



Clinical trial results:

A Randomized, Parallel Group, Double-Blind Study of Ticagrelor Compared with Aspirin for Prevention of Vascular Events in Patients Undergoing Coronary Artery Bypass Graft Operation TiCAB– Ticagrelor in CABG

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2012-003630-16 |
| Trial protocol | DE AT |
| Global end of trial date | 16 May 2018 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 08 March 2019 |
| First version publication date | 08 March 2019 |
| Summary attachment (see zip file) | Synopsis of Clinical Study Report (TiCAB_EudraCT 2012-003630-16_Synopsis of Final Study Report_20181122_final_geschwätzte Namen.pdf) |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GEIDENo.D00112 |
|-----------------------|----------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Deutsches Herzzentrum München |
| Sponsor organisation address | Lazarettstraße 36, München, Germany, 80636 |
| Public contact | Project Manager, ISAResearch Center, 49 8912182774, ticab@dhm.mhn.de |
| Scientific contact | Project Manager, ISAResearch Center, 49 8912182774, ticab@dhm.mhn.de |

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 | 20 September 2018 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 May 2018 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to test the hypothesis that Ticagrelor is superior to Aspirin (ASA) for the prevention of major cardiovascular and cerebrovascular events (MACCE; cardiovascular death, myocardial infarction, recurrent revascularization or stroke) in patients undergoing coronary artery bypass graft operation (CABG).

The primary efficacy MACCE-endpoint is the composite of cardiovascular death, myocardial infarction, recurrent revascularization, and stroke at twelve month after coronary artery bypass operation.

Protection of trial subjects:

not applicable

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 29 March 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------|
| Country: Number of subjects enrolled | Austria: 258 |
| Country: Number of subjects enrolled | Germany: 1614 |
| Country: Number of subjects enrolled | Switzerland: 21 |
| Worldwide total number of subjects | 1893 |
| EEA total number of subjects | 1872 |

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) | 721 |

| | |
|---------------------|------|
| From 65 to 84 years | 1161 |
| 85 years and over | 11 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

For inclusion in the study patients must fulfill the following criteria (1-3):

1. Patients 18 years of age or older
2. Informed, written consent by the patient
3. Indication for CABG surgery: - coronary three vessel disease, or - left main stenosis, or - two vessel disease with impaired left ventricular function (<50%)

Period 1

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

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Ticagrelor |

Arm description:

Patients randomised to Ticagrelor

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | ticagrelor |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

90 mg twice daily

| | |
|------------------|--------------------|
| Arm title | Acetylsalicyl acid |
|------------------|--------------------|

Arm description:

Patients randomised to ASA

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | ASA |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

100 mg once daily

| Number of subjects in period 1 | Ticagrelor | Acetylsalicyl acid |
|---------------------------------------|------------|--------------------|
| Started | 946 | 947 |
| Completed | 931 | 928 |
| Not completed | 15 | 19 |
| Lost to follow-up | 15 | 19 |

Baseline characteristics

End points

End points reporting groups

| | |
|---|--------------------|
| Reporting group title | Ticagrelor |
| Reporting group description: Patients randomised to Ticagrelor | |
| Reporting group title | Acetylsalicyl acid |
| Reporting group description: Patients randomised to ASA | |

Primary: Death

| | |
|---|---------|
| End point title | Death |
| End point description: All documented deaths | |
| End point type | Primary |
| End point timeframe: at 12 months after coronary artery bypass operation | |

| End point values | Ticagrelor | Acetylsalicyl acid | | |
|-----------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 931 | 928 | | |
| Units: 1 | 24 | 23 | | |

Statistical analyses

| | |
|--|---------------------------------|
| Statistical analysis title | Full analysis set (FAS) |
| Statistical analysis description: All patients who have been randomized to study treatment will be included irrespective of their protocol adherence and continued participation in the study. If a patient prematurely discontinues study medication, every effort will be made to determine the patient's status regarding MI, stroke, coronary revascularization procedures and mortality at the end of their scheduled study duration. Patients will be analyzed according to their randomized study medication irrespective of whether the event | |
| Comparison groups | Ticagrelor v Acetylsalicyl acid |
| Number of subjects included in analysis | 1859 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 1 ^[1] |
| Method | Cox Model |

Notes:

[1] - The p-values for the subgroup analyses will not be adjusted for multiple comparisons as the tests are exploratory and will be interpreted descriptively.

Primary: Death CV

| | |
|-----------------|-------------------------|
| End point title | Death CV ^[2] |
|-----------------|-------------------------|

End point description:

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

End point timeframe:
at 12 months after CABG

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: Several analyses to be performed

| End point values | Ticagrelor | Acetylsalicyl acid | | |
|-----------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 946 | 947 | | |
| Units: 1 | 17 | 19 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Myocard Infarction

| | |
|-----------------|-----------------------------------|
| End point title | Myocard Infarction ^[3] |
|-----------------|-----------------------------------|

End point description:

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

End point timeframe:
12 months after CABG

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: Several analyses to be performed

| End point values | Ticagrelor | Acetylsalicyl acid | | |
|-----------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 946 | 947 | | |
| Units: 1 | 17 | 31 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Stroke

| | |
|-----------------|--------|
| End point title | Stroke |
|-----------------|--------|

End point description:

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

End point timeframe:
12 months after CABG

| End point values | Ticagrelor | Acetylsalicyl acid | | |
|-----------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 946 | 947 | | |
| Units: 1 | 30 | 24 | | |

Statistical analyses

| Statistical analysis title | Full analysis set |
|----------------------------|-------------------|
|----------------------------|-------------------|

Statistical analysis description:

All patients who have been randomized to study treatment will be included irrespective of their protocol adherence and continued participation in the study. If a patient prematurely discontinues study medication, every effort will be made to determine the patient's status regarding MI, stroke, coronary revascularization procedures and mortality at the end of their scheduled study duration. Patients will be analyzed according to their randomized study medication irrespective of whether the event

| | |
|---|---------------------------------|
| Comparison groups | Ticagrelor v Acetylsalicyl acid |
| Number of subjects included in analysis | 1893 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[4] |
| P-value | = 0.5 ^[5] |
| Method | t-test, 2-sided |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.775 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.1 |
| upper limit | 0.9 |

Notes:

[4] - several analyses to be performed

[5] - The p-values for the subgroup analyses will not be adjusted for multiple comparisons as the tests are exploratory and will be interpreted descriptively.

Primary: Revascularisation

| | |
|-----------------|----------------------------------|
| End point title | Revascularisation ^[6] |
|-----------------|----------------------------------|

End point description:

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

End point timeframe:
12 months after CABG

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: Several analyses to be performed

| End point values | Ticagrelor | Acetylsalicyl acid | | |
|-----------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 946 | 947 | | |
| Units: 1 | 41 | 36 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Bleeding

| | |
|-----------------|-------------------------|
| End point title | Bleeding ^[7] |
|-----------------|-------------------------|

End point description:

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

End point timeframe:

12 months after CABG

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: Several analyses to be performed

| End point values | Ticagrelor | Acetylsalicyl acid | | |
|-----------------------------|-----------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 946 | 947 | | |
| Units: 1 | 30 | 29 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12 months after coronary artery bypass operation

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|----------|
| Dictionary name | Internal |
|-----------------|----------|

| | |
|--------------------|---|
| Dictionary version | 1 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | All patients |
|-----------------------|--------------|

Reporting group description:

All patients

| Serious adverse events | All patients | | |
|---|------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 377 / 1893 (19.92%) | | |
| number of deaths (all causes) | 59 | | |
| number of deaths resulting from adverse events | 58 | | |
| Cardiac disorders | | | |
| Several SAEs reported | | | |
| subjects affected / exposed | 377 / 1893 (19.92%) | | |
| occurrences causally related to treatment / all | 85 / 1052 | | |
| deaths causally related to treatment / all | 8 / 58 | | |

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

| Non-serious adverse events | All patients | | |
|---|------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 783 / 1893 (41.36%) | | |
| Vascular disorders | | | |
| Several different AEs documented | | | |
| subjects affected / exposed | 783 / 1893 (41.36%) | | |
| occurrences (all) | 1950 | | |

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