



## 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  $\geq 6$  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.

|                                       |                         |
|---------------------------------------|-------------------------|
| <b>Number of subjects in period 1</b> | 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**

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | 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.

| <b>Number of subjects in period 2</b> | 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<br>Units: Subjects                                  |                |       |  |
| Age continuous<br>Units: years<br>median<br>full range (min-max)    | 48<br>41 to 53 | -     |  |
| Gender categorical<br>Units: Subjects                               |                |       |  |
| Female  | 29             | 29    |  |
| Male  | 74             | 74    |  |
| High school or higher education<br>Units: Subjects                  |                |       |  |
| High school or higher education                                     | 50             | 50    |  |
| No higher education   | 53             | 53    |  |
| Injecting drug use in the past 6 months<br>Units: Subjects          |                |       |  |
| Injecting drug use in the past 6 months                             | 103            | 103   |  |
| Injecting drug use frequency in the past 30 days<br>Units: Subjects |                |       |  |
| Never   | 27             | 27    |  |
| Less than daily   | 49             | 49    |  |
| At least daily  | 27             | 27    |  |
| History of OST<br>Units: Subjects                                   |                |       |  |
| History of OST  | 84             | 84    |  |
| No history of OST   | 19             | 19    |  |
| Current OST<br>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)<br>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<br>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<br>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

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | 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  |

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| 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 %

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

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



## 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.<br>Disallowed agents: Clarification about Amiodarone was added. |

Notes:

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### 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:

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### Online references

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