



## 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
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##### 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
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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



## 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

<b>Arm title</b>	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 (ISENTRESS®) 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.

<b>Number of subjects in period 1</b>	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 <sup>[1]</sup>
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	

<b>Attachments (see zip file)</b>	SOFTRIH Endpoint data/SOFTRIH-endpoint.png
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### 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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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### Reporting groups

Reporting group title	Non-cirrhotic
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Reporting group description: -

Reporting group title	Cirrhotic
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Reporting group description: -

Reporting group title	Global
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Reporting group description: -

<b>Serious adverse events</b>	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
<b>Gastrointestinal disorders</b>			
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
<b>Respiratory, thoracic and mediastinal disorders</b>			
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
<b>Metabolism and nutrition disorders</b>			
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 %

<b>Non-serious adverse events</b>	Non-cirrhotic	Cirrhotic	Global
<b>Total subjects affected by non-serious adverse events</b>			
subjects affected / exposed	41 / 41 (100.00%)	27 / 27 (100.00%)	68 / 68 (100.00%)
<b>Vascular disorders</b>			
Hypertension			
subjects affected / exposed	10 / 41 (24.39%)	4 / 27 (14.81%)	14 / 68 (20.59%)
occurrences (all)	10	4	14
<b>General disorders and administration site conditions</b>			
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	2 / 41 (4.88%)	3 / 27 (11.11%)	5 / 68 (7.35%)
occurrences (all)	3	4	7
Nasopharyngitis			
subjects affected / exposed	4 / 41 (9.76%)	1 / 27 (3.70%)	5 / 68 (7.35%)
occurrences (all)	4	1	5
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	15 / 41 (36.59%)	8 / 27 (29.63%)	23 / 68 (33.82%)
occurrences (all)	25	12	37
Hypokalaemia			
subjects affected / exposed	6 / 41 (14.63%)	3 / 27 (11.11%)	9 / 68 (13.24%)
occurrences (all)	7	11	18
Hyponatraemia			
subjects affected / exposed	3 / 41 (7.32%)	3 / 27 (11.11%)	6 / 68 (8.82%)
occurrences (all)	4	3	7
Hypercholesterolaemia			
subjects affected / exposed	5 / 41 (12.20%)	1 / 27 (3.70%)	6 / 68 (8.82%)
occurrences (all)	5	1	6
Hypercreatininaemia			
subjects affected / exposed	9 / 41 (21.95%)	8 / 27 (29.63%)	17 / 68 (25.00%)
occurrences (all)	17	16	33
Hyperuricaemia			
subjects affected / exposed	3 / 41 (7.32%)	2 / 27 (7.41%)	5 / 68 (7.35%)
occurrences (all)	4	3	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: - 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: - 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: - 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: - 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:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/29214737>