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 inhibtor 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 osteoathritis 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 standard deviation	 68.2 ± 6.1	 68.6 ± 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 yeas	

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 asverse 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 no-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