Clinical trial results:
Multicenter trial for the treatment of acute Hepatitis C for 8 weeks with Sofosbuvir/Velpatasvir fix dose combination - The HepNet Acute HCV-V study

Summary

EudraCT number	2018-003474-27
Trial protocol	DE
Global end of trial date	08 June 2021

Results information

Result version number	v1 (current)
This version publication date	23 September 2022
First version publication date	23 September 2022

Trial information

Trial identification

Sponsor protocol code	HepNet-aHCV-V

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03818308
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hannover Medical School
Sponsor organisation address	Carl-Neuberg-Str. 1, Hannover, Germany, 30625
Public contact	Stabsstelle Qualitätsmanagement in der Klinischen Forschung, Hannover Medical School, EudraCT@mh-hannover.de
Scientific contact	Stabsstelle Qualitätsmanagement in der Klinischen Forschung, Hannover Medical School, EudraCT@mh-hannover.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	08 September 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 June 2021
Global end of trial reached?	Yes
Global end of trial date	08 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the efficacy of treatment with sofosbuvir/velpatasvir (SOF/VEL) Fixed-Dose Combination (FDC) for 8 weeks in patients with acute HCV infection as measured by the proportion of subjects with sustained viral response (undetectable HCV RNA) 12 weeks after stop of therapy (SVR 12)

Protection of trial subjects:

Before study enrolment all subjects got detailed information about study procedures, potential risks and benefits as well as alternative treatment options. The study was approved by regulatory authorities and independent monitoring was conducted to ensure subjects safety. The IMP is an approved drug with extensive data from clinical trials and favorable risk-benefit profile.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 June 2019
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: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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)	31
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patints were screened in 14 study centers in Germany. Overall 31 patients were screened for elegibility and signed informed consent. 11 of these screened patients had to be excluded due to inclusion/exclusion criteria (Screening failures). Recruitment period was between 06/2019 and 01/2020.

Pre-assignment

Screening details:

Adults (≥18 years) with acute HCV monoinfection. Leading inclusion criteria were HCV RNA > 10^3 IU/ml and proven antibody or RNA seroconversion or ALT > 10 ULN with known exposure within 4 month. Leading exclusion criteria were HIV co-infection, clinically significant illness (other than HCV) and contraindications against SOF/VEL.

Pre-assignment period milestones

Number of subjects started	31
Number of subjects completed	20

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screening Failure: 11

Period 1

Period 1 title	ITT Population (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	single-arm

Arm description:

single-arm study

Arm type	Experimental
Investigational medicinal product name	Epclusa®
Investigational medicinal product code	
Other name	sofosbuvir/ velpatasvir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Sofosbuvir/ velpatasvir (SOF/VEL, Epclusa®), film-coated, fixed-dose combination tablet, consisting of 400 mg SOF and 100 mg VEL for oral administration

Number of subjects in period 1[1]	single-arm
Started	20
End of treatment	19
Completed	18
Not completed	2

Lost to follow-up	2

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: 31 patients were screened for enrolment and 20 patients finally were enrolled in the study. 11 patients dit not met inclusion-/ exclusion criteria and thus must be excluded as screening failure. The number of patients in the baseline period reflects the number of patients who received at least one dose of study medication (ITT).

Baseline characteristics

Reporting groups	
Reporting group title	ITT Population
Reporting group description:	
The overall population is an ITT population and consists of all patients who received at least one dose of the study medication.	

Reporting group values	ITT Population	Total	
Number of subjects	20	20	
Age categorical 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)	20	20	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Adults >= 18 yr			
Units: years			
arithmetic mean	37.4		
standard deviation	± 9.3	-	
Gender categorical Units: Subjects			
Female	1	1	
Male	19	19	
HCV Genotype Units: Subjects			
1a.	12	12	
1b.	1	1	
2.	1	1	
3.	3	3	
4.	3	3	
5.	0	0	
6.	0	0	
HCV RNA Units: IU/ml			
median	104307		
inter-quartile range (Q1-Q3)	7842 to 1726734	-	
ALT/GPT Units: U/L			
arithmetic mean	393.2		
standard deviation	± 405.1	-	

Subject analysis sets

Subject analysis set title	PP Population
Subject analysis set type	Per protocol

Subject analysis set description:

The PP population comprises of all patients that were complying with the studyprotocol until the end of the observational period, particularly all patients that attended all study visits and have fully observed data for the primary endpoint.

Reporting group values	PP Population		
Number of subjects	18		
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)	18		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Adults >= 18 yr			
Units: years			
arithmetic mean	37.7		
standard deviation	± 9.4		
Gender categorical Units: Subjects			
Female	1		
Male	17		
HCV Genotype Units: Subjects			
1a.	10		
1b.	1		
2.	1		
3.	3		
4.	3		
5.	0		
6.	0		
HCV RNA Units: IU/ml			
median	156325		
inter-quartile range (Q1-Q3)	7875 to 2963448		
ALT/GPT Units: U/L			
arithmetic mean	400.7		
standard deviation	± 424.5		

End points

End points reporting groups

Reporting group title	single-arm
Reporting group description: single-arm study	
Subject analysis set title	PP Population
Subject analysis set type	Per protocol
Subject analysis set description: The PP population comprises of all patients that were complying with the studyprotocol until the end of the observational period, particularly all patients that attended all study visits and have fully observed data for the primary endpoint.	

Primary: Proportion of subjects with sustained virological response (SVR 12) 12 weeks after discontinuation of therapy

End point title	Proportion of subjects with sustained virological response (SVR 12) 12 weeks after discontinuation of therapy
End point description: Proportion of subjects with sustained virological response (undetectable HCV RNA) 12 weeks after discontinuation of therapy (SVR 12)	
End point type	Primary
End point timeframe: Follow up visit 12	

End point values	single-arm	PP Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	20	18		
Units: Patients				
sustained viral response 12 weeks in all patients	18	18		

Statistical analyses

Statistical analysis title	two-sided 95%-Wilson-confidence interval
Statistical analysis description: The two-sided 95%-Wilson-confidence interval for the proportion of subjects with sustained viral response 12 weeks after discontinuation of therapy (SVR 12). Since it is assumed that all patients will be HCV RNA negative, it is expected that the corresponding 95%-Wilson-confidence interval will be above 83% and it can be concluded that the treatment has an efficacy of at least 83% 12 weeks after a treatment period of 8 weeks. H0: pSVR12 < 0.83 and H1: pSVR12 ≥ 0.83.	
Comparison groups	single-arm v PP Population

Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.83 [2]
Method	95%Wilson-confidence interval

Notes:

[1] - Patients with missing values for the primary endpoint SVR 12 will be counted as treatment failures for the ITT analysis. These patients are hence counted as patients, which did not show a sustained viral response.
[2] - H0: pSVR12 < 0.83 and H1: pSVR12 ≥ 0.83.

Secondary: Proportion of subjects who reached ALT normalization after End of therapy

End point title	Proportion of subjects who reached ALT normalization after End of therapy

End point description:

Proportion of subjects who reached ALT normalization (ALT <ULN) after 8 weeks of therapy (EOT)

End point type	Secondary

End point timeframe:

Week 8

End point values	single-arm			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Patients	16			

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects who reached ALT normalization 12 weeks after discontinuation of therapy (FU12)

End point title	Proportion of subjects who reached ALT normalization 12 weeks after discontinuation of therapy (FU12)

End point description:

Proportion of subjects who reached ALT normalization (ALT <ULN) after 12 weeks after discontinuation of therapy (FU12)

End point type	Secondary

End point timeframe:

Follow Up Visit 12

End point values	single-arm			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Patients	17			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean HCV RNA at week 2

End point title	Mean HCV RNA at week 2

End point description:

End point type	Secondary

End point timeframe:

Week 2 after baseline

End point values	single-arm			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: IU/ml				
arithmetic mean (confidence interval 95%)	10.84 (3.56 to 18.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean HCV RNA at week 4

End point title	Mean HCV RNA at week 4

End point description:

End point type	Secondary

End point timeframe:

Week 4 after baseline

End point values	single-arm			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: IU/ml				
arithmetic mean (confidence interval 95%)	3.16 (0.86 to 5.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean HCV RNA at week 8

End point title	Mean HCV RNA at week 8

End point description:

End point type	Secondary

End point timeframe:

Week 8 after baseline

End point values	single-arm			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: IU/ml				
arithmetic mean (confidence interval 95%)	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean HCV RNA 12 weeks after end of treatment

End point title	Mean HCV RNA 12 weeks after end of treatment

End point description:

End point type	Secondary

End point timeframe:

12 weeks after end of treatment

End point values	single-arm			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: IU/ml				
arithmetic mean (confidence interval 95%)	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse event documentation period for this trial begins with informed consent and ends with the 12 weeks post-treatment visit.

Adverse event reporting additional description:

Numbers in the non-serious adverse events section reflect all adverse events occurring during the study (non-serious and serious).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	SOF/VEL

Reporting group description: -

Serious adverse events	SOF/VEL		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Poisoning	Additional description: Toxicity to various agents		
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	SOF/VEL		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 20 (65.00%)		
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Poisoning subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Reproductive system and breast disorders Genital erythema subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) Acne subjects affected / exposed occurrences (all) Sensitive skin	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		

subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Renal and urinary disorders Urethral disorder subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Sleep disorder subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Mycoplasma infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Pneumonia subjects affected / exposed occurrences (all) Post viral fatigue syndrome subjects affected / exposed occurrences (all) Syphilis	 1 / 20 (5.00%) 1 5 / 20 (25.00%) 6 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		

subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 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