



## Clinical trial results:

### A phase IIIb, open-label, multicentre, international randomised controlled trial of simplified treatment monitoring for 8 weeks glecaprevir (300mg)/pibrentasvir (120mg) in chronic HCV treatment naïve patients without cirrhosis

#### Summary

EudraCT number	2017-000694-37
Trial protocol	GB FR
Global end of trial date	14 December 2018

#### Results information

Result version number	v1 (current)
This version publication date	02 August 2019
First version publication date	02 August 2019

#### Trial information

##### Trial identification

Sponsor protocol code	VHCRP1701
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03117569
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	University of New South Wales Sydney
Sponsor organisation address	UNSW Sydney, Sydney, Australia,
Public contact	Philippa Marks, University of New South Wales Sydney, 61 293850886, pmarks@kirby.unsw.edu.au
Scientific contact	Gregory Dore, University of New South Wales Sydney, 61 293850900, 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	04 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 December 2018
Global end of trial reached?	Yes
Global end of trial date	14 December 2018
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To compare the proportion of participants with undetectable hepatitis C virus load in their blood (HCV RNA less than the lower limit of quantification- LLOQ) at 12 weeks post-treatment (SVR12); following 8 weeks treatment with glecaprevir (300mg)/pibrentasvir (120mg); in people infected with hepatitis C without liver scarring (HCV treatment naïve non-cirrhosis chronic HCV patients), who have received a standard versus simplified schedule of safety and virological monitoring.

Protection of trial subjects:

Participants received a telephone call from the nurse 4 weekly while on treatment to assess safety and adherence.

Background therapy:

Participants received a direct acting antiviral hepatitis C treatment in the form of a oral once-daily fixed dose of glecaprevir (300mg)/pibrentasvir (120mg).

Evidence for comparator: -

Actual start date of recruitment	14 August 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 24
Country: Number of subjects enrolled	France: 42
Country: Number of subjects enrolled	Germany: 41
Country: Number of subjects enrolled	Australia: 45
Country: Number of subjects enrolled	Canada: 86
Country: Number of subjects enrolled	New Zealand: 86
Country: Number of subjects enrolled	Switzerland: 23
Country: Number of subjects enrolled	United States: 33
Worldwide total number of subjects	380
EEA total number of subjects	107

Notes:

### Subjects enrolled per age group

In utero	0
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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)	342
From 65 to 84 years	38
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

From 21 August 2017 to 16 July 2018, participants were screened and enrolled at 33 sites in Australia (n=6), Canada (n=7), France (n=3), Germany (n=4), New Zealand (n=4), Switzerland (n=2), United Kingdom (n=3), and United States (n=4).

### Pre-assignment

Screening details:

Eligible participants were at least 18 years of age with chronic HCV, HCV treatment-naive and without cirrhosis. Participants who required additional treatment adherence support, self-reported injecting drug use within the previous six months, positive urinary drug screen or acute/chronic hepatitis B co-infection were excluded.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Simplified monitoring

Arm description:

Scheduled clinic study visits were only undertaken at screening, baseline and post-treatment week 12.

Arm type	Simplified Monitoring
Investigational medicinal product name	glecaprevir (300mg)/pibrentasvir (120mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

glecaprevir (300mg)/pibrentasvir (120mg) once daily for 8 weeks

<b>Arm title</b>	Standard monitoring
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Arm description:

Scheduled clinic study visits were undertaken at screening, baseline, treatment weeks four and eight (end of treatment), and post-treatment week 12.

Arm type	Standard Monitoring
Investigational medicinal product name	glecaprevir (300mg)/pibrentasvir (120mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

glecaprevir (300mg)/pibrentasvir (120mg) once daily for 8 weeks

<b>Number of subjects in period 1</b>	Simplified monitoring	Standard monitoring
Started	253	127
Completed	253	127

## Period 2

Period 2 title	Completed treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Simplified monitoring

### Arm description:

In the simplified arm, scheduled clinic study visits were undertaken at baseline and post-treatment week 12.

Arm type	Experimental
Investigational medicinal product name	glecaprevir (300mg)/pibrentasvir (120mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

### Dosage and administration details:

glecaprevir (300mg)/pibrentasvir (120mg) daily for 8 weeks

<b>Arm title</b>	Standard monitoring
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### Arm description:

In the standard arm, scheduled clinic study visits were undertaken at baseline, treatment weeks four and eight (end of treatment), and post-treatment week 12.

Arm type	Active comparator
Investigational medicinal product name	glecaprevir (300mg)/pibrentasvir (120mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

### Dosage and administration details:

glecaprevir (300mg)/pibrentasvir (120mg) daily for 8 weeks

<b>Number of subjects in period 2</b>	Simplified monitoring	Standard monitoring
Started	253	127
Completed	249	127
Not completed	4	0
Adverse event, non-fatal	1	-
Lost to follow-up	2	-
Protocol deviation	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	Simplified monitoring
Reporting group description: Scheduled clinic study visits were only undertaken at screening, baseline and post-treatment week 12.	
Reporting group title	Standard monitoring
Reporting group description: Scheduled clinic study visits were undertaken at screening, baseline, treatment weeks four and eight (end of treatment), and post-treatment week 12.	

Reporting group values	Simplified monitoring	Standard monitoring	Total
Number of subjects	253	127	380
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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Median Age			
Units: years			
median	52	50	
full range (min-max)	22 to 73	24 to 79	-
Gender categorical			
Units: Subjects			
Female	96	53	149
Male	157	72	229
Transgender	0	2	2
HCV Genotype			
HCV Genotype			
Units: Subjects			
Genotype 1	118	61	179
Genotype 2	35	17	52
Genotype 3	80	41	121
Genotype 4	14	4	18
Genotype 5	0	1	1
Genotype 6	5	3	8
Genotype indeterminate	1	0	1
Fibrosis Stage			
Units: Subjects			
No or mild fibrosis (F0/F1)	190	93	283

Moderate fibrosis (F2)	49	29	78
Severe fibrosis (F3)	14	5	19
HIV Infection			
HIV Infection			
Units: Subjects			
HIV infection	14	13	27
No HIV Infection	239	114	353
Ethnicity			
Ethnicity			
Units: Subjects			
White	194	97	291
Asian	22	12	34
Black	13	7	20
Other	24	11	35
Opioid Substitution Therapy (OST)			
Opioid Substitution Therapy (OST)			
Units: Subjects			
Opioid Substitution Therapy (OST)	21	17	38
No OST	232	110	342
Body Mass Index (BMI)			
Body Mass Index (BMI)			
Units: kg/m <sup>2</sup>			
median	25.3	24.7	
full range (min-max)	17.8 to 41.7	18.2 to 51.5	-
HCV RNA			
HCV RNA			
Units: Log <sub>10</sub> IU/mL			
median	6.27	6.29	
full range (min-max)	2.49 to 7.74	2.85 to 7.71	-

## End points

### End points reporting groups

Reporting group title	Simplified monitoring
Reporting group description: Scheduled clinic study visits were only undertaken at screening, baseline and post-treatment week 12.	
Reporting group title	Standard monitoring
Reporting group description: Scheduled clinic study visits were undertaken at screening, baseline, treatment weeks four and eight (end of treatment), and post-treatment week 12.	
Reporting group title	Simplified monitoring
Reporting group description: In the simplified arm, scheduled clinic study visits were undertaken at baseline and post-treatment week 12.	
Reporting group title	Standard monitoring
Reporting group description: In the standard arm, scheduled clinic study visits were undertaken at baseline, treatment weeks four and eight (end of treatment), and post-treatment week 12.	

### Primary: SVR12

End point title	SVR12
End point description:	
End point type	Primary
End point timeframe: Twelve weeks post-treatment.	

End point values	Simplified monitoring	Standard monitoring		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	123		
Units: Number of participants				
number (not applicable)	233	121		

### Statistical analyses

Statistical analysis title	Primary endpoint
Comparison groups	Simplified monitoring v Standard monitoring

Number of subjects included in analysis	362
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[1]</sup>
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	92
Confidence interval	
level	95 %
sides	2-sided
lower limit	88
upper limit	95

Notes:

[1] - The non-inferiority margin of 6% was selected in accordance with the principles outlined in guidance on conducting non-inferiority trials; the choice of margin ensured minimal to no loss of efficacy.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events up to 30 days after last dose

Adverse event reporting additional description:

Collected at clinic visits and during 4-weekly telephone call with the nurse while on treatment.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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### Reporting groups

Reporting group title	Simplified monitoring
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Reporting group description:

In the simplified arm, scheduled clinic study visits were undertaken at baseline and post-treatment week 12. Adverse events were also collected during the 4-weekly on-treatment telephone calls with the nurse. Adverse events are reported up to 30 days after last dose.

Reporting group title	Standard monitoring
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Reporting group description:

In the standard arm, scheduled clinic study visits were undertaken at baseline, treatment weeks four and eight (end of treatment), and post-treatment week 12. Adverse events were also collected during the 4-weekly on-treatment telephone calls with the nurse. Adverse events are reported up to 30 days after last dose.

Serious adverse events	Simplified monitoring	Standard monitoring	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 253 (1.19%)	0 / 127 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 253 (0.40%)	0 / 127 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Lung adenocarcinoma			
subjects affected / exposed	1 / 253 (0.40%)	0 / 127 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Acute psychosis			

subjects affected / exposed	1 / 253 (0.40%)	0 / 127 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Simplified monitoring	Standard monitoring	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	133 / 253 (52.57%)	70 / 127 (55.12%)	
Nervous system disorders			
Headache			
subjects affected / exposed	43 / 253 (17.00%)	26 / 127 (20.47%)	
occurrences (all)	43	26	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	52 / 253 (20.55%)	30 / 127 (23.62%)	
occurrences (all)	52	30	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	17 / 253 (6.72%)	25 / 127 (19.69%)	
occurrences (all)	17	25	

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported