



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 incomplete, 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 obtained 6 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 (\pm 12.85) | 18.92 (\pm 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 (\pm 5.53) | 8.99 (\pm 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 (\pm 1.23) | 3.55 (\pm 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

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|-----------------|--------|
| 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.

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| 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 |
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Notes: