



Clinical trial results:

Pilot study to assess efficacy and safety of Sofosbuvir/Ledipasvir (GS-5885) fixed-dose combination in NS3/4A protease inhibitor-experienced subjects with HCV genotype 1 infection and HIV co-infection

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2013-002607-33 |
| Trial protocol | FR |
| Global end of trial date | 04 December 2015 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 08 March 2024 |
| First version publication date | 08 March 2024 |

Trial information

Trial identification

| | |
|-----------------------|--------------------|
| Sponsor protocol code | ANRS HC 31 SOFTRIH |
|-----------------------|--------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02125500 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Inserm-ANRS |
| Sponsor organisation address | 101 rue de Tolbiac, Paris, France, 75013 |
| Public contact | Pr. Eric Rosenthal, Service de Médecine interne, +33 4 92 03 58 51, rosenthal.e@chu-nice.fr |
| Scientific contact | Pr. Eric Rosenthal, Service de Médecine interne, +33 4 92 03 58 51, rosenthal.e@chu-nice.fr |

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 | 11 March 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 December 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess, in patients with HCV genotype 1 infection and HIV co-infection, who had previously failed a NS3/4A protease inhibitor plus PEG/RBV regimen or stopped prematurely their treatment for intolerance, the rate of sustained virological response (SVR) 12 weeks after 24 weeks of treatment in cirrhotic patients and 12 weeks in non-cirrhotic patients with oral Sofosbuvir/Ledipasvir fixed-dose combination, and to determine whether this SVR rate is significantly above 50%.

Protection of trial subjects:

This study was conducted in accordance with the updated Declaration of Helsinki, in compliance with the approved protocol and its amendments, the International Council for Harmonisation guideline for Good Clinical Practice (ICH GCP), and French regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 18 August 2014 |
| 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 | France: 68 |
| Worldwide total number of subjects | 68 |
| EEA total number of subjects | 68 |

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) | 64 |
| From 65 to 84 years | 4 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from 30 clinical centers in France from August 2014 to March 2015.

Pre-assignment

Screening details:

Main criteria:

Inclusion: at least 18 years old, confirmed HIV infection, infection with HCV genotype 1 only (confirmed at screen visit)

Non-inclusion: Child-Pugh B or C cirrhosis or history of decompensated cirrhosis, co-infection with Hepatitis B virus (AgHBs)

Period 1

| | |
|------------------------------|---------------------------------|
| Period 1 title | Overall period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|--|-----------------------|
| Arm title | Global |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Sofosbuvir/Ledipasvir |
| Investigational medicinal product code | |
| Other name | SOF/LDV |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

SOF: 400 mg

LDV: 90 mg

The tablet is administered orally, once daily, without regard to food. It is recommended to take their dose in the morning.

To be taken during 12 weeks for non-cirrhotic patients and during 24 weeks for cirrhotic patients.

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Stable antiretroviral combination |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

The patients enrolled in the study had to receive a stable antiretroviral combination of emtricitabine/tenofovir (TRUVADA®) or lamivudine/tenofovir (EPIVIR® + VIREAD®) standard of care backbone plus efavirenz (SUSTIVA®) or raltegravir (ISENRESS®) or rilpivirine (EDURANT®) or enfuvirtide (FUZEON®).

Alternative combinations of the above listed medications were allowed.

Single tablets regimen containing emtricitabine/tenofovir plus efavirenz or rilpivirine (ATRIPLA® or EVIPLERA®) were permitted.

To be taken during 12 weeks for non-cirrhotic patients and during 24 weeks for cirrhotic patients.

| Number of subjects in period 1 | Global |
|---------------------------------------|--------|
| Started | 68 |
| Completed | 65 |
| Not completed | 3 |
| Protocol deviation | 3 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | Global |
|-----------------------|--------|

Reporting group description: -

| Reporting group values | Global | Total | |
|---|----------|-------|--|
| Number of subjects | 68 | 68 | |
| 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) | 64 | 64 | |
| From 65-84 years | 4 | 4 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 52 | | |
| inter-quartile range (Q1-Q3) | 49 to 54 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 14 | 14 | |
| Male | 54 | 54 | |

Subject analysis sets

| | |
|----------------------------|-----------|
| Subject analysis set title | Cirrhotic |
|----------------------------|-----------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subset formed by the cirrhotic patients.

| | |
|----------------------------|---------------|
| Subject analysis set title | Non-cirrhotic |
|----------------------------|---------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subset formed by non-cirrhotic patients

| Reporting group values | Cirrhotic | Non-cirrhotic | |
|---|-----------|---------------|--|
| Number of subjects | 27 | 41 | |
| 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) | 26 | 38 | |
| From 65-84 years | 1 | 3 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 53 | 52 | |
| inter-quartile range (Q1-Q3) | 51 to 55 | 48 to 54 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 8 | 6 | |
| Male | 19 | 35 | |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | Global |
| Reporting group description: - | |
| Subject analysis set title | Cirrhotic |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Subset formed by the cirrhotic patients. | |
| Subject analysis set title | Non-cirrhotic |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Subset formed by non-cirrhotic patients | |

Primary: SVR12

| | |
|--|----------------------|
| End point title | SVR12 ^[1] |
| End point description: | |
| The primary endpoint is the sustained virological response, defined by an undetectable HCV RNA 12 weeks post-treatment (SVR12) | |
| End point type | Primary |
| End point timeframe: | |
| Analyses made 12 weeks after treatment stop. | |
| W36 for cirrhotic patients and W24 for non-cirrhotic patients. | |
| Notes: | |

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This endpoint concerns a single arm, adding statistical analyses create errors. See attachments for data.

| End point values | Global | Cirrhotic | Non-cirrhotic | |
|-----------------------------|-----------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 68 | 27 | 41 | |
| Units: Number of patients | 65 | 25 | 40 | |

| | |
|-----------------------------------|--|
| Attachments (see zip file) | SOFTRIH Endpoint data/SOFTRIH-endpoint.png |
|-----------------------------------|--|

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Participants reported adverse events during the entire time of the trial.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Non-cirrhotic |
|-----------------------|---------------|

Reporting group description: -

| | |
|-----------------------|-----------|
| Reporting group title | Cirrhotic |
|-----------------------|-----------|

Reporting group description: -

| | |
|-----------------------|--------|
| Reporting group title | Global |
|-----------------------|--------|

Reporting group description: -

| Serious adverse events | Non-cirrhotic | Cirrhotic | Global |
|---|----------------|-----------------|------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | 8 / 27 (29.63%) | 11 / 68 (16.18%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | 1 / 27 (3.70%) | 2 / 68 (2.94%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | 1 / 27 (3.70%) | 3 / 68 (4.41%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|--|----------------|----------------|----------------|
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Arteritis | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 27 (3.70%) | 1 / 68 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Non-cirrhotic | Cirrhotic | Global |
|--|-------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 41 / 41 (100.00%) | 27 / 27 (100.00%) | 68 / 68 (100.00%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 10 / 41 (24.39%) | 4 / 27 (14.81%) | 14 / 68 (20.59%) |
| occurrences (all) | 10 | 4 | 14 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 6 / 41 (14.63%) | 11 / 27 (40.74%) | 17 / 68 (25.00%) |
| occurrences (all) | 6 | 11 | 17 |
| Influenza like illness | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | 1 / 27 (3.70%) | 4 / 68 (5.88%) |
| occurrences (all) | 4 | 1 | 5 |

| | | | |
|--------------------------------------|-----------------|------------------|------------------|
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | 2 / 27 (7.41%) | 4 / 68 (5.88%) |
| occurrences (all) | 2 | 2 | 4 |
| Depression | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | 2 / 27 (7.41%) | 5 / 68 (7.35%) |
| occurrences (all) | 3 | 2 | 5 |
| Insomnia | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | 3 / 27 (11.11%) | 6 / 68 (8.82%) |
| occurrences (all) | 3 | 3 | 6 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 6 / 41 (14.63%) | 5 / 27 (18.52%) | 11 / 68 (16.18%) |
| occurrences (all) | 8 | 6 | 14 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 8 / 41 (19.51%) | 9 / 27 (33.33%) | 17 / 68 (25.00%) |
| occurrences (all) | 13 | 10 | 23 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 5 / 41 (12.20%) | 7 / 27 (25.93%) | 12 / 68 (17.65%) |
| occurrences (all) | 5 | 8 | 13 |
| Blood HIV RNA increased | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | 2 / 27 (7.41%) | 4 / 68 (5.88%) |
| occurrences (all) | 3 | 2 | 5 |
| Blood bicarbonate decreased | | | |
| subjects affected / exposed | 8 / 41 (19.51%) | 12 / 27 (44.44%) | 20 / 68 (29.41%) |
| occurrences (all) | 11 | 19 | 30 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 6 / 41 (14.63%) | 5 / 27 (18.52%) | 11 / 68 (16.18%) |
| occurrences (all) | 11 | 11 | 22 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | 4 / 27 (14.81%) | 8 / 68 (11.76%) |
| occurrences (all) | 4 | 5 | 9 |
| Blood and lymphatic system disorders | | | |
| Thrombocytopenia | | | |

| | | | |
|---|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 2 / 41 (4.88%) 6 | 10 / 27 (37.04%) 18 | 12 / 68 (17.65%) 24 |
| Leukopenia subjects affected / exposed occurrences (all) | 4 / 41 (9.76%) 6 | 5 / 27 (18.52%) 13 | 9 / 68 (13.24%) 19 |
| Neutropenia subjects affected / exposed occurrences (all) | 2 / 41 (4.88%) 3 | 4 / 27 (14.81%) 8 | 6 / 68 (8.82%) 11 |
| Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 41 (2.44%) 1 | 3 / 27 (11.11%) 3 | 4 / 68 (5.88%) 4 |
| Nausea subjects affected / exposed occurrences (all) | 4 / 41 (9.76%) 4 | 2 / 27 (7.41%) 2 | 6 / 68 (8.82%) 6 |
| Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 3 / 41 (7.32%) 3 | 4 / 27 (14.81%) 5 | 7 / 68 (10.29%) 8 |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 2 / 41 (4.88%) 2 | 2 / 27 (7.41%) 4 | 4 / 68 (5.88%) 6 |
| Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all) | 24 / 41 (58.54%) 46 | 13 / 27 (48.15%) 22 | 37 / 68 (54.41%) 68 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 2 / 41 (4.88%) 2 | 2 / 27 (7.41%) 3 | 4 / 68 (5.88%) 5 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 41 (2.44%) 2 | 4 / 27 (14.81%) 4 | 5 / 68 (7.35%) 6 |
| Infections and infestations | | | |

| | | | |
|---|------------------------|-----------------------|------------------------|
| Bronchitis subjects affected / exposed occurrences (all) | 2 / 41 (4.88%) 3 | 3 / 27 (11.11%) 4 | 5 / 68 (7.35%) 7 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 4 / 41 (9.76%) 4 | 1 / 27 (3.70%) 1 | 5 / 68 (7.35%) 5 |
| Metabolism and nutrition disorders | | | |
| Hypophosphataemia subjects affected / exposed occurrences (all) | 15 / 41 (36.59%) 25 | 8 / 27 (29.63%) 12 | 23 / 68 (33.82%) 37 |
| Hypokalaemia subjects affected / exposed occurrences (all) | 6 / 41 (14.63%) 7 | 3 / 27 (11.11%) 11 | 9 / 68 (13.24%) 18 |
| Hyponatraemia subjects affected / exposed occurrences (all) | 3 / 41 (7.32%) 4 | 3 / 27 (11.11%) 3 | 6 / 68 (8.82%) 7 |
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 5 / 41 (12.20%) 5 | 1 / 27 (3.70%) 1 | 6 / 68 (8.82%) 6 |
| Hypercreatininaemia subjects affected / exposed occurrences (all) | 9 / 41 (21.95%) 17 | 8 / 27 (29.63%) 16 | 17 / 68 (25.00%) 33 |
| Hyperuricaemia subjects affected / exposed occurrences (all) | 3 / 41 (7.32%) 4 | 2 / 27 (7.41%) 3 | 5 / 68 (7.35%) 7 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 12 March 2014 | The substantial modifications included in the amendment 1 of the protocol are: <ul style="list-style-type: none">- review and modification of the criterion for discontinuation of treatment in case of virological rebound- rewording of the non-inclusion criterion concerning contraindications to the experimental treatment in order to be consistent with the "Contra-indicated treatments" part of the protocol. |
| 09 July 2014 | The substantial modifications included in the amendment 2 of the protocol are: <ul style="list-style-type: none">- modification of the trial's therapeutic strategy- clarification of the criterion for stopping HCV treatment for virological reasons- update of the list of prohibited treatments. |
| 10 December 2014 | The substantial modifications included in the amendment 3 of the protocol are: <ul style="list-style-type: none">- clarification of the conditions for changing antiretroviral treatment after stopping experimental anti-HCV treatment- modification of the list of contra-indicated antiviral treatments. |
| 11 February 2015 | The substantial modifications included in the amendment 4 of the protocol are: <ul style="list-style-type: none">- modification of the criteria for determining the fibrosis score- deletion of a virological criterion for discontinuation of HCV treatment- update of safety data- modification of the interaction data, the list of contra-indicated treatments and treatments to be used with caution- modification of the adverse event severity rating scale used for the "bicarbonate" item. |

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/29214737>