomas Berg, Universität Leipzig, 49 3419712330, thomas.berg@medizin.uni-leipzig.de
Scientific contact	Prof. Dr. Thomas Berg, Universität Leipzig, 49 3419712330, thomas.berg@medizin.uni-leipzig.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 December 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	03 March 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the rates of RVR – rapid virological response, defined as HCV RNA \leq LOQ (limit of quantification), defined as \leq 15 IU/mL at week four of an antiviral treatment with telaprevir, peginterferon alpha and ribavirin – between patients who either receive infusions of silibinin during the first ten consecutive working days of antiviral treatment or no infusions.

Protection of trial subjects:

see descriptions in Patient informed consent and the Trial protocol

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 December 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 2
Worldwide total number of subjects	2
EEA total number of subjects	2

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	2
From 65 to 84 years	0

Subject disposition

Recruitment

Recruitment details:

2 patients before premature trial termination

Pre-assignment

Screening details:

A total of 3 patients were to be included in the screening process of whom only one was eligible for randomisation and was randomised in the control arm.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	control

Arm description:

Telaprevir 1125 mg BID for a period of 12 weeks starting at baseline visite

Ribavirin 1000 or 1200 mg (depending on the body weight) divided in two daily doses for a period of 48 weeks starting at baseline Visite

Peginterferon alpha 2a 180 µg s.c. qweek for a period of 48 weeks starting at baseline Visite

Arm type	Active comparator
Investigational medicinal product name	Telaprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Telaprevir 1125 mg BID for a period of 12 weeks starting at baseline visite

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin 1000 or 1200 mg (depending on the body weight) divided in two daily doses for a period of 48 weeks starting at baseline visite

Investigational medicinal product name	Peginterferon alpha 2a
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Peginterferon alpha 2a 180 µg s.c. qweek for a period of 48 weeks starting at baseline visite

Arm title	experimental
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Arm description:

Silibinin infusions (20 mg/kg bw/d) on 10 consecutive working days (ideally Monday to Friday sparing the weekend)

+Telaprevir 1125 mg BID for a period of 12 weeks starting at baseline visite

+ Ribavirin 1000 or 1200 mg (depending on the body weight) divided in two daily doses for a period of 48 weeks starting at baseline visite

+ Peginterferon alpha 2a 180 µg s.c. qweek for a period of 48 weeks starting at baseline Visite

Arm type	Experimental
Investigational medicinal product name	Silibinin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Silibinin infusions (20 mg/kg bw/d) on 10 consecutive working days (ideally Monday to Friday sparing the weekend)

Investigational medicinal product name	Telaprevir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Telaprevir 1125 mg BID for a period of 12 weeks starting at baseline visite

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ribavirin 1000 or 1200 mg (depending on the body weight) divided in two daily doses for a period of 48 weeks starting at baseline visite

Investigational medicinal product name	Peginterferon alpha 2a
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Peginterferon alpha 2a 180 µg s.c. qweek for a period of 48 weeks starting at baseline visite

Number of subjects in period 1	control	experimental
Started	1	1
Completed	0	0
Not completed	1	1
Physician decision	1	-
screening failure	-	1

Baseline characteristics

Reporting groups

Reporting group title	overall trial
Reporting group description: not reported	

Reporting group values	overall trial	Total	
Number of subjects	2	2	
Age categorical			
age categories used in Trial information section			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	2	2	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Not recorded			
Units: Subjects			
Female	1	1	
Male	0	0	
not recorded	1	1	

End points

End points reporting groups

Reporting group title	control
Reporting group description: Telaprevir 1125 mg BID for a period of 12 weeks starting at baseline visite Ribavirin 1000 or 1200 mg (depending on the body weight) divided in two daily doses for a period of 48 weeks starting at baseline Visite Peginterferon alpha 2a 180 µg s.c. qweek for a period of 48 weeks starting at baseline Visite	
Reporting group title	experimental
Reporting group description: Silibinin infusions (20 mg/kg bw/d) on 10 consecutive working days (ideally Monday to Friday sparing the weekend) +Telaprevir 1125 mg BID for a period of 12 weeks starting at baseline visite + Ribavirin 1000 or 1200 mg (depending on the body weight) divided in two daily doses for a period of 48 weeks starting at baseline visite + Peginterferon alpha 2a 180 µg s.c. qweek for a period of 48 weeks starting at baseline Visite	

Primary: To compare the rates of RVR – rapid virological response, defined as HCV RNA ≤ LOQ (limit of quantification), defined as ≤ 15 IU/mL at week four of an antiviral treatment with telaprevir, peginterferon alpha and ribavirin – between patients who either rec

End point title	To compare the rates of RVR – rapid virological response, defined as HCV RNA ≤ LOQ (limit of quantification), defined as ≤ 15 IU/mL at week four of an antiviral treatment with telaprevir, peginterferon alpha and ribavirin – between patients who either rec ^[1]
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End point description:

End point type	Primary
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End point timeframe:

4 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The trial was stopped prematurely and only a very limited number of patients included, which does not allow an endpoint analysis. For further descriptions please see the attached trial synopsis.

End point values	control	experimental		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	1		
Units: whole	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Adverse events will be documented at every visit from the baseline visit (visit 2) until visit 18/week FU 12 = End of Event Reporting = EoER)

Adverse event reporting additional description:

Not recorded

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Frequency threshold for reporting non-serious adverse events: 1 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Please see the list of AEs related and not related to the IMP in the trial synopsis, uploaded together with the posting of this results report.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2013	Change of co-ordinating investigator Change of a principal Investigator at a trial site

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
03 March 2014	The study was aborted prematurely due to current developments in the field of treatment of chronic hepatitis C patients (i.e. approval of new antiviral agents).	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was aborted prematurely due to current developments in the field of treatment of chronic hepatitis C patients (i.e. approval of new antiviral agents).
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Notes: