Clinical trial results:
A phase II, open-label, single arm, multicentre, international trial of sofosbuvir and GS-5816 for people with chronic hepatitis C virus infection and recent injection drug use

Summary

EudraCT number	2015-000178-36
Trial protocol	GB
Global end of trial date	28 November 2018

Results information

Result version number	v1 (current)
This version publication date	18 December 2019
First version publication date	18 December 2019

Trial information

Trial identification

Sponsor protocol code	VHCRP1309

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02336139
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of New South Wales, The Kirby Institute
Sponsor organisation address	UNSW Sydney, Sydney, Australia, 2052
Public contact	Philippa Marks, University of New South Wales, 61 02 93850886, pmarks@kirby.unsw.edu.au
Scientific contact	Gregory Dore, University of New South Wales, 61 02 93850898, gdore@kirby.unsw.edu.au

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	19 April 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the proportion of patients with undetectable HCV RNA at 12 weeks post end of treatment (SVR12) following SOF/GS-5816 therapy for 12 weeks in people with chronic HCV infection and recent injection drug.

Protection of trial subjects:

Subjects were seen by a health practitioner at each study visit to assess safety and adherence.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 5
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Australia: 36
Country: Number of subjects enrolled	New Zealand: 7
Country: Number of subjects enrolled	Switzerland: 10
Country: Number of subjects enrolled	United States: 5
Country: Number of subjects enrolled	Canada: 35
Worldwide total number of subjects	103
EEA total number of subjects	10

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	102
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 19 sites, in Australia (seven sites), Canada (six sites), New Zealand (one site), Norway (one site), Switzerland (two sites), the UK (one site), and the USA (one site). Subjects were recruited from people from three drug treatment clinics, 12 hospital clinics, a private practice, and three community clinics.

Pre-assignment

Screening details:

Participants were 18 years or older, had chronic HCV genotypes 1–6 (confirmed ≥6 months), were naive to NS5A-based HCV therapy, and had recently injected drugs (self-reported injection drug use within 6 months of enrolment). Participants with HIV infection or decompensated liver disease, or both, were excluded.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable, the study was open-label.

Arms

Arm title	Single arm - open-label

Arm description:

The study was open-label. Subjects enrolled in the study received 12 weeks of SOF/GS-5816 in an oral once-daily fixed dose combination. Therapy was administered in weekly electronic blister packs for monitoring of adherence

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir/Velpatasvir
Investigational medicinal product code	SOF/VEL
Other name	Epclusa
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received a fixed-dose combination tablet that contained 400 mg of sofosbuvir and 100 mg of velpatasvir, administered orally once daily for 12 weeks.

Number of subjects in period 1	Single arm - open-label
Started	103
Completed	103

Period 2

Period 2 title	Primary endpoint SVR12
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Not applicable, the study was open-label.

Arms

Arm title	Single arm - open-label

Arm description:

The study was open-label. Subjects enrolled in the study received 12 weeks of SOF/GS-5816 in an oral once-daily fixed dose combination. Therapy was administered in weekly electronic blister packs for monitoring of adherence

Arm type	Experimental
Investigational medicinal product name	Sofosbuvir/Velpatasvir
Investigational medicinal product code	SOF/VEL
Other name	Epclusa
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received a fixed-dose combination tablet that contained 400 mg of sofosbuvir and 100 mg of velpatasvir, administered orally once daily for 12 weeks.

Number of subjects in period 2	Single arm - open-label
Started	103
End of treatment (ETR)	100
Completed	97
Not completed	6
Adverse event, serious fatal	1
Lost to follow-up	4
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	103	103	
Age categorical Units: Subjects			
Age continuous Units: years			
median	48		
full range (min-max)	41 to 53	-	
Gender categorical Units: Subjects			
Female	29	29	
Male	74	74	
High school or higher education Units: Subjects			
High school or higher education	50	50	
No higher education	53	53	
Injecting drug use in the past 6 months Units: Subjects			
Injecting drug use in the past 6 months	103	103	
Injecting drug use frequency in the past 30 days Units: Subjects			
Never	27	27	
Less than daily	49	49	
At least daily	27	27	
History of OST Units: Subjects			
History of OST	84	84	
No history of OST	19	19	
Current OST Units: Subjects			
Methadone	45	45	
Buprenorphine	4	4	
Buprenorphine-naloxone	12	12	
No current OST	42	42	
OST and had injected in past 30 days (baseline) Units: Subjects			
No OST, no recent injecting	12	12	
No OST, recent injecting	33	33	
OST, no recent injecting	15	15	

OST, recent injecting	43	43	
HCV genotype Units: Subjects			
genotype 1a	35	35	
genotype 1b	1	1	
genotype 2	5	5	
genotype 3	60	60	
genotype 4	2	2	
Stage of liver disease Units: Subjects			
No or mild fibrosis (F0–F1)	59	59	
Moderate or advanced fibrosis (F2–F3)	27	27	
Cirrhosis (F4)	9	9	
Not recorded	8	8	

End points

End points reporting groups

Reporting group title	Single arm - open-label

Reporting group description:

The study was open-label. Subjects enrolled in the study received 12 weeks of SOF/GS-5816 in an oral once-daily fixed dose combination. Therapy was administered in weekly electronic blister packs for monitoring of adherence

Reporting group title	Single arm - open-label

Reporting group description:

The study was open-label. Subjects enrolled in the study received 12 weeks of SOF/GS-5816 in an oral once-daily fixed dose combination. Therapy was administered in weekly electronic blister packs for monitoring of adherence

Primary: SVR12

End point title	SVR12

End point description:

The primary efficacy endpoint was the proportion of participants with SVR12, which was defined as a HCV RNA load below the limit of quantification 12 weeks after the end of treatment in all participants who received at least one dose of sofosbuvir and velpatasvir.

End point type	Primary

End point timeframe:

12 weeks post-treatment

End point values	Single arm - open-label	Single arm - open-label		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	103		
Units: Number of subjects	0	97		

Statistical analyses

Statistical analysis title	Intention to treat
Comparison groups	Single arm - open-label v Single arm - open-label
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	90

Confidence interval	
level	95 %
sides	2-sided
lower limit	88
upper limit	95

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events up to 28 days after last dose of study treatment

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Single arm - open-label

Reporting group description:

The study was open-label. Subjects enrolled in the study received 12 weeks of SOF/GS-5816 in an oral once-daily fixed dose combination. Therapy was administered in weekly electronic blister packs for monitoring of adherence

Serious adverse events	Single arm - open-label		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 103 (6.80%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Nervous system disorders			
Headache	Additional description: Hospitalisation for headache		
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Elevated Creatine kinase			
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Death	Additional description: Death due to multiple organ failure complicating amphetamines and opiates toxicity.		
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Skin and subcutaneous tissue disorders			
Erythroderma	Additional description: Hospitalisation for acute onset erythroderma		

subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation	Additional description: Hospitalisation for suicidal thoughts		
subjects affected / exposed	3 / 103 (2.91%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Alcohol withdrawal syndrome	Additional description: Hospitalisation for alcohol withdrawal		
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anxiety	Additional description: Hospitalisation due to increase in polysubstance use leading to anxiety, depression		
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Drug psychosis	Additional description: Hospitalisation due to psychosis thought to be provoked by use of cannabis		
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Overdose	Additional description: Hospitalisation for heroin overdose		
subjects affected / exposed	1 / 103 (0.97%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Single arm - open-label		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 103 (82.52%)		
Nervous system disorders			
Headache			

subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	19 / 103 (18.45%) 19 5 / 103 (4.85%) 5		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	 23 / 103 (22.33%) 23		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 14 / 103 (13.59%) 14 4 / 103 (3.88%) 4 4 / 103 (3.88%) 4		
Respiratory, thoracic and mediastinal disorders Nasopharyngitis subjects affected / exposed occurrences (all)	 5 / 103 (4.85%) 5		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 9 / 103 (8.74%) 9		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 6 / 103 (5.83%) 6 4 / 103 (3.88%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 March 2015	Inclusion criteria: Clarification about patients with cirrhosis was added. Disallowed agents: Clarification about Amiodarone was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Subjects were recruited from hospital-based HCV clinics and community health centres, 10% of participants who were assessed for eligibility were not enrolled. HIV-positive people were excluded because of the absence of data at the start of the study.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29310928