# Clinical trial results:
# Interferon-free Treatment of Acute Genotype 1 Hepatitis C Virus Infection with Ledipasvir/Sofosbuvir Fixed-Dose Combination - The HepNet Acute HCV IV Study

## Summary

| | |
|---|---|
| EudraCT number | 2013-001081-42 |
| Trial protocol | DE |
| Global end of trial date | 13 June 2016 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 31 December 2023 |
| First version publication date | 31 December 2023 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | HepNet-aHCV-IV |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02309918 |
| 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 Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de |
| Scientific contact | Stabsstelle Zentrum für Klinische Studien, 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 | 29 March 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 13 June 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 June 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objectives of this study are as follows:
• To evaluate the efficacy of treatment with ledipasvir (LDV)/sofosbuvir (SOF) FDC for 6 weeks in patients with acute genotype 1 HCV infection as measured by the proportion of subjects with sustained viral response (HCV RNA < LLOQ TND) 12 weeks after discontinuation of therapy (SVR12)
• To evaluate the safety and tolerability of LDV/SOF FDC -containing regimens administered for up to 6 weeks in patients with acute genotype 1 HCV infection

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.
Safety was assessed throughout the treatment and follow-up periods based on the AEs. Adverse events were documented within one week on the respective AE forms in the (e)CRF. The same documentation responsibilities as described for AEs applied to SAEs. In addition, SAEs were documented on a paper SAE-form and reported to the sponsor. Documentation of SAE was done as complete and detailed as possible. Safety Laboratory assessments were conducted at each single visit. The investigator had the right to withdraw a patient from the study if the patient’s safety or wellbeing was compromised by further study participation.

Background therapy:

-

Evidence for comparator:

-

| | |
|---|---|
| Actual start date of recruitment | 05 November 2014 |
| 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: 26 |
| Worldwide total number of subjects | 26 |
| EEA total number of subjects | 26 |

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) | 26 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Patints were screened in 10 study centers in Germany. Overall 26 patients were screened for elegibility and signed informed consent. Six patients were ineligible at screening. Recruitment period was between 11/2014 and 11/2015.

### Pre-assignment

Screening details:

Adults (≥18 years) with acute HCV genotype 1 monoinfection. Leading inclusion criteria: HCV RNA > 10.000 IU/mL and documented HCV antibody seroconversion, or known exposure with ALT > 10 ULN within 4 month.
Leading exclusion criteria: Liver cirrhosis, hepatic decompensation, systemic drug usage, contraindications against IMP.

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 26 |
| Number of subjects completed | 20 |

### Pre-assignment subject non-completion reasons

| | |
|---|---|
| Reason: Number of subjects | Screening Failure: 6 |

### Period 1

| | |
|---|---|
| Period 1 title | Study period (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 | Ledipasvir/ Sofosbuvir |
| Investigational medicinal product code | |
| Other name | Harvoni |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Ledipasvir/ Sofosbuvir fixed dose combination. Film-coated tablets containing 90 mg of Ledipasvir (LDV) and 400 mg of Sofosbuvir (SOF). LDV/SOF FDC tablet was administered once daily.

| **Number of subjects in period 1[1]** | Single-Arm |
|---|---|
| Started | 20 |
| End of treatment | 20 |
| Follow up week 12 | 20 |

| | |
|---|---|
| Completed | 19 |
| Not completed | 1 |
| Consent withdrawn by subject | 1 |

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: 26 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 | Study period |
| Reporting group description: | |
| Single Arm study | |

| Reporting group values | Study period | Total | |
|---|---|---|---|
| Number of subjects | 20 | 20 | |
| Age categorical<br>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<br>Units: years | | | |
| median | 49 | | |
| inter-quartile range (Q1-Q3) | 36 to 54 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 8 | 8 | |
| Male | 12 | 12 | |
| HCV Genotype<br>Units: Subjects | | | |
| 1a | 11 | 11 | |
| 1b | 9 | 9 | |
| HCV RNA<br>Units: Subjects | | | |
| <= 50.000 IU/ml | 12 | 12 | |
| < 15 IU/ml | 1 | 1 | |
| > 50.000 IU/ml | 7 | 7 | |
| Risk factors for infection<br>Units: Subjects | | | |
| Sexual transmission | 11 | 11 | |
| Medical procedures/needle stick injury | 5 | 5 | |
| Nail treatment | 1 | 1 | |
| Unspecified | 3 | 3 | |
| HCV RNA<br>Units: IU/ml | | | |
| median | 11000 | | |
| inter-quartile range (Q1-Q3) | 140 to 190000 | - | |

| | | | |
|---|---|---|---|
| Alanine Aminotransferase<br>Units: U/l<br>median<br>inter-quartile range (Q1-Q3) | <br><br>225<br>71 to 722 | <br><br><br>- | |
| Bilirubin<br>Units: µmol/l<br>median<br>inter-quartile range (Q1-Q3) | <br><br>13.7<br>10.2 to 25.1 | <br><br><br>- | |
| Aspartate aminotransferase<br>Units: U/l<br>median<br>inter-quartile range (Q1-Q3) | <br><br>76.5<br>34.5 to 286.5 | <br><br><br>- | |
| Gamma GT<br>Units: U/l<br>median<br>inter-quartile range (Q1-Q3) | <br><br>134<br>71 to 292 | <br><br><br>- | |
| Alkaline phosphatase<br>Units: U/l<br>median<br>inter-quartile range (Q1-Q3) | <br><br>104<br>80 to 138 | <br><br><br>- | |

| **Subject analysis sets** | |
|---|---|
| Subject analysis set title | IIT-Analysis |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

The overall population is an ITT population and consists of all patients who received at least one dose ofthe study medication.

| | |
|---|---|
| Subject analysis set title | Per Protocol Analysis |
| 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** | IIT-Analysis | Per Protocol Analysis | |
|---|---|---|---|
| Number of subjects | 20 | 19 | |
| Age categorical<br>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 | 19 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years<br>median | <br><br>49 | <br><br>49 | |

| | | | |
|---|---|---|---|
| inter-quartile range (Q1-Q3) | 36 to 54 | 35 to 54 | |

| | | | |
|---|---|---|---|
| Gender categorical<br>Units: Subjects | | | |
| Female | 8 | 7 | |
| Male | 12 | 12 | |
| HCV Genotype<br>Units: Subjects | | | |
| 1a | 11 | 11 | |
| 1b | 9 | 8 | |
| HCV RNA<br>Units: Subjects | | | |
| <= 50.000 IU/ml | 12 | 12 | |
| < 15 IU/ml | 1 | 1 | |
| > 50.000 IU/ml | 7 | 6 | |
| Risk factors for infection<br>Units: Subjects | | | |
| Sexual transmission | 11 | 11 | |
| Medical procedures/needle stick injury | 5 | 4 | |
| Nail treatment | 1 | 1 | |
| Unspecified | 3 | 3 | |
| HCV RNA<br>Units: IU/ml | | | |
| median | 11000 | 6750 | |
| inter-quartile range (Q1-Q3) | 140 to 190000 | 138 to 250000 | |
| Alanine Aminotransferase<br>Units: U/l | | | |
| median | 225 | 269 | |
| inter-quartile range (Q1-Q3) | 71 to 722 | 68 to 766 | |
| Bilirubin<br>Units: µmol/l | | | |
| median | 13.7 | 15.4 | |
| inter-quartile range (Q1-Q3) | 10.2 to 25.1 | 10.1 to 27.4 | |
| Aspartate aminotransferase<br>Units: U/l | | | |
| median | 77 | 72 | |
| inter-quartile range (Q1-Q3) | 35 to 287 | 32 to 294 | |
| Gamma GT<br>Units: U/l | | | |
| median | 134 | 135 | |
| inter-quartile range (Q1-Q3) | 71 to 292 | 75 to 292 | |
| Alkaline phosphatase<br>Units: U/l | | | |
| median | 104 | 108 | |
| inter-quartile range (Q1-Q3) | 80 to 138 | 84 to 139 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Single-Arm |
| Reporting group description: | |
| Single-arm study | |
| Subject analysis set title | IIT-Analysis |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| The overall population is an ITT population and consists of all patients who received at least one dose ofthe study medication. | |
| Subject analysis set title | Per Protocol Analysis |
| 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: sustained virological response (SVR 12)

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

| End point values | Single-Arm | IIT-Analysis | Per Protocol Analysis | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 20 | 20 | 19 | |
| Units: Patients | | | | |
| sustained virological response (SVR 12) week 12 | 20 | 20 | 19 | |

### 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) was evaluated. Since all patients (ITT or PP) were expected to be HCV-RNA negative, the lower limit of the confidence interval was expected to be above 80%. | |
| Comparison groups | Single-Arm v IIT-Analysis v Per Protocol Analysis |

| | |
|---|---|
| Number of subjects included in analysis | 59 |
| Analysis specification | Pre-specified |
| Analysis type | other[1] |
| P-value | < 0.05 [2] |
| Method | 95%Wilson-confidence interval |

Notes:

[1] - 95%Wilson-confidence interval

[2] - H0: pSVR12 < 0.83 and H1: pSVR12 ≥ 0.83.

## Secondary: sustained virological response (SVR 24)

| | |
|---|---|
| End point title | sustained virological response (SVR 24) |

End point description:

Proportion of subjects with durability of sustained virological response (SVR 24) 24 weeks after discontinuation of therapy

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Follow up week 24

| End point values | Single-Arm | IIT-Analysis | Per Protocol Analysis | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 20 | 20 | 19[3] | |
| Units: patients | | | | |
| Patients sustained virological response (SVR 24) | 19 | 19 | 19 | |

Notes:

[3] - FU24 data were available for 19 patients, 1 patient was lost to follow up

## 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 upon first administration of the IMPs and ends with the end-of-trial visit of the respective patient.

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 | 18.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | LDV/SOF FDC |

Reporting group description: -

| **Serious adverse events** | LDV/SOF FDC | | |
|---|---|---|---|
| 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 | | | |
| Ligament rupture | | | |
| 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** | LDV/SOF FDC | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 19 / 20 (95.00%) | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 20 (20.00%) | | |
| occurrences (all) | 5 | | |
| Performance status decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Mood altered | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Irritability | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Sleep disorder | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Investigations | | | |
| Blood uric acid increased | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Meniscus injury | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Ligament rupture | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Wrist fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | | |
| occurrences (all) | 2 | | |
| Multiple sclerosis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Transient global amnesia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Transient ischemic attack | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Eye disorders | | | |
| Blepharospasm | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 2 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | | |
| occurrences (all) | 3 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Diarrhea | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | | |
| occurrences (all) | 2 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Feces discolored | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1 | | |
| Flatulence<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1 | | |
| Nausea<br>subjects affected / exposed<br>occurrences (all) | 4 / 20 (20.00%)<br>4 | | |
| Oral discomfort<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1 | | |
| Vomiting<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1 | | |
| Hepatobiliary disorders | | | |
| Hepatic pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1 | | |
| Hepatic steatosis<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia<br>subjects affected / exposed<br>occurrences (all) | 3 / 20 (15.00%)<br>3 | | |
| Rash<br>subjects affected / exposed<br>occurrences (all) | 2 / 20 (10.00%)<br>2 | | |
| Skin reaction<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1 | | |
| Arthralgia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | | |
| occurrences (all) | 3 | | |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |
| Otitis media | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | | |
| occurrences (all) | 1 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 25 February 2015 | Inclusion criterium changed and inclusion of a prohibited concomitant medication |
| 12 June 2015 | secondary objectives were defined more precisely and shipping of samples for the cytokine analysis was changed to the end of the study. |

Notes:

### 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/28029529

http://www.ncbi.nlm.nih.gov/pubmed/33517457

http://www.ncbi.nlm.nih.gov/pubmed/30548086

http://www.ncbi.nlm.nih.gov/pubmed/34843107