



Clinical trial results:

A randomized, comparative effectiveness study of complete versus culprit-only revascularization strategies to treat multi-vessel disease after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction

Summary

EudraCT number	2013-002210-12
Trial protocol	ES
Global end of trial date	07 June 2019

Results information

Result version number	v1 (current)
This version publication date	25 June 2022
First version publication date	25 June 2022

Trial information

Trial identification

Sponsor protocol code	COMPLETE-2013-05-01
-----------------------	---------------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01740479
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Population Health Research Institute
Sponsor organisation address	237 Barton Street East, Hamilton, Canada,
Public contact	COMPLETE Project Office, Population Health Research Institute, 1 9055274322 x40444, complete@phri.ca
Scientific contact	COMPLETE Project Office, Population Health Research Institute, 1 9055274322 x40444, complete@phri.ca

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	07 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 June 2019
Global end of trial reached?	Yes
Global end of trial date	07 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether, on a background of optimal medical therapy with low dose ASA and ticagrelor, a strategy of multi-vessel revascularization involving staged PCI using drug eluting stents of all suitable non-infarct related artery lesions is superior to a strategy of culprit lesion only revascularization in reducing the composite outcome of CV death or new MI in patients with multi-vessel disease who have undergone successful culprit lesion primary PCI for STEMI.

Protection of trial subjects:

Consent process: The study was verbally described in detail to the subject. The subjects were given time to review the informed consent form, ask questions, discuss with family, and consider participation before they enrolled into the study.

Measures were put in place to protect the personal health information of subjects: Access to medical records and study data were limited to authorized personnel only, access to electronic data was password protected and auditable, electronic data is stored on a network with firewalls and other security and back-up measures in place.

Background therapy:

Guideline-based medical therapy was recommended in both treatment groups. Dual antiplatelet therapy with aspirin and ticagrelor for at least 1 year was recommended. Beyond 1 year, aspirin was recommended for all patients, and ticagrelor (60 mg twice daily) was recommended for patients who were not at high risk for bleeding. High-dose statin therapy, angiotensin-converting-enzyme inhibitors or angiotensin-receptor blockers, mineralocorticoid-receptor antagonists, and beta-blockers were recommended.

Evidence for comparator: -

Actual start date of recruitment	01 February 2013
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	Spain: 265
Country: Number of subjects enrolled	Australia: 60
Country: Number of subjects enrolled	Austria: 36
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Brazil: 102
Country: Number of subjects enrolled	Canada: 1580
Country: Number of subjects enrolled	China: 89
Country: Number of subjects enrolled	Colombia: 3
Country: Number of subjects enrolled	Czechia: 39
Country: Number of subjects enrolled	Finland: 36

Country: Number of subjects enrolled	France: 119
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Greece: 75
Country: Number of subjects enrolled	Hungary: 42
Country: Number of subjects enrolled	Israel: 22
Country: Number of subjects enrolled	Italy: 272
Country: Number of subjects enrolled	Kuwait: 9
Country: Number of subjects enrolled	Lithuania: 21
Country: Number of subjects enrolled	Mexico: 18
Country: Number of subjects enrolled	North Macedonia: 108
Country: Number of subjects enrolled	Poland: 10
Country: Number of subjects enrolled	Portugal: 7
Country: Number of subjects enrolled	Romania: 5
Country: Number of subjects enrolled	Saudi Arabia: 24
Country: Number of subjects enrolled	Serbia: 83
Country: Number of subjects enrolled	South Africa: 28
Country: Number of subjects enrolled	Sweden: 40
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Tunisia: 19
Country: Number of subjects enrolled	United Kingdom: 713
Country: Number of subjects enrolled	United States: 180
Worldwide total number of subjects	4041
EEA total number of subjects	999

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)	2428
From 65 to 84 years	1546
85 years and over	67

Subject disposition

Recruitment

Recruitment details:

From February 1, 2013, through March 6, 2017, a total of 4041 patients from 140 centers in 31 countries were recruited and randomized.

Pre-assignment

Screening details:

Patients who presented to the hospital with STEMI were considered for inclusion in the trial if they could undergo randomization within 72 hours after successful culprit-lesion PCI.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Complete Revascularization

Arm description:

A strategy of complete revascularization (consisting of PCI of all suitable nonculprit lesions) in patients with STEMI and multivessel coronary artery disease who had undergone successful culprit-lesion PCI.

Arm type	standard treatment
Investigational medicinal product name	N/A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

Guideline-based medical therapy was recommended in both treatment groups. Dual antiplatelet therapy with aspirin and ticagrelor for at least 1 year was recommended. Beyond 1 year, aspirin was recommended for all patients, and ticagrelor (60 mg twice daily) was recommended for patients who were not at high risk for bleeding. High-dose statin therapy, angiotensin-converting-enzyme inhibitors or angiotensin-receptor blockers, mineralocorticoid-receptor antagonists, and beta-blockers were recommended.

Arm title	Culprit Lesion Only Revascularization
------------------	---------------------------------------

Arm description:

A strategy of no further revascularization in patients with STEMI and multivessel coronary artery disease who had undergone successful culprit-lesion PCI.

Arm type	standard treatment
Investigational medicinal product name	N/A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Not mentioned

Dosage and administration details:

Guideline-based medical therapy was recommended in both treatment groups. Dual antiplatelet therapy with aspirin and ticagrelor for at least 1 year was recommended. Beyond 1 year, aspirin was recommended for all patients, and ticagrelor (60 mg twice daily) was recommended for patients who were not at high risk for bleeding. High-dose statin therapy, angiotensin-converting-enzyme inhibitors or angiotensin-receptor blockers, mineralocorticoid-receptor antagonists, and beta-blockers were recommended.

Number of subjects in period 1	Complete Revascularization	Culprit Lesion Only Revascularization
Started	2016	2025
Completed	1881	1634
Not completed	135	391
Did not receive allocated intervention	135	391

Baseline characteristics

Reporting groups

Reporting group title	Complete Revascularization
Reporting group description: A strategy of complete revascularization (consisting of PCI of all suitable nonculprit lesions) in patients with STEMI and multivessel coronary artery disease who had undergone successful culprit-lesion PCI.	
Reporting group title	Culprit Lesion Only Revascularization
Reporting group description: A strategy of no further revascularization in patients with STEMI and multivessel coronary artery disease who had undergone successful culprit-lesion PCI.	

Reporting group values	Complete Revascularization	Culprit Lesion Only Revascularization	Total
Number of subjects	2016	2025	4041
Age categorical			
Units: Subjects			
Adults (18-64 years)	1233	1195	2428
Adults (65 years and over)	783	830	1613
Gender categorical			
Units: Subjects			
Female	393	423	816
Male	1623	1602	3225
Time from symptom onset to index PCI			
Units: Subjects			
<6 hr	1383	1341	2724
6 to 12 hr	322	354	676
>12 hr	289	305	594
Not recorded	22	25	47
Glycated hemoglobin			
Units: percent			
arithmetic mean	6.3	6.3	
standard deviation	± 1.6	± 1.6	-
Low-density lipoprotein cholesterol			
Units: millimole(s)/litre			
arithmetic mean	3.1	3.1	
standard deviation	± 1.2	± 1.2	-
Peak creatinine			
Units: micromole(s)/litre			
arithmetic mean	84.7	85.2	
standard deviation	± 30.8	± 26.8	-

End points

End points reporting groups

Reporting group title	Complete Revascularization
Reporting group description: A strategy of complete revascularization (consisting of PCI of all suitable nonculprit lesions) in patients with STEMI and multivessel coronary artery disease who had undergone successful culprit-lesion PCI.	
Reporting group title	Culprit Lesion Only Revascularization
Reporting group description: A strategy of no further revascularization in patients with STEMI and multivessel coronary artery disease who had undergone successful culprit-lesion PCI.	

Primary: Co-Primary Outcomes

End point title	Co-Primary Outcomes
End point description:	
End point type	Primary
End point timeframe: Outcome events were assessed up to the date of each patient's final follow-up visit, which ranged from September 1, 2018, to June 7, 2019, when the database was locked. The mean follow-up time was 36.2 months, and the median follow-up time was 35.8 months	

End point values	Complete Revascularization	Culprit Lesion Only Revascularization		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2016	2025		
Units: subjects				
Cardiovascular death or myocardial infarction(MI)	158	213		
Cardiovascular death, MI,or ischemia-driven revasc	179	339		

Statistical analyses

Statistical analysis title	Analysis of co-primary outcome 1
Statistical analysis description: Cardiovascular death or myocardial infarction	
Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization

Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	0.91

Statistical analysis title	Analysis of co-primary outcome 2
Statistical analysis description:	
Cardiovascular death or myocardial infarction, or ischemia-driven revascularization	
Comparison groups	Culprit Lesion Only Revascularization v Complete Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.61

Secondary: Key Secondary Outcomes

End point title	Key Secondary Outcomes
End point description:	
Cardiovascular death, myocardial infarction, ischemia-driven revascularization, unstable angina, or NYHA class IV heart failure	
End point type	Secondary
End point timeframe:	
Outcome events were assessed up to the date of each patient's final follow-up visit, which ranged from September 1, 2018, to June 7, 2019, when the database was locked. The mean follow-up time was 36.2 months, and the median follow-up time was 35.8 months	

End point values	Complete Revascularization	Culprit Lesion Only Revascularization		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2016	2025		
Units: subjects				
Key secondary outcome	272	426		

Statistical analyses

Statistical analysis title	Analysis of key secondary outcome
Statistical analysis description: Composite of cardiovascular death, myocardial infarction, ischemia-driven revascularization, unstable angina, or NYHA class IV heart failure	
Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.72

Secondary: Other Secondary Outcomes

End point title	Other Secondary Outcomes
End point description:	
End point type	Secondary
End point timeframe: Outcome events were assessed up to the date of each patient's final follow-up visit, which ranged from September 1, 2018, to June 7, 2019, when the database was locked. The mean follow-up time was 36.2 months, and the median follow-up time was 35.8 months	

End point values	Complete Revascularization	Culprit Lesion Only Revascularization		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2016	2025		
Units: subjects				
Myocardial infarction	109	160		
Ischemia-driven revascularization	29	160		
Unstable angina	70	130		
Death from cardiovascular causes	59	64		
Death from any cause	96	106		

Statistical analyses

Statistical analysis title	Analysis of secondary outcomes - MI
Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.86

Statistical analysis title	Analysis of secondary outcomes - IDR
Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.26

Statistical analysis title	Analysis of secondary outcomes - Unstable Angina
Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	0.53

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	0.71

Statistical analysis title	Analysis of secondary outcomes - Death CV causes
Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.32

Statistical analysis title	Analysis of secondary outcomes - Death Any Cause
Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.2

Other pre-specified: Other Outcomes

End point title	Other Outcomes
End point description:	
End point type	Other pre-specified

End point timeframe:

Outcome events were assessed up to the date of each patient's final follow-up visit, which ranged from September 1, 2018, to June 7, 2019, when the database was locked. The mean follow-up time was 36.2 months, and the median follow-up time was 35.8 months

End point values	Complete Revascularization	Culprit Lesion Only Revascularization		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2016	2025		
Units: subjects				
Stroke	38	29		
NYHA class IV heart failure	58	56		
Stent thrombosis	26	19		

Statistical analyses

Statistical analysis title	Analysis of other outcomes - Stroke
Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	2.13

Statistical analysis title	Analysis of other - NYHA class IV heart failure
Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.5

Statistical analysis title	Analysis of other outcomes - Stent thrombosis
-----------------------------------	---

Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	2.49

Other pre-specified: Safety Outcomes

End point title	Safety Outcomes
-----------------	-----------------

End point description:

End point type	Other pre-specified
----------------	---------------------

End point timeframe:

Outcome events were assessed up to the date of each patient's final follow-up visit, which ranged from September 1, 2018, to June 7, 2019, when the database was locked. The mean follow-up time was 36.2 months, and the median follow-up time was 35.8 months

End point values	Complete Revascularization	Culprit Lesion Only Revascularization		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2016	2025		
Units: subjects				
Major bleeding	58	44		
Contrast-associated acute kidney injury	30	19		

Statistical analyses

Statistical analysis title	Analysis of safety outcomes - Major bleeding
Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	1.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.97

Statistical analysis title	Analysis of safety-contrast-assoc acute kidney inj
Comparison groups	Complete Revascularization v Culprit Lesion Only Revascularization
Number of subjects included in analysis	4041
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	2.84

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Not applicable to this trial

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

Dictionary used

Dictionary name	Not Applicable
-----------------	----------------

Dictionary version	0
--------------------	---

Frequency threshold for reporting non-serious adverse events: 0 %

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: NOT APPLICABLE TO THIS TRIAL

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 February 2017	<p>To ensure that COMPLETE is adequately powered to detect a meaningful clinical difference, the primary outcome of the trial was expanded to a co-primary outcome of 1) cardiovascular death or new myocardial infarction, and 2) cardiovascular death, new myocardial infarction or ischemia-driven revascularization. The sample size was re-calculated resulting in a modest increase in sample size from 3900 to 4000 participants.</p> <p>This amendment also incorporates results from recently published trials into the study background and rationale, harmonizes study objectives and hypotheses with revised study outcomes, and provides additional guidance for the conduct and timing of follow-up visits.</p> <p>For those participants whose qualifying early PCI for STEMI was a pharmacoinvasive strategy, the window for enrolment was extended from 3-12 hours to 3-24 hours after initial PCI. A definition for the outcome event of Unstable Angina and untoward medical event were added and minor changes to the definitions for ischemia-driven revascularization, stent thrombosis and heart failure were updated in accordance with the definitions used by the Event Adjudication Committee.</p>

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.

We did not evaluate non-culprit-lesion PCI that was performed during the same procedure as that for the index culprit-lesion PCI for STEMI. Although cardiogenic shock was not an exclusion criterion, no patients with cardiogenic shock were enrolled.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/31475795>

<http://www.ncbi.nlm.nih.gov/pubmed/31779786>

<http://www.ncbi.nlm.nih.gov/pubmed/32912441>

<http://www.ncbi.nlm.nih.gov/pubmed/34320839>

<http://www.ncbi.nlm.nih.gov/pubmed/32646305>