Clinical trial results:
Four weeks treatment for chronic hepatitis C in patients under 50 years of age with no significant liver fibrosis

Summary

EudraCT number	2017-005179-21
Trial protocol	DK
Global end of trial date	11 August 2021

Results information

Result version number	v1 (current)
This version publication date	17 September 2022
First version publication date	17 September 2022

Trial information

Trial identification

Sponsor protocol code	4RIBC-2018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Clinical Institute, University of Southern Denmark
Sponsor organisation address	J.B. Winsløwsvej 4, Indgang 18, Penthous, Odense C, Denmark, 5000
Public contact	Deparment of infectious Diseases, Odense University Hospital, 0045 28834681, lone.wulff.madsen@rsyd.dk
Scientific contact	Deparment of infectious Diseases, Odense University Hospital, lone.wulff.madsen@rsyd.dk

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	22 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 August 2021
Global end of trial reached?	Yes
Global end of trial date	11 August 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the percentage of subjects achieving a 12-week sustained virological response, SVR 12 (HCV RNA below lower limit of quantification at week 12 after end of treatment) after 4 weeks of treatment (including forward moving arm from phase 1) compared to 8 weeks of treatment in the intention to treat population including all subjects taking at least one dose of study medication.

Protection of trial subjects:

because of the study criteria, no one suffered from severe liver disease, and based on previous retreatment studies after
short treatment, the likelihood of cure after retreatment was high.

All patients who experienced treatment failure have been offered retreatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 May 2018
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	Denmark: 61
Worldwide total number of subjects	61
EEA total number of subjects	61

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)	61
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first 33 patients were all included at the outpatient clinic at Odense University hospital.
The 28 last patients were included at outreach clinics at drug treatment centers and at the outpatient clinic at Odense University hospital.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	61
Number of subjects completed	53

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Protocol deviation: 2
Reason: Number of subjects	Consent withdrawn by subject: 6

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	Intervention

Arm description:

Glecaprevir/Pibrentasvir was given with ribavirin for 4 weeks

Arm type	Experimental
Investigational medicinal product name	Maviret
Investigational medicinal product code	
Other name	Glecaprevir/Pibrentasvir
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

100mg glecaprevir and 40 mg pibrentasvir, 3 tablets once daily at the same time with food.

Investigational medicinal product name	Ribavirin
Investigational medicinal product code	
Other name	Moderiba/copegus/
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

15mg/kg with a maximum of 1400mg. Dosed twice daily for the first 15 patients and for the rest in this intervention group once daily

Arm title	Intervention 2

Arm description:

Glecaprevir/pibrentasvir given for 4 weeks

Arm type	Experimental

Investigational medicinal product name	Maviret
Investigational medicinal product code	
Other name	Glecaprevir/pibrentasvir
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

100mg glecaprevir/40 mg pibrentasvir, 3 tablets once daily with food

Arm title	GLE/PIB for 8 weeks

Arm description:

Standard of care with GLE/PIB for 8 weeks for treatment of chronic hepatitis C

Arm type	standard of care
Investigational medicinal product name	Maviret
Investigational medicinal product code	
Other name	Glecaprevir/Pibrentasvir
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

100mg glecaprevir and 40 mg pibrentasvir, 3 tablets once daily at the same time with food.

Number of subjects in period 1[1]	Intervention	Intervention 2	GLE/PIB for 8 weeks
Started	28	17	8
Completed	28	17	8

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 61 patients were enrolled. A total of 53 patients started treatment divided at the three treatment arms.

Baseline characteristics

Reporting groups	
Reporting group title	Intervention
Reporting group description:	
Glecaprevir/Pibrentasvir was given with ribavirin for 4 weeks	
Reporting group title	Intervention 2
Reporting group description:	
Glecaprevir/pibrentasvir given for 4 weeks	
Reporting group title	GLE/PIB for 8 weeks
Reporting group description:	
Standard of care with GLE/PIB for 8 weeks for treatment of chronic hepatitis C	

Reporting group values	Intervention	Intervention 2	GLE/PIB for 8 weeks
Number of subjects	28	17	8
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	28	17	8
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	43	41	36
inter-quartile range (Q1-Q3)	39 to 45	33 to 48	33.5 to 43.5
Gender categorical Units: Subjects			
Female	7	3	4
Male	21	14	4

Reporting group values	Total		
Number of subjects	53		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	53		

From 65-84 years	0		
85 years and over	0		

Age continuous Units: years median inter-quartile range (Q1-Q3)	- -		
Gender categorical Units: Subjects			
Female	14		
Male	39		

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description: Glecaprevir/Pibrentasvir was given with ribavirin for 4 weeks	
Reporting group title	Intervention 2
Reporting group description: Glecaprevir/pibrentasvir given for 4 weeks	
Reporting group title	GLE/PIB for 8 weeks
Reporting group description: Standard of care with GLE/PIB for 8 weeks for treatment of chronic hepatitis C	

Primary: SVR12

End point title	SVR12
End point description: How many were cured of hepatitis C	
End point type	Primary
End point timeframe: 12 weeks after end of treatment	

End point values	Intervention	Intervention 2	GLE/PIB for 8 weeks	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	27[1]	17	7[2]	
Units: %	67	59	100	

Notes:

[1] - one patient lost to follow up

[2] - one patient lost to follow up

Statistical analyses

Statistical analysis title	percent
Comparison groups	Intervention v Intervention 2 v GLE/PIB for 8 weeks
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.749 [4]
Method	Fisher exact
Parameter estimate	Mean difference (final values)

Notes:

[3] - The study closed prematurely due to the low number of included patients due to the COVID-19 pandemic.

[4] - 4 weeks treatment with maviret + ribavirin compared to maviret for 4 weeks

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 12 weeks after end of treatment	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20
Reporting groups	
Reporting group title	4 weeks maviret+ ribavirin
Reporting group description: -	
Reporting group title	maviret 4 weeks
Reporting group description: -	
Reporting group title	maviret 8 weeks
Reporting group description: -	

Serious adverse events	4 weeks maviret+ ribavirin	maviret 4 weeks	maviret 8 weeks
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	1 / 8 (12.50%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
drug use			
subjects affected / exposed	1 / 28 (3.57%)	0 / 17 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	4 weeks maviret+ ribavirin	maviret 4 weeks	maviret 8 weeks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 28 (89.29%)	15 / 17 (88.24%)	8 / 8 (100.00%)
Nervous system disorders			
headache			
subjects affected / exposed	10 / 28 (35.71%)	11 / 17 (64.71%)	5 / 8 (62.50%)
occurrences (all)	10	11	5
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	18 / 28 (64.29%)	13 / 17 (76.47%)	5 / 8 (62.50%)
occurrences (all)	18	13	5
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 28 (17.86%)	7 / 17 (41.18%)	3 / 8 (37.50%)
occurrences (all)	5	7	3
diarrhea			
subjects affected / exposed	5 / 28 (17.86%)	4 / 17 (23.53%)	1 / 8 (12.50%)
occurrences (all)	5	4	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	5 / 28 (17.86%)	3 / 17 (17.65%)	1 / 8 (12.50%)
occurrences (all)	5	3	1
Pruritus			
subjects affected / exposed	5 / 28 (17.86%)	4 / 17 (23.53%)	1 / 8 (12.50%)
occurrences (all)	5	4	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/34154034

http://www.ncbi.nlm.nih.gov/pubmed/35337021