Clinical trial results:
A Phase 4, 6-week, randomized double-blind, multicenter, active-controlled trial to evaluate the effects of Celecoxib (Celebrex®) or Naproxen on blood pressure in paediatric subjects with juvenile idiopathic arthritis

Summary

EudraCT number	2014-003737-26
Trial protocol	Outside EU/EEA
Global end of trial date	17 December 2012

Results information

Result version number	v1 (current)
This version publication date	04 May 2016
First version publication date	01 August 2015

Trial information

Trial identification

Sponsor protocol code	A3191342

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00807846
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 May 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 December 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of treatment with celecoxib on systolic blood pressure (SBP) compared to treatment with naproxen in subjects with juvenile idiopathic arthritis (JIA) (oligoarticular, polyarticular arthritis and children with systemic onset disease but inactive systemic features).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 September 2009
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	Russian Federation: 21
Country: Number of subjects enrolled	Peru: 21
Country: Number of subjects enrolled	Philippines: 18
Country: Number of subjects enrolled	South Africa: 3
Country: Number of subjects enrolled	Ukraine: 27
Country: Number of subjects enrolled	Serbia: 29
Country: Number of subjects enrolled	Costa Rica: 2
Country: Number of subjects enrolled	United States: 66
Country: Number of subjects enrolled	Chile: 8
Country: Number of subjects enrolled	Switzerland: 3
Worldwide total number of subjects	198
EEA total number of subjects	0

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)	96
Adolescents (12-17 years)	102
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a phase 4, 6-week, randomized double-blind, multicenter, active-controlled trial in subjects with JIA. A total of 221 subjects were screened into the study in 32 investigator sites.

Pre-assignment

Screening details:

A total of 101 subjects were randomized to treatment with Celecoxib and 100 subjects to treatment with Naproxen. Of these randomized, 100 subjects received treatment with Celecoxib and 98 subjects received treatment with Naproxen. Three subjects were randomized but did not receive any treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Celecoxib

Arm description:

Subjects received celecoxib for 6 weeks. The volume per (/) dose of the study medications was determined by the subject's weight at baseline visit.

Arm type	Experimental
Investigational medicinal product name	Celecoxib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received celecoxib capsules 50 millligram (mg) twice daily (BID) or 100 mg BID for 6 weeks.

Arm title	Naproxen

Arm description:

Subjects received naproxen for 6 weeks. The volume/dose of the study medications was determined by the subject's weight at baseline visit.

Arm type	Experimental
Investigational medicinal product name	Naproxen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Subjects received naproxen suspension 7.5 mg/kilogram (kg) BID (maximum dose of 500 mg BID) for 6 weeks.

Number of subjects in period 1	Celecoxib	Naproxen
Started	100	98
Completed	88	94
Not completed	12	4
'Protocol Violation '	2	1
Consent withdrawn by subject	2	1
'Adverse Event '	5	-
'Other Not Specified '	1	2
Lack of efficacy	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Celecoxib
Reporting group description:	
Subjects received celecoxib for 6 weeks. The volume per (/) dose of the study medications was determined by the subject's weight at baseline visit.	
Reporting group title	Naproxen
Reporting group description:	
Subjects received naproxen for 6 weeks. The volume/dose of the study medications was determined by the subject's weight at baseline visit.	

Reporting group values	Celecoxib	Naproxen	Total
Number of subjects	100	98	198
Age categorical Units: Subjects			
Greater than or equal to(>=)2-lessthan (<)8 years	22	18	40
>=8 - <13 Years	34	47	81
>=13 - <18 Years	44	33	77
Gender categorical Units: Subjects			
Female	76	64	140
Male	24	34	58

End points

End points reporting groups

Reporting group title	Celecoxib
Reporting group description:	
Subjects received celecoxib for 6 weeks. The volume per (/) dose of the study medications was determined by the subject's weight at baseline visit.	
Reporting group title	Naproxen
Reporting group description:	
Subjects received naproxen for 6 weeks. The volume/dose of the study medications was determined by the subject's weight at baseline visit.	

Primary: Change From Baseline in Systolic Blood Pressure (SBP) at Week 6/Final Visit

End point title	Change From Baseline in Systolic Blood Pressure (SBP) at Week 6/Final Visit
End point description:	
Value at 6 weeks minus value at baseline. Safety population included all randomized subjects who received at least one dose of study medication. The safety analysis set was used to analyze all BP (blood pressure) measurements. For early terminations the last observation carried forward (LOCF) was used to impute missing data.	
End point type	Primary
End point timeframe:	
6 Weeks/Final Visit	

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	98		
Units: millimeter of mercury (mmHg)				
least squares mean (standard error)	0.366 (± 0.7)	-0.734 (± 0.7)		

Statistical analyses

Statistical analysis title	Change from baseline in SBP at Week 6/Final Visit
Statistical analysis description:	
The primary analysis was based on 90 percentage (%) confidence interval (CI) for the difference across treatment groups (celecoxib – naproxen) in mean change from baseline in SBP. Change from Baseline in BP was analyzed using analysis of covariance (ANCOVA) with model terms for treatment with baseline height, baseline weight, baseline age, and baseline SBP as covariates. No formal hypothesis testing was applied to the primary analysis.	
Comparison groups	Celecoxib v Naproxen

Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.274
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.56
upper limit	2.76

Secondary: Change From Baseline to Week 2 in SBP

End point title	Change From Baseline to Week 2 in SBP

End point description:

Value at 2 weeks minus value at baseline. Safety population included all randomized subjects who received at least one dose of study medication. The Safety Analysis set was used to analyze all BP measurements. For early terminations the LOCF was used to impute missing data.

End point type	Secondary

End point timeframe:

2 weeks

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	97		
Units: mmHg				
least squares mean (standard error)	-0.202 (± 0.53)	-1.29 (± 0.53)		

Statistical analyses

Statistical analysis title	Change from baseline in SBP at Week 2

Statistical analysis description:

For secondary analyses, 95% CIs for the differences across treatment groups (celecoxib – naproxen) in the mean change from baseline were generated. The change from baseline in BP was analyzed using an ANCOVA model with terms for treatment, baseline height, weight, age and baseline BP as covariates.

Comparison groups	Naproxen v Celecoxib
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.148 [1]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.088

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.39
upper limit	2.57

Notes:

[1] - Secondary analyses were conducted using a two-sided test with α=0.05.

Secondary: Change From Baseline in SBP at Week 4

End point title	Change From Baseline in SBP at Week 4

End point description:

Value at 4 weeks minus value at baseline. Safety population included all randomized subjects who received at least one dose of study medication. The Safety Analysis set was used to analyze all BP measurements. For early terminations the LOCF was used to impute missing data.

End point type	Secondary

End point timeframe:

4 weeks

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	98		
Units: mmHg				
least squares mean (standard error)	-0.17 (± 0.58)	-2.007 (± 0.58)		

Statistical analyses

Statistical analysis title	Change from baseline in SBP at Week 4

Statistical analysis description:

For secondary analyses, 95% CIs for the differences across treatment groups (celecoxib – naproxen) in the mean change from baseline were generated. The change from baseline in blood pressure was analyzed using an ANCOVA model with terms for treatment, baseline height, weight, age and baseline BP as covariates.

Comparison groups	Celecoxib v Naproxen
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.027 [2]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	1.837
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	3.46

Notes:

[2] - Secondary analyses were conducted using a two-sided test with α=0.05.

Secondary: Change From Baseline in Diastolic Blood Pressure (DBP) at Week 2

End point title	Change From Baseline in Diastolic Blood Pressure (DBP) at Week 2

End point description:

Value at 2 weeks minus value at baseline. Safety population included all randomized subjects who received at least one dose of study medication. The Safety Analysis set was used to analyze all BP measurements. For early terminations the LOCF was used to impute missing data.

End point type	Secondary

End point timeframe:

2 weeks

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	97	97		
Units: mmHg				
least squares mean (standard error)	-1.346 (± 0.52)	-0.139 (± 0.52)		

Statistical analyses

Statistical analysis title	Change from baseline in DBP at Week 2

Statistical analysis description:

For secondary analyses, 95% CIs for the differences across treatment groups (celecoxib – naproxen) in the mean change from baseline were
generated. The change from baseline in BP was analyzed using an ANCOVA model with terms for treatment, baseline height, weight, age and baseline BP as covariates.

Comparison groups	Celecoxib v Naproxen
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.106 [3]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.207
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.67
upper limit	0.26

Notes:

[3] - Secondary analyses were conducted using a two-sided test with α=0.05.

Secondary: Change From Baseline in DBP at Week 4

End point title	Change From Baseline in DBP at Week 4

End point description:

Value at 4 weeks minus value at baseline. Safety population included all randomized subjects who received at least one dose of study medication. The Safety Analysis set was used to analyze all BP measurements. For early terminations the LOCF was used to impute missing data.

End point type	Secondary

End point timeframe:

4 weeks

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	98		
Units: mmHg				
least squares mean (standard error)	-0.628 (± 0.54)	-0.848 (± 0.54)		

Statistical analyses

Statistical analysis title	Change from baseline in DBP at Week 4

Statistical analysis description:

For secondary analyses, 95% CIs for the differences across treatment groups (celecoxib – naproxen) in the mean change from baseline were generated. The change from baseline in BP was analyzed using an ANCOVA model with terms for treatment, baseline height, weight, age and baseline BP as covariates.

Comparison groups	Celecoxib v Naproxen
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.776 [4]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.74

Notes:

[4] - Secondary analyses were conducted using a two-sided test with α=0.05.

Secondary: Change From Baseline in DBP at Week 6/Final Visit

End point title	Change From Baseline in DBP at Week 6/Final Visit

End point description:

Value at 6 weeks/Final Visit minus value at baseline. Safety population included all randomized subjects who received at least one dose of study medication. The Safety Analysis set was used to analyze all BP measurements. For early terminations the LOCF was used to impute missing data.

End point type	Secondary

End point timeframe:

6 weeks

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	98		
Units: mmHg				
least squares mean (standard error)	-0.535 (± 0.54)	-0.356 (± 0.54)		

Statistical analyses

Statistical analysis title	Change from baseline in DBP at Week 6

Statistical analysis description:

For secondary analyses, 95% CIs for the differences across treatment groups (celecoxib – naproxen) in the mean change from baseline were generated. The change from baseline in BP was analyzed using an ANCOVA model with terms for treatment, baseline height, weight, age and baseline blood pressure as covariates.

Comparison groups	Celecoxib v Naproxen
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.815 [5]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.179
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	1.33

Notes:

[5] - Secondary analyses were conducted using a two-sided test with α=0.05.

Secondary: Change From Baseline in Parent's Assessment of Overall Well-Being at Week 6/Final Visit

End point title	Change From Baseline in Parent's Assessment of Overall Well-Being at Week 6/Final Visit

End point description:

The parent/legal guardian evaluated the subject's overall well-being at Baseline and at Week 6 (or Final Visit) by placing one vertical line on the visual analog scale (VAS). The VAS ranged from 0 to 100, with 0 being 'very well' and 100 being 'very poor. Modified-Intent-to-Treat (MITT) Population included all randomized subjects who received at least one dose of study medication and had at least one post-baseline efficacy measurement.

End point type	Secondary

End point timeframe:

6 weeks

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	98		
Units: millimeter (mm)				
least squares mean (standard error)	-10.581 (± 2.081)	-13.614 (± 2.06)		

Statistical analyses

Statistical analysis title	Parent's assessment of overall well-being

Statistical analysis description:

Change from Baseline to Week 6 was analyzed using ANCOVA model as well with treatment and Baseline value as a covariate. The LS mean change from Baseline was compared between treatment groups and an appropriate p-value and 95% CI for the difference between the two treatment groups was generated.

Comparison groups	Celecoxib v Naproxen
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.303 [6]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.033
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.76
upper limit	8.82

Notes:

[6] - This analysis was conducted using a two-sided test with α=0.05.

Secondary: Number of Subjects with >= 30% Improvement in the Parent's Global Assessment of Overall Well-Being at Week 6/Final Visit

End point title	Number of Subjects with >= 30% Improvement in the Parent's Global Assessment of Overall Well-Being at Week 6/Final Visit

End point description:

The parent/legal guardian evaluated the subject's overall well-being at Baseline and at Week 6 (or Final Visit) by placing one vertical line on the visual analog scale (VAS). The VAS ranged from 0 to 100, with 0 being 'very well' and 100 being 'very poor. The MITT Population included all randomized subjects who received at least one dose of study medication and had at least one post-baseline efficacy measurement.

End point type	Secondary

End point timeframe:

Week 6/Final Visit

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	98		
Units: Subjects	47	54		

Statistical analyses

Statistical analysis title	Parent’s global assessment of overall well-being

Statistical analysis description:

The number of subjects with at least a 30% improvement in Parent/Guardian's Global Assessment of Overall Well-Being was compared between the two treatment groups using a chi-square test. A 95% CI for the difference in incidence between groups was also computed. Mean Difference (Final Values) indicates difference in incidence between treatments.

Comparison groups	Celecoxib v Naproxen
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.392
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	-0.061
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.202
upper limit	0.079

Secondary: Change From Baseline in Subject's Assessment of Overall Well-Being at Week 6/Final Visit

End point title	Change From Baseline in Subject's Assessment of Overall Well-Being at Week 6/Final Visit

End point description:

Subjects, >= 8 years of age at the baseline, evaluated their own overall well-being at Baseline and at Week 6 (or Final Visit) by placing one vertical line on the VAS. The VAS ranges from 0 to 100, with 0 being ‘very well’ and 100 being ‘very poor’. MITT population was used. Additional 3 subjects aged <8 yrs at Baseline in Naproxen Arm provided self-assessments. In Celecoxib Arm, 2 subjects (>=8 yrs) did not provide self-assessment and 2 (>=8 yrs) provided but they were not from MITT and were excluded; additional 1 subject (<8 yrs) provided self-assessment and was included in analysis.

End point type	Secondary

End point timeframe:

6 weeks

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	83		
Units: mm				
least squares mean (standard error)	-12.99 (± 2.226)	-12.588 (± 2.115)		

Statistical analyses

Statistical analysis title	Subject's assessment of overall well-being

Statistical analysis description:

Change from Baseline to Week 6 was analyzed using ANCOVA model as well with treatment and Baseline value as a covariate. The LS mean change from Baseline was compared between treatment groups and an appropriate p-value and 95% CI for the difference between the two treatment groups was generated.

Comparison groups	Celecoxib v Naproxen
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.897 [7]
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.402
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.5
upper limit	5.69

Notes:

[7] - This analysis was conducted using a two-sided test with α=0.05.

Secondary: Number of Subjects with >= 30% Improvement in the Subject's Global Assessment of Overall Well-Being at Week 6/Final Visit

End point title	Number of Subjects with >= 30% Improvement in the Subject's Global Assessment of Overall Well-Being at Week 6/Final Visit

End point description:

Subjects, >=8 years of age at the baseline, evaluated their own overall well-being at Baseline and at Week 6 (or Final Visit) by placing one vertical line on the VAS. The VAS ranges from 0 to 100, with 0 being 'very well' and 100 being 'very poor'. MITT population was used. Additional 3 subjects aged <8 yrs at Baseline in Naproxen Arm provided self-assessments. In Celecoxib Arm, 2 subjects (>=8 yrs) not provided self-assessment and 2 (>=8 yrs) provided but they were not from MITT and were excluded; additional 1 subject (<8 yrs) provided self-assessment and included in analysis.

End point type	Secondary

End point timeframe:

Week 6/Final Visit

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	83		
Units: Subjects	33	45		

Statistical analyses

Statistical analysis title	Subject's global assessment of overall well-being

Statistical analysis description:

The number of subjects with at least a 30% improvement in subject's Global Assessment of Overall Well-Being was compared between the two treatment groups using a chi-square test. A 95% CI for the difference in incidence between groups was also computed. Mean Difference (Final Values) indicates difference in incidence between treatments.

Comparison groups	Celecoxib v Naproxen
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	-0.102
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.257
upper limit	0.053

Other pre-specified: Change From Baseline in Assessment of Ambulatory Blood Pressure Monitoring (ABPM) for SBP and DBP at Week 6/Final Visit

End point title	Change From Baseline in Assessment of Ambulatory Blood Pressure Monitoring (ABPM) for SBP and DBP at Week 6/Final Visit

End point description:

Ambulatory BP measurements were obtained from 24 subjects (in addition to the BP measurements obtained by the cuff technique) participating in the exploratory 24-hour ABPM sub-study. BP was monitored by a 24 hour Ambulatory BP device provided by a central vendor. Safety population included all randomized subjects who received at least one dose of study medication. For one subject in Naproxen Arm the device failed to collect 11 out of 24 readings at Week 6 and this subject was not included in analysis. ABPM data were analyzed for 12 and 11 subjects in Celecoxib and Naproxen Arms respectively.

End point type	Other pre-specified

End point timeframe:

6 weeks/Final Visit

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: mmHg				
arithmetic mean (standard deviation)				
SBP	2.4 (± 7.02)	-1.7 (± 12.4)		
DBP	0.9 (± 4.23)	-1.1 (± 5.36)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Assessment of ABPM for Heart Rate at Week 6/Final Visit

End point title	Change From Baseline in Assessment of ABPM for Heart Rate at Week 6/Final Visit

End point description:

Ambulatory BP measurements were obtained from 24 subjects (in addition to the BP measurements obtained by the cuff technique) participating in the exploratory 24-hour ABPM sub-study. A summary of ABPM 24-hour averages for heart rate is presented in this Outcome Measure. Safety population included all randomized subjects who received at least one dose of study medication. For one subject in Naproxen Arm the device failed to collect 11 out of 24 readings at Week 6 and this subject was not included in analysis. ABPM data were analyzed for 12 and 11 subjects in Celecoxib and Naproxen Arms respectively.

End point type	Other pre-specified

End point timeframe:

6 weeks/Final Visit

End point values	Celecoxib	Naproxen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	11		
Units: beats per minute (bpm)				
arithmetic mean (standard deviation)	2.5 (± 6.34)	3.7 (± 8.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Week 6/Final Visit	
Adverse event reporting additional description:	
The same event may appear as both an adverse event (AE) and a serious adverse event (SAE). However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups	
Reporting group title	Celecoxib
Reporting group description:	
Subjects received celecoxib for 6 weeks. The volume per (/) dose of the study medications was determined by the subject's weight at baseline visit	
Reporting group title	Naproxen
Reporting group description:	
Subjects received naproxen for 6 weeks. The volume/dose of the study medications was determined by the subject's weight at baseline visit	

Serious adverse events	Celecoxib	Naproxen	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 100 (0.00%)	1 / 98 (1.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Celecoxib	Naproxen	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 100 (10.00%)	18 / 98 (18.37%)	
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	7 / 100 (7.00%) 7	4 / 98 (4.08%) 4	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	4 / 100 (4.00%) 4	9 / 98 (9.18%) 10	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	5 / 98 (5.10%) 5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 April 2009	1. To correct and extend information given on the volume per dose naproxen/placebo in reference to body weight.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported