Clinical trial results:
Personal monitoring of liver transplant patients infected with Hepatitis C Virus. Pilot study to compare the evolution of Hepatitis C by receiving immunosuppression with tacrolimus in combination with Mycophenolate Mofetil or Everolimus.

Summary

EudraCT number	2012-002105-22
Trial protocol	ES
Global end of trial date	01 September 2020

Results information

Result version number	v1 (current)
This version publication date	29 November 2021
First version publication date	29 November 2021

Trial information

Trial identification

Sponsor protocol code	EVL-VHC-HVH.12

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	VHIR
Sponsor organisation address	Passeig Vall Hebron 119-129, Barcelona, Spain, 08035
Public contact	Joaquin Lopez-Soriano, VHIR, joaquin.lopez.soriano@vhir.org
Scientific contact	Dra Itxarone Bilbao, VHIR, 0034 932746113, ibilbao@vhebron.net

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	01 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Compare the evolution of hepatitis C recurrence as determined by progression of liver fibrosis (F ? 2, as ranked by ISHAK) a year post-liver transplantation in patients receiving low dose tacrolimus in combination with mycophenolate mofetil vs everolimus.

Since recruitment of patients was imcomplete, the assay only comprised the study of viral populations. HCV genomes isolated from pre-LT and 15-day post-LT serum samples of ten patients, who underwent orthotopic LT, were quantified and sequenced using a next-generation sequencing platform. Sequence alignments, phylogenetic trees, quasispecies complexity measures, biostatistics analyses, adjusted R2 values, and analysis of variance (ANOVA) were carried out. Viral populations were then used as predictor of the future degree of liver damage.

Protection of trial subjects:

This study was approved by the local institutional review board for clinical research, and all patients gave written informed consent in accordance with the 1975 Declaration of Helsinki

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2012
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	Spain: 10
Worldwide total number of subjects	10
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 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	8
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Ten patients were included in the study, five being infected with HCV genotype 1 subtype a (G1a), four with G1b, and one with G3a.

Pre-assignment

Screening details:

All patients were assigned to the single group in the study

Period 1

Period 1 title	Pre-transplantation
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Liver transplantation

Arm description: -

Arm type	Single arm, no intervention
Investigational medicinal product name	No product was administered
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solvent for...
Routes of administration	Unknown use

Dosage and administration details:

There was no administration of products in this assay

Number of subjects in period 1	Liver transplantation
Started	10
Completed	10

Period 2

Period 2 title	Post-transplantation
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	No treatment
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	No treatment
Started	10
Completed	10

Baseline characteristics

Reporting groups	
Reporting group title	Pre-transplantation

Reporting group description: -

Reporting group values	Pre-transplantation	Total	
Number of subjects	10	10	
Age categorical Units: Subjects			
Adults (18-64 years)	8	8	
From 65-84 years	2	2	
Gender categorical Units: Subjects			
Female	2	2	
Male	8	8	

End points

End points reporting groups

Reporting group title	Liver transplantation
Reporting group description: -	
Reporting group title	No treatment
Reporting group description: -	
Subject analysis set title	Pre-LT
Subject analysis set type	Full analysis
Subject analysis set description:	
10 patients with samples obtained6 weeks before liver transplantation	
Subject analysis set title	Post-LT
Subject analysis set type	Full analysis
Subject analysis set description:	
10 patients with samples taken 2 weeks after liver transplantation	

Primary: Hill D1

End point title	Hill D1
End point description:	
The following diversity index was used to define the viral quasispecies complexity at the molecular level: Hill numbers (see article)	
End point type	Primary
End point timeframe:	
Overall study	

End point values	Pre-LT	Post-LT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: Units				
arithmetic mean (standard deviation)	19.80 (± 12.85)	18.92 (± 11.03)		

Statistical analyses

Statistical analysis title	Hill D1
Comparison groups	Post-LT v Pre-LT
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5
Method	Wilcoxon (Mann-Whitney)

Primary: Hill D2

End point title	Hill D2

End point description:

End point type	Primary

End point timeframe:

15 days after liver transplantation

End point values	Pre-LT	Post-LT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: units				
arithmetic mean (standard deviation)	8.70 (± 5.53)	8.99 (± 6.86)		

Statistical analyses

Statistical analysis title	Hill D2
Comparison groups	Post-LT v Pre-LT
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.539
Method	Wilcoxon (Mann-Whitney)

Primary: Hill Dinf

End point title	Hill Dinf

End point description:

End point type	Primary

End point timeframe:

15 days after transplantation

End point values	Pre-LT	Post-LT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	10		
Units: units				
arithmetic mean (standard deviation)	3.35 (± 1.23)	3.55 (± 2.18)		

Statistical analyses

Statistical analysis title	Hill Dinf
Comparison groups	Post-LT v Pre-LT
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.615
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

15 days after transplantation

Adverse event reporting additional description:

There were no adverse events, since the assay only reached the phase of blood sampling, with no further treatments (they were suspended).
Blood samples were taken in order to characterize VHC virus populations in each patient.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Post-LT

Reporting group description: -

Serious adverse events	Post-LT		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Post-LT		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The assay only included blood sampling for VHC population study. There were no pharmacological interventions, contrary to what was initially proposed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

None of the viral complexity measures studied at 15 days after liver transplantation were significantly associated with liver damage progression at 1 year following the procedure. Full article available at: https://doi.org/10.3390/genes12111731

Notes: