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

Published: 09-12-2019
Last updated: 10-04-2024

The main objective:- 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 primarycoronary angioplasty.- To assess the PK properties of a single subcutaneous injection...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Myocardial disorders
Study type	Interventional

Summary

ID

NL-OMON49794

Source
ToetsingOnline

Brief title
CEL-02

Condition

- Myocardial disorders

Synonym
heart attack, ST-elevation myocardial infarction

Research involving
Human

Sponsors and support

Primary sponsor: CeleCor Therapeutics, Inc.
Source(s) of monetary or material Support: Celecor Therpeutics;Inc (sponsor/verrichter van het onderzoek)

Intervention

Keyword: pharmacodynamics, pharmacokinetics, platelet inhibitor, ST-elevation myocardial infarction

Outcome measures

Primary outcome

- Inhibition of TRAP-induced platelet aggregation (%) assessed by VerifyNow at

baseline, and at 15, 45, 60, 90, 120, 180 and 240 minutes after administration

of RUC-4 (the 240 minute time point is only applicable if the RUC-4 dose is

increased in cohort 2 and/or 3)

- RUC-4 concentration (ng/mL) versus time profiles (at baseline and at 15, 45,

90, 120 and 180 minutes after administration of RUC 4) and associated PK

parameters

- Safety and tolerability parameters at baseline and at hospital discharge

Secondary outcome

- Platelet count (µL) at baseline, and at 15, 45, 90, 120 and 180 minutes after

administration of RUC-4 and at hospital discharge

- Bleeding events (according to BARC II, III and V criteria for safety

assessment and according to ISTH Major and TIMI Major for information only) at

baseline, discharge and at 15-day and at 30-day follow-up

- Intraprocedural thrombosis (assessed by PI)

- Injection site reactions at baseline, 1-hour post-PCI, hospital discharge,

and at 15-day and at 30-day follow-up

- Inhibition of ADP-induced platelet aggregation (%) assessed by VerifyNow at

baseline, and at 15, 45, 60, 90, 120, 180 and 240 minutes after administration

of RUC-4 (the 240 minute time point is only applicable if the RUC-4 dose is

increased in cohort 2 and/or 3)

- Differences in PD or PK among the patients (gender, weight, BMI, age)

Study description

Background summary

The use of αIIbβ3 antagonists has been validated as an effective therapy of MI for patients undergoing percutaneous coronary interventions (PCI). Treatment with one of the three currently available agents (abciximab, tirofiban, eptifibatide) has been shown to result in an approximately 20% reduction in mortality and an approximately 33% reduction in death or reinfarction at 30 days after treatment. Early treatment of MI with αIIbβ3 antagonists at first medical contact (i.e., by Emergency Medical System [EMS] personnel or personnel in emergency departments of either *spoke* hospitals or PCI-capable hospitals) compared to catheterization lab treatment has been associated with increased pre-procedure blood flow in the target coronary artery using the Thrombolysis in Myocardial Infarction (TIMI) scale and indices of myocardial perfusion, smaller infarcts, fewer early and late complications of MI, and reduced mortality. The improvement in outcome correlates with the time at which the drugs were administered after the onset of symptoms.

Despite these data, αIIbβ3 antagonists are not routinely administered at first medical contact, in part because they require intravenous (IV) administration of a bolus dose followed by a continuous infusion regulated by an infusion pump. In addition, all of the agents are associated with thrombocytopenia in a small percentage of patients (0.5%-2%), with abciximab associated with the highest frequency.

RUC-4 is being developed to facilitate pre-hospital and emergency department therapy at the earliest time point, thus maximizing the chance of preserving the cardiac muscle. RUC-4 is differentiated from current αIIbβ3 antagonists because it is based on newer information on the receptor structure and is specifically designed to facilitate early administration. RUC-4 inhibits ligand binding to αIIbβ3 by binding to both the αIIb and β3 subunits and displacing the Mg2+ metal from the ion-dependent adhesion site (MIDAS) required for ligand binding; this locks the β3 subunit of the receptor in its inactive conformation. This may decrease the likelihood of developing thrombocytopenia because data indicate that much of the thrombocytopenia caused by the current αIIbβ3 antagonists is due to the presence of antibodies to conformations of the receptor induced by the binding of the drugs.

Study objective

The main objective:
- 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

Secundary objectives:
- To assess platelet count at select time points before and after RUC-4 administration
- To assess bleeding events* of a single SC injection of RUC-4 at select timepoints after RUC-4 administration, at discharge and at 15-day and at 30-day follow-up
- To assess intraprocedural thrombosis
- To assess the injection site reactions of a single subcutaneous injection of RUC-4 at select timepoints after RUC-4 administration and at 15-day and at 30 day follow-up
- To evaluate any differences in PD or PK within each treatment group (gender, weight, BMI, age)

* According to the BARC (II, III and V), ISTH Major and TIMI Major criteria

Study design

This is an open-label, phase 2 single center study.
The anticipated study duration is 18-20 weeks including 1-month follow-up from last patient in; with 14-16 weeks enrollment period including up to two interim analyses for review of data by the SRC (Safety Review Committee) at the completion of each dose cohort before a dose-escalation. The interim analyses

can be performed without the 30-day follow-up data.
The decision to escalate to a higher (or lower, or maintain the same) dose level will be based on review of the interim analysis by the SRC.
The duration of participation for each patient will be 1 month (± 7 days) including enrollment into study, dosing and 30-day post RUC-4 administration follow-up.

Intervention

A single subcutaneous injection of RUC-4.
3 cohorts:
Initial dose / First Cohort: 0.075 mg/kg.
Second and third Cohort: Decrease dose, increase dose (up to 0.015 mg/kg) or maintain dose.

Study burden and risks

Burden:
7 or 8 x blood sample collection for which 2 to 4 x intravenous injections.

Risks and inconveniences:
- The following side effects of RUC-4 are known:
- the occurrence of skin irritations at the injection site of RUC-4
- the occurrence of small bleeding events, limited to the injection site of RUC-4
- The following research tests may involve the following risks/conveniences:
- Blood sampling: Local pain and/or bruising.

Contacts

Public
CeleCor Therapeutics, Inc.

Merryfield Row 3210
San Diego CA 92121
US
Scientific
CeleCor Therapeutics, Inc.

Merryfield Row 3210
San Diego CA 92121
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Patients with STEMI, presenting with persistent chest pain (>30 min) and ongoing >= 1 mm ST-segment elevation in two adjacent ECG-leads, with > 6 mm cumulative ST-segment deviation, in whom the total duration of symptom to first intracoronary device deployment (excluding a wire) is anticipated to be within 6 hours
- Adult males and females 18 years of age or older
- Females must be non-pregnant, non-lactating, and of non-childbearing potential (postmenopausal or surgically sterilized)
- Weight (by history) of between 52 and 120 kg
- Written informed consent (following short-form of the informed consent form at CCL)

Exclusion criteria

- High probability in the opinion of the cardiologist that current STEMI is caused by stent thrombosis and the previous PCI related to this stent thrombosis is < 1 month
- High suspicion of COVID-19 infection (known exposure, hypoxia, fever, cough)
- High suspicion of type II MI
- Out of hospital cardiac arrest (OHCA)
- Therapy resistant cardiogenic shock (systolic blood pressure <= 80 mm Hg for > 30 minutes)
- Persistent severe hypertension (systolic blood pressure > 180 mm Hg or diastolic blood pressure > 110 mm Hg)
- Presentation with atrial fibrillation de novo
- Known severe liver disease
- Known history of severe renal dysfunction (glomerular filtration rate < 30

mL/min or serum creatinine > 200 mmol/L [> 2.5 mg/dL])
- Known left bundle branch block
- Requirement of oral anticoagulation (Vitamin K antagonists {VKA} or direct oral antagonists {DOACs})
- Chronic use of P2Y12 antagonists
- Current treatment with αIIbβ3 receptor antagonist (other than RUC-4)
- Coagulation abnormality, known bleeding disorder, or history of documented prior hemorrhagic or thrombotic stroke < 6 months
- History of upper or lower GI bleeding within the past 6 months
- Known clinically important anemia
- Known clinically important thrombocytopenia (platelet count of less than 150,000/µL)
- Known history of allergy to any of the ingredients in the RUC-4 formulation (i.e., acetate buffer, sucrose)
- Major surgery within the past 6 months
- Life expectancy of less than 6 months
- Any clinically significant abnormality identified prior to enrollment that in the judgment of the Investigator would preclude safe completion of the study
- Unwillingness or inability to comply with the requirements of this protocol including the presence of any condition (physical, mental, or social) that is likely to affect the patient's ability to comply with the study protocol.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-06-2020
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	RUC-4
Generic name:	RUC-4

Ethics review

Approved WMO Date:	09-12-2019
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-02-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-04-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-05-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-05-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-09-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	10-09-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2019-004282-41-NL
ClinicalTrials.gov	NCT04284995
CCMO	NL72032.100.19