



Clinical trial results:

GLOBAL LEADERS: Comparative effectiveness of 1 month of ticagrelor plus aspirin followed by ticagrelor monotherapy versus a current-day intensive dual antiplatelet therapy in all-comers patients undergoing percutaneous coronary intervention with bivalirudin and BioMatrix family drug-eluting stent use.

Summary

| | |
|--------------------------|----------------------------------|
| EudraCT number | 2012-003515-58 |
| Trial protocol | IT DE GB AT ES BE NL DK HU PT BG |
| Global end of trial date | 16 February 2018 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 17 February 2019 |
| First version publication date | 17 February 2019 |
| Summary attachment (see zip file) | Global Leaders main paper (Global Leaders main paper_Lancet August 2018.pdf) Global leaders supplementary appendix (supplementary appendix.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | ECRI-12-001 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01813435 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | ECRI b.v. |
| Sponsor organisation address | Westblaak 98, Rotterdam, Netherlands, |
| Public contact | Managing Director, ECRI b.v., 0031 0102062850, GA.vEs@ecri-trials.com |
| Scientific contact | Managing Director, ECRI b.v., 0031 0102062850, GA.vEs@ecri-trials.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 | 16 February 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 16 February 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 February 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To determine in all-comers patients undergoing PCI under standardised treatment (including the BioMatrix family of drug-eluting stents and bivalirudin), whether treatment with 1 month of ticagrelor and aspirin followed by 23 months of ticagrelor monotherapy is superior with respect to the composite of all-cause mortality or non-fatal new Q-wave MI compared to treatment with 12 months of standard dual anti platelet therapy (DAPT) followed by aspirin monotherapy.

Protection of trial subjects:

NA, phase IV trial

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 01 May 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 | Netherlands: 1159 |
| Country: Number of subjects enrolled | Poland: 1532 |
| Country: Number of subjects enrolled | Portugal: 113 |
| Country: Number of subjects enrolled | Spain: 951 |
| Country: Number of subjects enrolled | United Kingdom: 1713 |
| Country: Number of subjects enrolled | Austria: 672 |
| Country: Number of subjects enrolled | Belgium: 2185 |
| Country: Number of subjects enrolled | Bulgaria: 943 |
| Country: Number of subjects enrolled | Denmark: 131 |
| Country: Number of subjects enrolled | France: 849 |
| Country: Number of subjects enrolled | Germany: 2267 |
| Country: Number of subjects enrolled | Hungary: 527 |
| Country: Number of subjects enrolled | Italy: 1578 |
| Country: Number of subjects enrolled | Switzerland: 705 |
| Country: Number of subjects enrolled | Australia: 83 |
| Country: Number of subjects enrolled | Brazil: 248 |
| Country: Number of subjects enrolled | Singapore: 142 |

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Canada: 170 |
| Worldwide total number of subjects | 15968 |
| EEA total number of subjects | 14620 |

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) | 7877 |
| From 65 to 84 years | 7854 |
| 85 years and over | 237 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

please refer to the manuscript for screening details

Period 1

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

Arms

| | |
|------------------------------|---------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | experimental intervention group |

Arm description: -

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | dual antiplatelet regimen for 30 days after revasc |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

NA

| | |
|------------------|---------------|
| Arm title | control group |
|------------------|---------------|

Arm description: -

| | |
|--|---|
| Arm type | control |
| Investigational medicinal product name | dual antiplatelet regimen for 365 days after revasc |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

NA

| Number of subjects in period 1 | experimental intervention group | control group |
|---------------------------------------|---------------------------------|---------------|
| Started | 7980 | 7988 |
| Completed | 7980 | 7988 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values | overall trial | Total | |
|---|---------------|-------|--|
| Number of subjects | 15968 | 15968 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 64.5 | | |
| standard deviation | ± 10.3 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 3714 | 3714 | |
| Male | 12254 | 12254 | |

End points

End points reporting groups

| | |
|--------------------------------|---------------------------------|
| Reporting group title | experimental intervention group |
| Reporting group description: - | |
| Reporting group title | control group |
| Reporting group description: - | |

Primary: all-cause mortality or new Q-wave myocardial infarction

| | |
|----------------------------------|---|
| End point title | all-cause mortality or new Q-wave myocardial infarction |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| up to 2 years post randomisation | |

| End point values | experimental intervention group | control group | | |
|-----------------------------|---------------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7980 | 7988 | | |
| Units: % | 304 | 349 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | primary endpoint |
| Comparison groups | experimental intervention group v control group |
| Number of subjects included in analysis | 15968 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[1] |
| P-value | < 0.001 |
| Method | Mantel-Cox |

Notes:

[1] - Mantel-Cox method

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

AE needed to be reported from ICF signature until last follow-up visit

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

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: see results in manuscript

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported