Clinical trial results:
A Pilot Self Selection Trial of an Extended-Release Over-the-Counter Analgesic

Summary

EudraCT number	2014-005305-20
Trial protocol	Outside EU/EEA
Global end of trial date	29 August 2011

Results information

Result version number	v2 (current)
This version publication date	07 September 2016
First version publication date	04 July 2015
Version creation reason	• New data added to full data set • Correction of full data set Bayer sponsor contact information to be updated

Trial information

Trial identification

Sponsor protocol code	BAYH6689/15833

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01383486
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, D-51368, Leverkusen, Germany,
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.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	29 August 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 August 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

A pilot trial to demonstrate that consumers can appropriately select Aleve 24 Hour for their own use based on expected duration of pain greater than 12 hours.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects and/or their legally authorized representatives. Participating subjects and/or their legally authorized representatives signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 July 2011
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	United States: 246
Worldwide total number of subjects	246
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)	0
Adolescents (12-17 years)	2
Adults (18-64 years)	205

From 65 to 84 years	38
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 10 pharmacies across the United States between 05 July 2011 (first subject first visit) and 29 August 2011 (last subject last visit). Of 435 subjects screened, 384 were qualified for participation, 259 presented at pharmacy to begin enrollment procedures, 254 gave informed consent and 1 refused to give pregnancy test.

Pre-assignment

Screening details:

Of 253 subjects provided with the study drugs, 18 subjects did not receive any study drug due to incomplete information for analysis in 2 subjects, 6 subjects did not take any product and 10 subjects were lost to follow up. Overall, 237 subjects were treated out of which 235 subjects gave estimated pain duration.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Naproxen Sodium ER (BAY H6689) or Advil IR

Arm description:

Eligible subjects were treated with 24 Advil immediate release (IR) caplets containing 200 milligram (mg) ibuprofen and 20 Aleve 24 Hour extended release (ER) tablets containing 660 mg naproxen sodium. Upon single incidence of pain, subjects were instructed to review both the packages and choose one product to use. Subjects were not offered any additional instructions for use beyond what was on the packages.

Arm type	Experimental
Investigational medicinal product name	Ibuprofen
Investigational medicinal product code	
Other name	Advil
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Eligible subjects were treated with 24 Advil IR caplets containing 200 mg ibuprofen orally.

Investigational medicinal product name	Naproxen sodium
Investigational medicinal product code	BAYH6689
Other name	Aleve 24 Hour
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Eligible subjects were treated with 20 Aleve 24 Hour ER tablets containing 660 mg naproxen sodium orally.

Number of subjects in period 1[1]	Naproxen Sodium ER (BAY H6689) or Advil IR
Started	235
Completed	235

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Not all enrolled subjects were treated with study drugs and gave estimated duration of pain. As baseline included only treated subjects who gave estimated duration of pain, the worldwide number enrolled in the trial differs with the number of subjects reported in the baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	Naproxen Sodium ER (BAY H6689) or Advil IR

Reporting group description:

Eligible subjects were treated with 24 Advil immediate release (IR) caplets containing 200 milligram (mg) ibuprofen and 20 Aleve 24 Hour extended release (ER) tablets containing 660 mg naproxen sodium. Upon single incidence of pain, subjects were instructed to review both the packages and choose one product to use. Subjects were not offered any additional instructions for use beyond what was on the packages.

Reporting group values	Naproxen Sodium ER (BAY H6689) or Advil IR	Total	
Number of subjects	235	235	
Age categorical Units: Subjects			
Age continuous			
Selection evaluation population included subjects who took any study medication and gave estimated duration of pain.			
Units: years			
arithmetic mean	51.4		
standard deviation	± 14.3	-	
Gender categorical			
Selection evaluation population. 1 'not recorded' subject refused to provide gender information.			
Units: Subjects			
Female	119	119	
Male	115	115	
Not recorded	1	1	

End points

End points reporting groups

Reporting group title	Naproxen Sodium ER (BAY H6689) or Advil IR

Reporting group description:

Eligible subjects were treated with 24 Advil immediate release (IR) caplets containing 200 milligram (mg) ibuprofen and 20 Aleve 24 Hour extended release (ER) tablets containing 660 mg naproxen sodium. Upon single incidence of pain, subjects were instructed to review both the packages and choose one product to use. Subjects were not offered any additional instructions for use beyond what was on the packages.

Subject analysis set title	Selection evaluation population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Selection evaluation population (N=235) included subjects who took any study medication and gave estimated duration of pain.

Primary: The Percentage of Subjects Who Selected Naproxen Sodium ER and Expected Their Pain to Last More Than 12 Hours

End point title	The Percentage of Subjects Who Selected Naproxen Sodium ER and Expected Their Pain to Last More Than 12 Hours[1]

End point description:

Subjects were instructed to select a product for use upon their pain episode and then call a toll-free number for an interview within 30 minutes of the selection decision. Subjects who did not call were interviewed after 14 days for data collection. The primary endpoint was derived from 2 variables: 1) number of subjects who selected naproxen sodium ER and reported expected duration of pain less than or equal to 12 hours (A); 2) number of subjects who selected naproxen sodium ER and report expected duration of pain greater than 12 hours (B). The result was calculated as B/(A+B).

End point type	Primary

End point timeframe:

Up to 14 days

Notes:

[1] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Naproxen Sodium ER (BAY H6689) or Advil IR			
Subject group type	Reporting group			
Number of subjects analysed	182[2]			
Units: Percentage of subjects (%)				
number (not applicable)	72			

Notes:

[2] - Only subjects who chose naproxen sodium were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: The Percentage of Subjects Who Selected Naproxen Sodium ER, Expected Their Pain to Last More Than 12 Hours and Reported Their Selection Decision Within First 24 Hours

End point title	The Percentage of Subjects Who Selected Naproxen Sodium ER, Expected Their Pain to Last More Than 12 Hours and

	Reported Their Selection Decision Within First 24 Hours

End point description:

End point type	Secondary

End point timeframe:

Within 24 hours of their selection decision taken up to 14 days

End point values	Naproxen Sodium ER (BAY H6689) or Advil IR			
Subject group type	Reporting group			
Number of subjects analysed	151[3]			
Units: Percentage of subjects (%)				
number (not applicable)	71.5			

Notes:

[3] - Subgroup of selection evaluation population.

Statistical analyses

No statistical analyses for this end point

Secondary: The Percentage of Low Literacy Subjects Who Selected Naproxen Sodium ER and Expected Their Pain to Last More Than 12 Hours

End point title	The Percentage of Low Literacy Subjects Who Selected Naproxen Sodium ER and Expected Their Pain to Last More Than 12 Hours

End point description:

In addition to the primary endpoint evaluated for all selection evaluable subjects, this secondary endpoint was evaluated separately for low literacy subjects. Low literacy subjects were defined as those who had REALM (Rapid Estimate of Adult Literacy in Medicine) score less than or equal to 60 at visit 1.

End point type	Secondary

End point timeframe:

Up to 14 days

End point values	Naproxen Sodium ER (BAY H6689) or Advil IR			
Subject group type	Reporting group			
Number of subjects analysed	31[4]			
Units: Percentage of subjects (%)				
number (not applicable)	64.5			

Notes:

[4] - Subgroup of selection evaluation population: low literacy subjects who chose naproxen sodium.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Subjects were followed for adverse events from the date of informed consent signed until the use of the product and follow up use phone call, or until the end of follow-up period (approximately 14 days)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	Naproxen Sodium ER (BAYH6689) or Advil IR)

Reporting group description:

Eligible subjects were treated with 24 Advil IR caplets containing 200 mg ibuprofen and 20 Aleve 24Hour ER tablets containing 660 mg naproxen sodium. Upon single incidence of pain, subjects wereinstructed to review both the packages and choose one product to use. Subjects were not offered anyadditional instructions for use beyond what was on the packages.

Serious adverse events	Naproxen Sodium ER (BAYH6689) or Advil IR)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 237 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Naproxen Sodium ER (BAYH6689) or Advil IR)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 237 (5.91%)		
Injury, poisoning and procedural complications			
Injuries NEC			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences (all)	1		
Nervous system disorders			
Headaches			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences (all)	1		
Neurological disorders NEC			

subjects affected / exposed	1 / 237 (0.42%)		
occurrences (all)	1		
General disorders and administration site conditions			
General system disorders NEC			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences (all)	1		
Gastrointestinal disorders			
Dental and gingival conditions			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Respiratory disorders NEC			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences (all)	1		
Renal and urinary disorders			
Urolithiases			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders NEC			
subjects affected / exposed	4 / 237 (1.69%)		
occurrences (all)	4		
Joint disorders			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences (all)	1		
Muscle disorders			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences (all)	1		
Infections and infestations			
Infections - pathogen unspecified			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences (all)	1		
Viral infectious disorders			
subjects affected / exposed	1 / 237 (0.42%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 May 2011	In the original protocol, subjects were to only receive one pill of each product. However, since Advil is commercially available in a 24-count box, it was determined that providing a commercial product in the commercial packaging would be more naturalistic. To maintain consistency between the two products, a 20-count Aleve 24 Hour bottle in a proposed commercial outer carton was provided as well. The protocol was amended to change the amount of both the Aleve 24 Hour and Advil that was provided to subjects during the treatment period of the clinical trial.
28 June 2011	The protocol was amended to (1) clarify screening procedures, (2) clarify analysis of the primary endpoint, and (3) to add questions to the interview questions for the enrollment period and End of Trial follow up period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Since this study was a self-selection study made by consumer, 7 out of 253 enrolled subjects did not report their age as providing their age was optional. Hence, subjects enrolled per country and age was provided for 246 subjects.

Notes: