



Clinical trial results:

The Standard care versus Celecoxib Outcome Trial (SCOT): A Large Streamlined Safety Study

Dansk:

Klinisk forsøg med standardbehandling versus celecoxib (SCOT-forsøget)

Et stort, strømlinet forsøg i lægemiddelsikkerhed

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2007-000012-90 |
| Trial protocol | GB DK NL |
| Global end of trial date | 28 August 2015 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 04 August 2017 |
| First version publication date | 04 August 2017 |
| Summary attachment (see zip file) | SCOT Abstract (SCOT Study Abstract.docx) |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 9.6(v16) |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00447759 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | The University of Dundee |
| Sponsor organisation address | Nethergate, Dundee, United Kingdom, DD1 4HN |
| Public contact | Dr Catrina Forde (Senior Research Governance Manager), The University of Dundee, 01382 383890, c.forde@dundee.ac.uk |
| Scientific contact | Dr Catrina Forde (Senior Research Governance Manager), The University of Dundee, 01382 383890, c.forde@dundee.ac.uk |

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 | No |

| |
|--------------------------------|
| 1901/2006 apply to this trial? |
|--------------------------------|

Notes:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 28 August 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 28 August 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 August 2015 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to compare the cardiovascular safety of celecoxib and traditional NSAIDs prescribed for the treatment of arthritis.

Protection of trial subjects:

All subjects were treated in normal care by family physicians. The intervention randomised subjects to continue to receive their standard non selective non-steroidal anti-inflammatory drug (nsNSAID) or to switch to celecoxib both prescribed in usual care.

Background therapy:

All subjects received nsNSAID at baseline prescribed for osteoarthritis or rheumatoid arthritis.

Evidence for comparator:

The purpose of the trial was to compare the cardiovascular safety of celecoxib, an effective selective cyclo-oxygenase 2 inhibitor with non-selective cyclooxygenase inhibitors (nsNSAIDs)

| | |
|---|------------------|
| Actual start date of recruitment | 29 January 2008 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 5 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|----------------------|
| Country: Number of subjects enrolled | United Kingdom: 5045 |
| Country: Number of subjects enrolled | Denmark: 2209 |
| Country: Number of subjects enrolled | Netherlands: 43 |
| Worldwide total number of subjects | 7297 |
| EEA total number of subjects | 7297 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|--|------|
| wk | |
| 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 to 84 years | 7297 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects aged 60 or over and free from established cardiovascular disease and who were taking chronic nsNSAIDs for osteoarthritis or rheumatoid arthritis were identified in primary care and invited to participate.

Pre-assignment

Screening details:

Subjects underwent screening by a study nurse including baseline bloods to exclude significant renal or hepatic dysfunction. The full study protocol is published at: [bmjopen-2012-002295](#)

Pre-assignment period milestones

| | |
|------------------------------|------|
| Number of subjects started | 7297 |
| Number of subjects completed | 7297 |

Period 1

| | |
|------------------------------|---|
| Period 1 title | Screening (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind ^[1] |
| Roles blinded | Investigator, Data analyst, Assessor ^[2] |

Blinding implementation details:

The study was a Prospective Open Blinded-end-point (PROBE) design.

Arms

| | |
|------------------------------|----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Standard NSAID |

Arm description:

Subjects in this arm continued their baseline nsNSAID

| | |
|--|---|
| Arm type | Active comparator |
| Investigational medicinal product name | nsNSAID |
| Investigational medicinal product code | |
| Other name | Any licenced nsNSAID except COX2 selective NSAIDs |
| Pharmaceutical forms | Capsule, Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Any licenced dose of and nsNSAID

| | |
|------------------|-----------|
| Arm title | Celecoxib |
|------------------|-----------|

Arm description:

Subjects switched from standard NSAID to celecoxib prescribing

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | celecoxib |
| Investigational medicinal product code | |
| Other name | celebrex |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Any licenced dose could be prescribed

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: This was a Prospective Open Blinded End Point (PROBE) design

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This was a Prospective Open Blinded End-point study (PROBE) design

| Number of subjects in period 1 | Standard NSAID | Celecoxib |
|---------------------------------------|----------------|-----------|
| Started | 3650 | 3647 |
| Completed | 3650 | 3647 |

Baseline characteristics

Reporting groups

| | |
|--|----------------|
| Reporting group title | Standard NSAID |
| Reporting group description: Subjects in this arm continued their baseline nsNSAID | |
| Reporting group title | Celecoxib |
| Reporting group description: Subjects switched from standard NSAID to celecoxib prescribing | |

| Reporting group values | Standard NSAID | Celecoxib | Total |
|---------------------------------------|----------------|-----------|-------|
| Number of subjects | 3650 | 3647 | 7297 |
| Age categorical Units: Subjects | | | |
| Age 60+ | 3650 | 3647 | 7297 |
| Age continuous | | | |
| Age 60 or over | | | |
| Units: years | | | |
| arithmetic mean | 68.2 | 68.6 | |
| standard deviation | ± 6.1 | ± 6.2 | - |
| Gender categorical Units: Subjects | | | |
| Female | 2218 | 2120 | 4338 |
| Male | 1432 | 1527 | 2959 |
| Type or arthritis Units: Subjects | | | |
| Osteoarthritis | 3422 | 3421 | 6843 |
| Rheumatoid | 228 | 226 | 454 |
| Mean age Units: years | | | |
| arithmetic mean | 68.2 | 68.6 | |
| standard deviation | ± 6.1 | ± 6.2 | - |

Subject analysis sets

| | |
|---|--------------------|
| Subject analysis set title | Standard NSAID |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects switched to celecoxib | |
| Subject analysis set title | Celecoxib |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Subjects continuing with nsNSAID | |

| Reporting group values | Standard NSAID | Celecoxib | |
|------------------------|----------------|-----------|--|
| Number of subjects | 3650 | 3647 | |

| | | | |
|--------------------|-------|-------|--|
| Age categorical | | | |
| Units: Subjects | | | |
| Age 60+ | 3650 | 3647 | |
| Age continuous | | | |
| Age 60 or over | | | |
| Units: years | | | |
| arithmetic mean | 68.2 | 68.6 | |
| standard deviation | ± 6.1 | ± 6.2 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |
| Type or arthritis | | | |
| Units: Subjects | | | |
| Osteoarthritis | | | |
| Rheumatoid | | | |
| Mean age | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | Standard NSAID |
| Reporting group description: | |
| Subjects in this arm continued their baseline nsNSAID | |
| Reporting group title | Celecoxib |
| Reporting group description: | |
| Subjects switched from standard NSAID to celecoxib prescribing | |
| Subject analysis set title | Standard NSAID |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Subjects switched to celecoxib | |
| Subject analysis set title | Celecoxib |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Subjects continuing with nsNSAID | |

Primary: APTC Composite

| | |
|------------------------|----------------|
| End point title | APTC Composite |
| End point description: | |
| Time to first event | |
| End point type | Primary |
| End point timeframe: | |
| Mean 3.2 years | |

| End point values | Standard NSAID | Celecoxib | | |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3650 ^[1] | 3647 ^[2] | | |
| Units: subjects | | | | |
| APTC Composite | 124 | 125 | | |

Notes:

[1] - nsNSAID

[2] - celecoxib

| | |
|-----------------------------------|------------------|
| Attachments (see zip file) | ITT Analysis.doc |
|-----------------------------------|------------------|

Statistical analyses

| | |
|-----------------------------------|----------------------------|
| Statistical analysis title | Primary Analysis |
| Statistical analysis description: | |
| Time to first APTC endpoint | |
| Comparison groups | Standard NSAID v Celecoxib |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 7297 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[3] |
| P-value | < 0.05 |
| Method | Logrank |
| Parameter estimate | Cox proportional hazard |
| Point estimate | 1.04 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 0.81 |
| upper limit | 1.33 |
| Variability estimate | Standard deviation |

Notes:

[3] - NI margin 1.4

Adverse events

Adverse events information

Timeframe for reporting adverse events:

At end of trial

Adverse event reporting additional description:

Only treatment related adverse reactions captured but all SAEs

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 18 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | nsNSAIDs |
|-----------------------|----------|

Reporting group description:

Stayed on prescribed NSAID

| | |
|-----------------------|-----------|
| Reporting group title | celecoxib |
|-----------------------|-----------|

Reporting group description:

Subjects switched to celecoxib

| Serious adverse events | nsNSAIDs | celecoxib | |
|---|-------------------------|-------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1183 / 3650 (32.41%) | 1155 / 3647 (31.67%) | |
| number of deaths (all causes) | 41 | 35 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Cardiac disorders | | | |
| Any SAE | | | |
| subjects affected / exposed | 1183 / 3650 (32.41%) | 1155 / 3647 (31.67%) | |
| occurrences causally related to treatment / all | 0 / 1183 | 0 / 1155 | |
| deaths causally related to treatment / all | 0 / 116 | 0 / 102 | |

Frequency threshold for reporting non-serious adverse events: 0.05 %

| Non-serious adverse events | nsNSAIDs | celecoxib | |
|---|------------------------|------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 586 / 3650 (16.05%) | 804 / 3647 (22.05%) | |
| Cardiac disorders | | | |
| All non-serious | | | |

| | | | |
|-----------------------------|------------------------|------------------------|--|
| subjects affected / exposed | 586 / 3650 (16.05%) | 804 / 3647 (22.05%) | |
| occurrences (all) | 586 | 804 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------|---|
| 07 May 2015 | Relaxation of the non-inferiority margin from 1.3 to 1.4 due to the very low (0.9%) event rate. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported