



Clinical trial results:

A Phase-2 open label study to assess the pharmacodynamic and pharmacokinetic properties of a single subcutaneous injection of RUC-4 in patients with ST-elevation myocardial infarction presenting to cardiac catheterization lab with planned primary coronary angioplasty

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2019-004282-41 |
| Trial protocol | NL |
| Global end of trial date | 04 November 2020 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 29 March 2022 |
| First version publication date | 29 March 2022 |
| Summary attachment (see zip file) | CEL-02 Summary Results 28May2021 (M2. CEL-02 CSR Synopsis 28May2021.pdf) |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | CEL-02 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04284995 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | CeleCor Therapeutics, Inc. |
| Sponsor organisation address | 1155 Camino Del Mar Suite 481, Del Mar, United States, CA 92014 |
| Public contact | S. Postma, Diagram BV, 0031 38426 2999, s.postma@diagram-zwolle.nl |
| Scientific contact | S. Postma, Diagram BV, 0031 38426 2999, s.postma@diagram-zwolle.nl |

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 | 28 May 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 04 November 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 November 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To assess the PD properties of a single subcutaneous injection of RUC-4 in STEMI patients presenting to the CCL with the aim to perform primary coronary angioplasty.
- To assess the PK properties of a single subcutaneous injection of RUC-4 in STEMI patients presenting to the CCL with the aim to perform primary coronary angioplasty.
- To assess safety and tolerability of RUC-4

Protection of trial subjects:

At the end of each cohort, the SRC (Safety Review Committee) has received an interim analysis of the safety, laboratory, and PK/PD data. After reviewing the interim analysis, the SRC has provided written recommendation to the PI whether to proceed with the same dose, or escalate to a higher dose or lower the dose to be studied in the next cohort.

Background therapy:

The use of aspirin or an oral P2Y12 antagonist before catheterization is allowed, but not mandated. Heparin is also allowed, as these medications are standard of care for STEMI patients. If heparin was administered pre-hospital, an activated clotting time (ACT) measurement should be performed at the CCL. If the ACT is <200 seconds, additional heparin is recommended.

There are no particular prohibitions and restrictions in this study.

Regular standard of care is performed from the provision of informed consent through the last study mandated patient visit.

Evidence for comparator:

N/A; no comparator used in this trial.

| | |
|---|--------------|
| Actual start date of recruitment | 03 June 2020 |
| 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: 27 |
| Worldwide total number of subjects | 27 |
| EEA total number of subjects | 27 |

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) | 16 |
| From 65 to 84 years | 10 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted in subjects with documented STEMI with onset of the cardiac ischemic symptoms within 6 hr before enrollment who are planned for primary PCI. Evaluation for eligibility performed in the CCL and witnessed verbal ICF was obtained. Before hospital discharge written ICF was obtained

Pre-assignment

Screening details:

Screening period: 03Jun - 07Oct2020.

73 patients screened, 27 patients enrolled.

Main reasons not enrolled:

- Eligibility criteria not met (20)
- Patient admitted outside business hours (14)

Period 1

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

Blinding implementation details:

N/A

Arms

| | |
|------------------------------|----------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cohort 1 |

Arm description:

All patients received a single SC dose of RUC-4 of 0.075 mg/kg.

| | |
|--|--------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | RUC-4 |
| Investigational medicinal product code | 140962 |
| Other name | |
| Pharmaceutical forms | Solution for injection in vial |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of RUC-4 of 0.075 mg/kg.

| | |
|------------------|----------|
| Arm title | Cohort 2 |
|------------------|----------|

Arm description:

All patients received a single SC dose of RUC-4 of 0.090 mg/kg.

| | |
|--|--------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | RUC-4 |
| Investigational medicinal product code | 140962 |
| Other name | |
| Pharmaceutical forms | Solution for injection in vial |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of RUC-4 of 0.090 mg/kg.

| | |
|------------------|----------|
| Arm title | Cohort 3 |
|------------------|----------|

Arm description:

All patients received a single SC dose of RUC-4 of 0.110 mg/kg.

| | |
|--|--------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | RUC-4 |
| Investigational medicinal product code | 140962 |
| Other name | |
| Pharmaceutical forms | Solution for injection in vial |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose of RUC-4 of 0.110 mg/kg.

| Number of subjects in period 1 | Cohort 1 | Cohort 2 | Cohort 3 |
|---------------------------------------|----------|----------|----------|
| Started | 8 | 9 | 10 |
| Completed | 8 | 9 | 9 |
| Not completed | 0 | 0 | 1 |
| Consent withdrawn by subject | - | - | 1 |

Baseline characteristics

Reporting groups

| | |
|---|----------|
| Reporting group title | Cohort 1 |
| Reporting group description: | |
| All patients received a single SC dose of RUC-4 of 0.075 mg/kg. | |
| Reporting group title | Cohort 2 |
| Reporting group description: | |
| All patients received a single SC dose of RUC-4 of 0.090 mg/kg. | |
| Reporting group title | Cohort 3 |
| Reporting group description: | |
| All patients received a single SC dose of RUC-4 of 0.110 mg/kg. | |

| Reporting group values | Cohort 1 | Cohort 2 | Cohort 3 |
|------------------------|----------|----------|----------|
| Number of subjects | 8 | 9 | 10 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 5 | 6 | 5 |
| From 65-84 years | 3 | 2 | 5 |
| 85 years and over | 0 | 1 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 59 | 63 | 62.60 |
| standard deviation | ± 12.51 | ± 13.84 | ± 13.09 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 2 | 2 | 3 |
| Male | 6 | 7 | 7 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 27 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 16 | | |
| From 65-84 years | 10 | | |
| 85 years and over | 1 | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 7 | | |
| Male | 20 | | |

Subject analysis sets

| | |
|----------------------------|-------------------|
| Subject analysis set title | Safety Population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

The Safety population included all enrolled subjects who received a SC dose of RUC-4.

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | PK Population |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

The PK Analysis Set included all subjects who receive a SC dose of RUC-4 and who had evaluable PK data.

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | PD Population |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

The PD Analysis Set included all subjects who receive a SC dose of RUC-4 and who had evaluable PD data.

| Reporting group values | Safety Population | PK Population | PD Population |
|---------------------------------------|-------------------|---------------|---------------|
| Number of subjects | 27 | 26 | 24 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 16 | 15 | 14 |
| From 65-84 years | 10 | 10 | 9 |
| 85 years and over | 1 | 1 | 1 |
| Age continuous Units: years | | | |
| arithmetic mean | 61.67 | 62.07 | 61.79 |
| standard deviation | ± 12.79 | ± 12.86 | ± 13.36 |
| Gender categorical Units: Subjects | | | |
| Female | 7 | 7 | 6 |
| Male | 20 | 19 | 18 |

End points

End points reporting groups

| | |
|--|-----------------------------|
| Reporting group title | Cohort 1 |
| Reporting group description: All patients received a single SC dose of RUC-4 of 0.075 mg/kg. | |
| Reporting group title | Cohort 2 |
| Reporting group description: All patients received a single SC dose of RUC-4 of 0.090 mg/kg. | |
| Reporting group title | Cohort 3 |
| Reporting group description: All patients received a single SC dose of RUC-4 of 0.110 mg/kg. | |
| Subject analysis set title | Safety Population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: The Safety population included all enrolled subjects who received a SC dose of RUC-4. | |
| Subject analysis set title | PK Population |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: The PK Analysis Set included all subjects who receive a SC dose of RUC-4 and who had evaluable PK data. | |
| Subject analysis set title | PD Population |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: The PD Analysis Set included all subjects who receive a SC dose of RUC-4 and who had evaluable PD data. | |

Primary: Inhibition of TRAP-induced platelet aggregation 15 min post dose

| | |
|---|---|
| End point title | Inhibition of TRAP-induced platelet aggregation 15 min post dose ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: At 15 minutes after administration of RUC-4 | |

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: No statistical analysis was performed for this endpoint. All statistical summaries were descriptive in nature. No hypothesis testing was planned for primary and secondary analyses.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PD Population |
|--------------------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 8 | 8 | 24 |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | 77.48 (± 9.06) | 87.46 (± 6.52) | 91.70 (± 7.66) | 85.54 (± 9.64) |

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic Parameter area under the curve from time zero to time of last quantifiable concentration [AUC0-last]

| | |
|-----------------|---|
| End point title | Pharmacokinetic Parameter area under the curve from time zero to time of last quantifiable concentration [AUC0-last] ^[2] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

PK parameters will be determined from blood concentrations at baseline (before study drug administration), 15, 45, 90, 120 and 180 minutes after administration of a single SC injection of RUC-4

Notes:

[2] - 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: No statistical analysis was performed for this endpoint. All statistical summaries were descriptive in nature. No hypothesis testing was planned for primary and secondary analyses.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PK Population |
|---|-----------------|------------------|------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 9 | 9 | 26 |
| Units: h*ng/ml | | | | |
| geometric mean (geometric coefficient of variation) | 93.39 (± 25.61) | 126.20 (± 66.12) | 117.74 (± 29.37) | 112.30 (± 43.99) |

Statistical analyses

No statistical analyses for this end point

Primary: Inhibition of TRAP-induced platelet aggregation 120 min post dose

| | |
|-----------------|--|
| End point title | Inhibition of TRAP-induced platelet aggregation 120 min post dose ^[3] |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

120 minutes post dose

Notes:

[3] - 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: No statistical analysis was performed for this endpoint. All statistical summaries were descriptive in nature. No hypothesis testing was planned for primary and secondary analyses.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PD Population |
|--------------------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 8 | 8 | 24 |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | 33.59 (± 8.33) | 44.46 (± 30.85) | 46.18 (± 7.52) | 41.41 (± 18.99) |

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic Parameter Observed maximum blood concentration (C_{max})

| | |
|-----------------|---|
| End point title | Pharmacokinetic Parameter Observed maximum blood concentration (C _{max}) ^[4] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

PK parameters will be determined from blood concentrations at baseline (before study drug administration), 15, 45, 90, 120 and 180 minutes after administration of a single SC injection of RUC-4

Notes:

[4] - 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: No statistical analysis was performed for this endpoint. All statistical summaries were descriptive in nature. No hypothesis testing was planned for primary and secondary analyses.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PK Population |
|---|-----------------|------------------|------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 9 | 9 | 26 |
| Units: ng/ml | | | | |
| geometric mean (geometric coefficient of variation) | 93.63 (± 27.70) | 131.04 (± 55.30) | 133.02 (± 21.24) | 118.78 (± 39.70) |

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic Parameter area under the curve from time zero extrapolated to infinite time[AUC_{0-inf}]

| | |
|-----------------|---|
| End point title | Pharmacokinetic Parameter area under the curve from time zero extrapolated to infinite time[AUC _{0-inf}] ^[5] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

PK parameters will be determined from blood concentrations at baseline (before study drug administration), 15, 45, 90, 120 and 180 minutes after administration of a single SC injection of RUC-4

Notes:

[5] - 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: No statistical analysis was performed for this endpoint. All statistical summaries were descriptive in nature. No hypothesis testing was planned for primary and secondary analyses.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PK Population |
|---|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 9 | 9 | 26 |
| Units: h*ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 106.27 (\pm 20.67) | 136.85 (\pm 61.77) | 139.28 (\pm 31.51) | 127.38 (\pm 41.75) |

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic Parameter Observed last blood concentration (Clast)

| | |
|-----------------|--|
| End point title | Pharmacokinetic Parameter Observed last blood concentration (Clast) ^[6] |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

PK parameters will be determined from blood concentrations at baseline (before study drug administration), 15, 45, 90, 120 and 180 minutes after administration of a single SC injection of RUC-4

Notes:

[6] - 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: No statistical analysis was performed for this endpoint. All statistical summaries were descriptive in nature. No hypothesis testing was planned for primary and secondary analyses.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PK Population |
|---|---------------------|---------------------|----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 9 | 9 | 26 |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 8.09 (\pm 31.70) | 9.28 (\pm 22.88) | 11.12 (\pm 42.75) | 9.47 (\pm 34.78) |

Statistical analyses

No statistical analyses for this end point

Primary: Inhibition of TRAP + PAR-4 induced platelet aggregation 15 min post dose

| | |
|-----------------|---|
| End point title | Inhibition of TRAP + PAR-4 induced platelet aggregation 15 min post dose ^[7] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

At 15 minutes after administration of RUC-4

Notes:

[7] - 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: No statistical analysis was performed for this endpoint. All statistical summaries were

descriptive in nature. No hypothesis testing was planned for primary and secondary analyses.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PD Population |
|--------------------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 8 | 8 | 24 |
| Units: percentage | | | | |
| arithmetic mean (standard deviation) | 86.03 (± 8.07) | 92.75 (± 3.71) | 93.04 (± 5.28) | 90.61 (± 6.59) |

Statistical analyses

No statistical analyses for this end point

Primary: Inhibition of TRAP + PAR-4 induced platelet aggregation 120 min post dose

| | |
|-----------------|--|
| End point title | Inhibition of TRAP + PAR-4 induced platelet aggregation 120 min post dose ^[8] |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

At 120 minutes after administration of RUC-4

Notes:

[8] - 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: No statistical analysis was performed for this endpoint. All statistical summaries were descriptive in nature. No hypothesis testing was planned for primary and secondary analyses.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PD Population |
|--------------------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 8 | 8 | 8 |
| Units: percentage | | | | |
| arithmetic mean (standard deviation) | 20.43 (± 16.38) | 33.61 (± 37.43) | 34.10 (± 16.23) | 29.38 (± 25.10) |

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of subjects that showed persistence, >= 50% inhibition TRAP induced platelet aggregation

| | |
|-----------------|--|
| End point title | Proportion of subjects that showed persistence, >= 50% inhibition TRAP induced platelet aggregation ^[9] |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:
120 minutes post dose

Notes:

[9] - 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: No statistical analysis was performed for this endpoint. All statistical summaries were descriptive in nature. No hypothesis testing was planned for primary and secondary analyses.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PD Population |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 8 | 8 | 24 |
| Units: number | | | | |
| >= 50% | 0 | 2 | 4 | 6 |

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of subjects that showed persistence, >= 50% inhibition TRAP + PAR-4 induced platelet aggregation

| | |
|-----------------|---|
| End point title | Proportion of subjects that showed persistence, >= 50% inhibition TRAP + PAR-4 induced platelet aggregation ^[10] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:
120 minutes post dose

Notes:

[10] - 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: No statistical analysis was performed for this endpoint. All statistical summaries were descriptive in nature. No hypothesis testing was planned for primary and secondary analyses.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PD Population |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 8 | 8 | 24 |
| Units: number | | | | |
| >= 50% | 0 | 2 | 1 | 3 |

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of subjects that showed >= 77% inhibition TRAP induced platelet aggregation

| | |
|-----------------|--|
| End point title | Proportion of subjects that showed >= 77% inhibition TRAP induced platelet aggregation ^[11] |
|-----------------|--|

End point description:

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: | |
| 15 minutes post dose | |
| Notes: | |
| [11] - 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: No statistical analysis was performed for this endpoint. All statistical summaries were descriptive in nature. No hypothesis testing was planned for primary and secondary analyses. | |

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PD Population |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 8 | 8 | 24 |
| Units: number | | | | |
| >= 77% | 3 | 7 | 7 | 17 |

Statistical analyses

No statistical analyses for this end point

Primary: Proportion of subjects that showed >= 77% inhibition TRAP + PAR-4 induced platelet aggregation

| | |
|-----------------|--|
| End point title | Proportion of subjects that showed >= 77% inhibition TRAP + PAR-4 induced platelet aggregation ^[12] |
|-----------------|--|

End point description:

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| 15 minutes post dose | |

Notes:

[12] - 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: No statistical analysis was performed for this endpoint

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | PD Population |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 8 | 8 | 24 |
| Units: number | | | | |
| >= 77% | 7 | 8 | 8 | 23 |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Injection Site Reaction

| | |
|-------------------------------------|-------------------------|
| End point title | Injection Site Reaction |
| End point description: | |
| Safety and tolerability parameters. | |
| End point type | Other pre-specified |

End point timeframe:

At baseline, hospital discharge, 15 days Follow-UP and 30 days Follow-Up.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Safety Population |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 8 | 9 | 10 | 27 |
| Units: number | 0 | 1 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected beginning after witnessed verbal IC is obtained till end of study, i.e. 30 days after study treatment.

Adverse event reporting additional description:

All (S)AEs reported spontaneously by the patient or observed by the investigator or his staff were recorded.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | Cohort 1 |
|-----------------------|----------|

Reporting group description:

All patients received a single SC dose of RUC-4 of 0.075 mg/kg.

| | |
|-----------------------|----------|
| Reporting group title | Cohort 2 |
|-----------------------|----------|

Reporting group description:

All patients received a single SC dose of RUC-4 of 0.090 mg/kg.

| | |
|-----------------------|----------|
| Reporting group title | Cohort 3 |
|-----------------------|----------|

Reporting group description:

All patients received a single SC dose of RUC-4 of 0.110 mg/kg.

| Serious adverse events | Cohort 1 | Cohort 2 | Cohort 3 |
|---|----------------|----------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 2 / 9 (22.22%) | 4 / 10 (40.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 9 (11.11%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Vascular access site haematoma | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 9 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |

| | | | |
|---|----------------|----------------|-----------------|
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 9 (11.11%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 9 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 9 (11.11%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 9 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 9 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 9 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 9 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 4 %

| Non-serious adverse events | Cohort 1 | Cohort 2 | Cohort 3 |
|--|--|--|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 8 / 8 (100.00%) | 7 / 9 (77.78%) | 8 / 10 (80.00%) |
| Injury, poisoning and procedural complications Vascular access site complication subjects affected / exposed occurrences (all) | 3 / 8 (37.50%) 1 | 0 / 9 (0.00%) 1 | 3 / 10 (30.00%) 1 |
| Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 1 / 9 (11.11%) 1 | 1 / 10 (10.00%) 1 |
| General disorders and administration site conditions Injection site bruising subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) | 3 / 8 (37.50%) 1 2 / 8 (25.00%) 2 | 4 / 9 (44.44%) 1 1 / 9 (11.11%) 1 | 4 / 10 (40.00%) 1 0 / 10 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 2 / 9 (22.22%) 2 | 0 / 10 (0.00%) 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 30 April 2020 | <ul style="list-style-type: none">- Additional PD measurement at 240 minutes if the dose of the study drug is increased (cohort 2 and/or 3)- Add exclusion criteria regarding COVID-19 infection- Definition of causal relationships with study drug and PCI procedure has been added- As the impact of STEMI on RUC-4 PK and PD in patients is not known, study CEL-02 is designed to assess PD and PK properties of the weight-adjusted dose of RUC-4 (mg/kg) required to achieve 77% or greater inhibition of TRAP-induced platelet aggregation (amendment: 77% instead of 90%). |
| 10 September 2020 | <ul style="list-style-type: none">-Additional heparin administration if ACT is <200 seconds instead of <250 seconds. The ACT cutoff value for administration of an additional dose of heparin is lowered to <200 instead of below <250 seconds, according to standard treatment guidelines to reduce heparin administration when using an αIIbβ3 inhibitor-Adapt exclusion criteria regarding COVID-19 infection. Instead of suspicion for COVID-19 infection it is preferred to only exclude confirmed COVID-19 infection. There were a number of exclusions based on this criterion of suspected infection, whereas afterwards these patients appeared not to be infected and could have participated in the trial.-Adapt inclusion criteria regarding persistent vs ongoing ST elevation. Has been adapted to include subjects with resolved ST elevation as well, as for the response to the study drug it does not matter whether ST elevation is persistent or has been resolved.-Remove exclusion criterium regarding de novo AF. De novo AF has been removed, as this criterion was included in order to exclude type 2 myocardial infarction, which is already an exclusion criterion (no. 2), therefore this criterion is redundant.-VerifyNow measurement now includes additional BASE channel; P2Y12 Test cartridges instead of PRU. This channel identifies the percentage inhibition directly related to the study drug, while filtering the inhibitory effects from the P2Y12 blocker ticagrelor. |

Notes:

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.

N/A.

Notes: