# Clinical trial results:
# Multicenter, Randomized Phase 2B Study to Evaluate the Efficacy, Safety and Tolerability of OCR-002 (ornithine phenylacetate) in Hospitalized Patients with Cirrhosis and Associated Hyperammonemia with an Episode of Hepatic Encephalopathy

## Summary

| | |
|---|---|
| EudraCT number | 2013-005412-10 |
| Trial protocol | EE CZ AT HU IT DE NL BE DK BG |
| Global end of trial date | 29 December 2016 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 22 November 2020 |
| First version publication date | 22 November 2020 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | OCR002-HE209 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01966419 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Acronym: STOP-HE |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Ocera Therapeutics, Inc. |
| Sponsor organisation address | 1425 U.S. Route 206, Bedminster, NJ, United States, 07921 |
| Public contact | Mallinckrodt Medical Information Call Center, Ocera Therapeutics, Inc., +1 800-556-3314 Ext. 5, clinicaltrials@mnk.com |
| Scientific contact | Mallinckrodt Medical Information Call Center, Ocera Therapeutics, Inc., +1 800-556-3314 Ext. 5, clinicaltrials@mnk.com |

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 | 23 August 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 29 December 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to determine whether ornithine phenylacetate can speed recovery from an acute hepatic encephalopathy episode requiring hospitalization in cirrhotic patients.

The primary objectives of the study were to evaluate the efficacy of OCR-002 for treatment of an acute hepatic encephalopathy (HE) episode in cirrhotic patients requiring hospitalization and the safety and tolerability of OCR-002 in hospitalized cirrhotic patients with an acute episode of HE.

Protection of trial subjects:

The investigator ensured that this study was conducted in accordance with the principles of the Declaration of Helsinki (as amended in Tokyo, Venice, Hong Kong, South Africa, and Edinburgh), International Council for Harmonisation guidelines, or with the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the study patient. Further, protection of trial participants was ensured by an Independent Data Monitoring Committee (IDMC).

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 07 January 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 | Netherlands: 1 |
| Country: Number of subjects enrolled | Spain: 13 |
| Country: Number of subjects enrolled | Austria: 7 |
| Country: Number of subjects enrolled | Belgium: 7 |
| Country: Number of subjects enrolled | Bulgaria: 3 |
| Country: Number of subjects enrolled | Czech Republic: 5 |
| Country: Number of subjects enrolled | Denmark: 2 |
| Country: Number of subjects enrolled | France: 21 |
| Country: Number of subjects enrolled | Hungary: 5 |
| Country: Number of subjects enrolled | Italy: 2 |
| Country: Number of subjects enrolled | United States: 128 |
| Country: Number of subjects enrolled | Russian Federation: 12 |
| Country: Number of subjects enrolled | Israel: 22 |
| Country: Number of subjects enrolled | Australia: 1 |
| Country: Number of subjects enrolled | Canada: 2 |

| | |
|---|---|
| Worldwide total number of subjects | 231 |
| EEA total number of subjects | 66 |

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) | 160 |
| From 65 to 84 years | 71 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

A total of 231 participants were enrolled (randomized) into the trial at multiple (68) sites in 15 countries, including the United States, Australia and Europe.

### Pre-assignment

Screening details:

Of all potential patients screened, 231 patients were randomized in a 1:1 ratio.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

While the study was double-blind (participant and investigator blinded), the care provider and outcomes assessor were also blinded.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo |

Arm description:

Patients receive matching placebo via continuous IV infusion for up to 5 days, in addition to standard of care (SOC)

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | Matching placebo |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo for continuous IV infusion that is visually identical to the experimental product

| | |
|---|---|
| **Arm title** | OCR-002 |

Arm description:

Patients receive ornithine phenylacetate by continuous IV infusion for up to 5 days in addition to SOC

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ornithine phenylacetate |
| Investigational medicinal product code | |
| Other name | OCR-002 |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Ornithine phenylacetate for continuous IV infusion at dose levels predicated on level of hepatic decompensation

| **Number of subjects in period 1** | Placebo | OCR-002 |
|---|---|---|
| Started | 115 | 116 |
| Intention to Treat (ITT) Population | 115 | 116 |
| Safety Population | 112 | 114 |
| Completed | 74 | 80 |
| Not completed | 41 | 36 |
| Voluntary withdrawal by patient or representative | 8 | 4 |
| Adverse event, non-fatal | 2 | 3 |
| Death | 14 | 8 |
| Investigator decision | - | 1 |
| Patient had liver transplant | 7 | 4 |
| Lost to follow-up | 2 | 2 |
| Reason not specified | 7 | 14 |
| Missing | 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Patients receive matching placebo via continuous IV infusion for up to 5 days, in addition to standard of care (SOC) | |
| Reporting group title | OCR-002 |
| Reporting group description: | |
| Patients receive ornithine phenylacetate by continuous IV infusion for up to 5 days in addition to SOC | |

| Reporting group values | Placebo | OCR-002 | Total |
|---|---|---|---|
| Number of subjects | 115 | 116 | 231 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 81 | 79 | 160 |
| From 65-84 years | 34 | 37 | 71 |
| Age continuous | | | |
| The aggregate mean and standard deviation of patient age (in years) is reported for the Intent to Treat (ITT) population. | | | |
| Units: years | | | |
| arithmetic mean | 60 | 50 | |
| standard deviation | ± 9.5 | ± 9.8 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 37 | 44 | 81 |
| Male | 78 | 72 | 150 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Patients receive matching placebo via continuous IV infusion for up to 5 days, in addition to standard of care (SOC) | |
| Reporting group title | OCR-002 |
| Reporting group description: | |
| Patients receive ornithine phenylacetate by continuous IV infusion for up to 5 days in addition to SOC | |

### Primary: Percentage of Participants in each HE Stage

| | |
|---|---|
| End point title | Percentage of Participants in each HE Stage[1] |
| End point description: | |
| To support the primary endpoint of confirmed clinical response, the investigator rated patients twice daily to determine the percentage of patients in each HE stage on a 4-point scale (from 4=coma to 0/1=no disorientation), where a lower score is better.<br><br>Percentages less than 1 are entered as 0 due to database constraints.<br>Not all patients were assessed at all post-baseline time points. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline to End of Study (at 3 hours Post End-of-Infusion or Early Hospital Discharge or Early Termination) | |
| 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.<br>Justification: No statistical analyses were performed to arrive at these summary aggregate data values. | |

| End point values | Placebo | OCR-002 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 115[2] | 116[3] | | |
| Units: percentage of patients | | | | |
| number (not applicable) | | | | |
| Baseline, Stage 4 | 10 | 5 | | |
| Baseline, Stage 3 | 26 | 34 | | |
| Baseline, Stage 2 | 62 | 59 | | |
| Baseline, Stage 0/1 | 0 | 0 | | |
| Baseline, Missing | 3 | 2 | | |
| Day 1- 7 am, Stage 4 | 0 | 0 | | |
| Day 1- 7 am, Stage 3 | 0 | 3 | | |
| Day 1- 7 am, Stage 2 | 2 | 3 | | |
| Day 1- 7 am, Stage 0/1 | 0 | 0 | | |
| Day 1- 7 am, Missing | 0 | 0 | | |
| Day 1- 5 pm, Stage 4 | 0 | 5 | | |
| Day 1- 5 pm, Stage 3 | 7 | 14 | | |
| Day 1- 5 pm, Stage 2 | 32 | 36 | | |
| Day 1- 5 pm, Stage 0/1 | 0 | 1 | | |
| Day 1- 5 pm, Missing | 0 | 0 | | |
| Day 2- 7 am, Stage 4 | 3 | 4 | | |

| | | | | |
|---|---|---|---|---|
| Day 2 - 7 am, Stage 3 | 21 | 15 | | |
| Day 2 - 7 am, Stage 2 | 61 | 69 | | |
| Day 2 - 7 am, Stage 0/1 | 10 | 10 | | |
| Day 2 - 7 am, Missing | 0 | 0 | | |
| Day 2 - 5 pm, Stage 4 | 3 | 4 | | |
| Day 2 - 5 pm, Stage 3 | 14 | 9 | | |
| Day 2 - 5 pm, Stage 2 | 57 | 61 | | |
| Day 2 - 5 pm, Stage 0/1 | 16 | 16 | | |
| Day 2 - 5 pm, Missing | 0 | 0 | | |
| Day 3 - 7 am, Stage 4 | 3 | 2 | | |
| Day 3 - 7 am, Stage 3 | 15 | 10 | | |
| Day 3 - 7 am, Stage 2 | 50 | 55 | | |
| Day 3 - 7 am, Stage 0/1 | 21 | 25 | | |
| Day 3 - 7 am, Missing | 0 | 0 | | |
| Day 3 - 5 pm, Stage 4 | 3 | 3 | | |
| Day 3 - 5 pm, Stage 3 | 7 | 9 | | |
| Day 3 - 5 pm, Stage 2 | 46 | 45 | | |
| Day 3 - 5 pm, Stage 0/1 | 20 | 27 | | |
| Day 3 - 5 pm, Missing | 0 | 0 | | |
| Day 4 - 7 am, Stage 4 | 2 | 0 | | |
| Day 4 - 7 am, Stage 3 | 5 | 9 | | |
| Day 4 - 7 am, Stage 2 | 42 | 40 | | |
| Day 4 - 7 am, Stage 0/1 | 28 | 30 | | |
| Day 4 - 7 am, Missing | 0 | 0 | | |
| Day 4 - 5 pm, Stage 4 | 2 | 0 | | |
| Day 4 - 5 pm, Stage 3 | 7 | 7 | | |
| Day 4 - 5 pm, Stage 2 | 29 | 34 | | |
| Day 4 - 5 pm, Stage 0/1 | 25 | 28 | | |
| Day 4 - 5 pm, Missing | 0 | 0 | | |
| Day 5 - 7 am, Stage 4 | 0 | 0 | | |
| Day 5 - 7 am, Stage 3 | 9 | 7 | | |
| Day 5 - 7 am, Stage 2 | 29 | 28 | | |
| Day 5 - 7 am, Stage 0/1 | 23 | 32 | | |
| Day 5 - 7 am, Missing | 0 | 0 | | |
| Day 5 - 5 pm, Stage 4 | 0 | 0 | | |
| Day 5 - 5 pm, Stage 3 | 8 | 3 | | |
| Day 5 - 5 pm, Stage 2 | 24 | 22 | | |
| Day 5 - 5 pm, Stage 0/1 | 23 | 28 | | |
| Day 5 - 5 pm, Missing | 0 | 0 | | |
| Day 6 - 7 am, Stage 4 | 0 | 0 | | |
| Day 6 - 7 am, Stage 3 | 10 | 3 | | |
| Day 6 - 7 am, Stage 2 | 21 | 24 | | |
| Day 6 - 7 am, Stage 0/1 | 23 | 27 | | |
| Day 6 - 7 am, Missing | 0 | 0 | | |
| Day 6 - 5 pm, Stage 4 | 0 | 0 | | |
| Day 6 - 5 pm, Stage 3 | 3 | 3 | | |
| Day 6 - 5 pm, Stage 2 | 5 | 7 | | |
| Day 6 - 5 pm, Stage 0/1 | 6 | 5 | | |
| Day 6 - 5 pm, Missing | 0 | 0 | | |
| End of Study, Stage 4 | 5 | 3 | | |
| End of Study, Stage 3 | 10 | 7 | | |
| End of Study, Stage 2 | 31 | 28 | | |

| | | | | |
|---|---|---|---|---|
| End of Study, Stage 0/1 | 45 | 55 | | |
| End of Study, Missing | 0 | 0 | | |

Notes:

[2] - ITT patients with data at the given time point - patients did not all start at the same time

[3] - ITT patients with data at the given time point - patients did not all start at the same time

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| 20 days | |
| Adverse event reporting additional description: | |
| Adverse events are reported in the safety population | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 14.1 |

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Matching placebo up to 5 days continuous IV infusion in addition to standard of care (SOC) | |
| Reporting group title | OCR-002 |
| Reporting group description: | |
| Continuous intravenous infusion of ornithine phenylacetate for up to 5 days on top of standard of care at dose levels predicated on level of hepatic decompensation | |

| Serious adverse events | Placebo | OCR-002 | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 34 / 112 (30.36%) | 29 / 114 (25.44%) | |
| number of deaths (all causes) | 15 | 11 | |
| number of deaths resulting from adverse events | 15 | 11 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Hepatocellular carcinoma | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multi-organ failure | | | |
| subjects affected / exposed | 4 / 112 (3.57%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 1 / 4 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Pelvic haemorrhage | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 2 / 112 (1.79%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hepatic hydrothorax | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Respiratory distress | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |

| | | | |
|---|---|---|---|
| Nervous system disorders | | | |
| Encephalopathy | | | |
| subjects affected / exposed | 2 / 112 (1.79%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 9 / 112 (8.04%) | 9 / 114 (7.89%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Intracranial pressure increased | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thalamus haemorrhage | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Ascites | | | |
| subjects affected / exposed | 2 / 112 (1.79%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 112 (0.89%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Localised intraabdominal fluid collection | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Chronic hepatic failure | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 2 / 114 (1.75%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hepatic failure | | | |
| subjects affected / exposed | 2 / 112 (1.79%) | 2 / 114 (1.75%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 2 | |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Renal and urinary disorders | | | |
| Anuria | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Renal failure | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure acute | | | |
| subjects affected / exposed | 3 / 112 (2.68%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Infections and infestations** | | | |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lobar pneumonia | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis bacterial | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 3 / 114 (2.63%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 2 / 112 (1.79%) | 2 / 114 (1.75%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 1 / 114 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| **Metabolism and nutrition disorders** | | | |

| | | | |
|---|---|---|---|
| Hypovolaemia | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 114 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Placebo | OCR-002 | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 31 / 112 (27.68%) | 30 / 114 (26.32%) | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 8 / 112 (7.14%) | 13 / 114 (11.40%) | |
| occurrences (all) | 11 | 14 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 112 (6.25%) | 6 / 114 (5.26%) | |
| occurrences (all) | 7 | 6 | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 4 / 112 (3.57%) | 8 / 114 (7.02%) | |
| occurrences (all) | 4 | 8 | |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 8 / 112 (7.14%) | 9 / 114 (7.89%) | |
| occurrences (all) | 10 | 9 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 9 / 112 (8.04%) | 5 / 114 (4.39%) | |
| occurrences (all) | 9 | 5 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 25 February 2014 | The protocol was updated to facilitate participation of countries outside of North America and to improve recruitment rates. |
| 19 March 2014 | The protocol was modified to optimize the dosing paradigm. |
| 24 October 2014 | The protocol was updated to improve recruitment rate. |
| 01 July 2015 | The protocol was updated to incorporate recommendations from the Independent Data Monitoring Committee (IDMC). |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported