EU Clinical Trials Register

Clinical trial results:
Evaluation Of The Efficacy Of A Novel Ibuprofen Formulation In The Treatment Of Post Surgical Dental Pain: Study I

Summary

EudraCT number	2014-004176-35
Trial protocol	Outside EU/EEA
Global end of trial date	09 July 2010

Results information

Result version number	v1 (current)
This version publication date	25 May 2016
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	AH-09-10

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01098747
WHO universal trial number (UTN)	-
Other trial identifiers	Alias: B3411004

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Clinical Trials.gov Call Center, Pfizer Inc, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Clinical Trials.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	04 May 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 July 2010
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of a single-dose of a novel ibuprofen formulation, ibuprofen sodium tablets (IBU Na; 2 multiplied (*) 256 milligram (mg) [equivalent to 400 mg ibuprofen]) in the third molar extraction model of dental pain compared to a single-dose of 1) Advil Tablets, (standard ibuprofen; 2*200 mg), 2) Motrin IB Tablets (standard ibuprofen; 2*200 mg), and 3) placebo.

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	01 April 2010
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: 316
Worldwide total number of subjects	316
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)	112
Adults (18-64 years)	204
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 407 subjects were screened in 1 country and 316 studies were assigned to placebo and 3 active treatment groups in a ratio of 1:2:2:2.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Single oral dose of 2 placebo tablets.

Arm type	Placebo Comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single oral dose of 2 placebo tablets.

Arm title	Ibuprofen Sodium

Arm description:

Single oral dose of 2 ibuprofen sodium 256 mg tablets, equivalent to 400 mg ibuprofen.

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

Dosage and administration details:

Subjects received single oral dose of 2 ibuprofen sodium 256 mg tablets, equivalent to 400 mg ibuprofen.

Arm title	Ibuprofen (Advil)

Arm description:

Single oral dose of 2 ibuprofen (Advil) 200 mg tablets (total dose of 400 mg ibuprofen).

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

Dosage and administration details:

Subjects received single oral dose of 2 ibuprofen (Advil) 200 mg tablets (total dose of 400 mg ibuprofen).

Arm title	Ibuprofen (Motrin IB)

Arm description:

Single oral dose of 2 ibuprofen [Motrin ibuprofen (IB)] 200 mg tablets (total dose of 400 mg ibuprofen).

Arm type	Experimental
Investigational medicinal product name	Ibuprofen (Motrin IB)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received single oral dose of 2 ibuprofen [Motrin ibuprofen (IB)] 200 mg tablets (total dose of 400 mg ibuprofen).

Number of subjects in period 1	Placebo	Ibuprofen Sodium	Ibuprofen (Advil)
Started	48	95	86
Completed	48	95	86

Number of subjects in period 1	Ibuprofen (Motrin IB)
Started	87
Completed	87

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Single oral dose of 2 placebo tablets.	
Reporting group title	Ibuprofen Sodium
Reporting group description:	
Single oral dose of 2 ibuprofen sodium 256 mg tablets, equivalent to 400 mg ibuprofen.	
Reporting group title	Ibuprofen (Advil)
Reporting group description:	
Single oral dose of 2 ibuprofen (Advil) 200 mg tablets (total dose of 400 mg ibuprofen).	
Reporting group title	Ibuprofen (Motrin IB)
Reporting group description:	
Single oral dose of 2 ibuprofen [Motrin ibuprofen (IB)] 200 mg tablets (total dose of 400 mg ibuprofen).	

Reporting group values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil)
Number of subjects	48	95	86
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	18.1	18.6	18.6
standard deviation	± 1.6	± 2.1	± 2.3
Gender categorical			
Units: Subjects			
Female	25	48	44
Male	23	47	42
Number of Subjects with Pain Severity Score			
Units: Subjects			
Moderate	27	51	43
Severe	21	44	43

Reporting group values	Ibuprofen (Motrin IB)	Total	
Number of subjects	87	316	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	18.4		
standard deviation	± 2	-	
Gender categorical			
Units: Subjects			
Female	44	161	
Male	43	155	

Number of Subjects with Pain Severity Score Units: Subjects			
Moderate	43	164	
Severe	44	152	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Single oral dose of 2 placebo tablets.	
Reporting group title	Ibuprofen Sodium
Reporting group description:	
Single oral dose of 2 ibuprofen sodium 256 mg tablets, equivalent to 400 mg ibuprofen.	
Reporting group title	Ibuprofen (Advil)
Reporting group description:	
Single oral dose of 2 ibuprofen (Advil) 200 mg tablets (total dose of 400 mg ibuprofen).	
Reporting group title	Ibuprofen (Motrin IB)
Reporting group description:	
Single oral dose of 2 ibuprofen [Motrin ibuprofen (IB)] 200 mg tablets (total dose of 400 mg ibuprofen).	
Subject analysis set title	Ibuprofen (Advil + Motrin IB)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Pooled data for Ibuprofen (Advil + Motrin IB) ITT population was compared with placebo and Ibuprofen Sodium. ITT population included all randomized subjects who received study medication and provided a baseline assessment.	

Primary: Time-weighted Sum of Pain Relief Rating and Pain Intensity Difference From 0-8 Hours (SPRID 0-8)

End point title	Time-weighted Sum of Pain Relief Rating and Pain Intensity Difference From 0-8 Hours (SPRID 0-8)[1]
End point description:	
SPRID: time-weighted sum of pain relief rating combined with pain intensity difference (PRID) over 8 hours. SPRID 0-8 score range: -8 (worst) to 56 (best). PRID: sum of Pain intensity differences (PID) and pain relief rating (PRR) at each time point. PRID score range: - 1=worst to 7=best. PID: baseline pain severity score minus pain severity score at a given time point (pain severity score range 0=none to 3=severe; baseline score range 2=moderate to 3=severe). PID score range: -1(worst) to 3 (best). PRR: assessed on 5-point pain relief rating scale (0=No relief to 4=Complete relief). Intent-to-treat (ITT) population included all randomized subjects who received study medication and provided a baseline assessment.	
End point type	Primary
End point timeframe:	
0 - 8 hours	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared
with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	95		
Units: Units on a scale				
arithmetic mean (standard deviation)	5.4 (± 14.1)	29.8 (± 14.2)		

Statistical analyses

Statistical analysis title	Placebo vs Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and 95 percent (%) confidence interval (CI): based on LS means from analysis of variance (ANOVA). Type I error controlled at 5% significance level (2 sided) by testing primary endpoints sequentially: Ibuprofen sodium (IBU Na) versus (vs.) Placebo for SPRID 0-8 then time to meaningful relief (TMR), IBU Na vs. IBU (Advil and Motrin IB) for TMR. If comparison at preceding step was significant only then subsequent comparisons were significant.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	ANOVA
Parameter estimate	Least Square (LS) Mean difference
Point estimate	24.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.32
upper limit	29.09

Notes:

[2] - p-value was calculated using ANOVA model with treatment, baseline Pain Severity Rating (PSR) and gender terms.

Primary: Time to Onset of Meaningful Relief

End point title	Time to Onset of Meaningful Relief[3]

End point description:

Subjects evaluated the time to meaningful relief by stopping a second stopwatch labelled 'meaningful relief' at the moment they first began to experience meaningful relief. Stopwatch was active up to 8 hours after dosing or until stopped by the subject, or rescue medication was administered. ITT population included all randomized subjects who received study medication and provided a baseline assessment. 99999 here indicates median because data was not summarized as median time to meaningful relief was greater than (>) 480 minutes (>8 hours) for placebo group. -99999 and 99999 indicates lower and upper limits of 95% CI as CI was not estimable.

End point type	Primary

End point timeframe:

0 - 8 hours

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: minutes				
median (confidence interval 95%)	99999 (-99999 to 99999)	42.4 (38.5 to 46.6)	55.3 (49.6 to 64.3)	

Statistical analyses

Statistical analysis title	Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Hazard Ratio (HR) and corresponding 95% CI were calculated based on the Wald statistic from the proportional hazards (PH) model. Type I error controlled at 5% significance level (2-sided) by testing primary endpoints sequentially: IBU Na vs. Placebo for SPRID 0-8 then TMR, IBU Na vs. IBU (Advil and Motrin IB) for TMR. If comparison at preceding step was significant only then subsequent comparisons were significant.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [4]
Method	Proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.78
upper limit	24.15

Notes:

[4] - p-value was calculated using the PH model with treatment, baseline PSR and gender terms.

Statistical analysis title	Ibuprofen Sodium vs. Ibuprofen (Advil + Motrin IB)

Statistical analysis description:

Hazard Ratio (HR) and corresponding 95% CI were calculated based on the Wald statistic from the proportional hazards (PH) model. Type I error controlled at 5% significance level (2-sided) by testing primary endpoints sequentially: IBU Na vs. Placebo for SPRID 0-8 then TMR, IBU Na vs. IBU (Advil and Motrin IB) for TMR. If comparison at preceding step was significant only then subsequent comparisons were significant.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [5]
Method	Proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.22
upper limit	2.06

Notes:

[5] - p-value was calculated using the PH model with treatment, baseline PSR and gender terms.

Secondary: Time to Confirmed First Perceptible Relief

End point title	Time to Confirmed First Perceptible Relief[6]

End point description:

Subjects evaluated the time to first perceptible relief by stopping a stopwatch labelled 'first perceptible relief' at the moment they first began to experience any relief. Stopwatch was active up to 8 hours after

dosing or until stopped by the subject, or rescue medication was administered. The first perceptible relief was considered confirmed if the subject also stopped the second stopwatch indicating meaningful relief. ITT population included all randomized subjects who received study medication and provided a baseline assessment. 99999 here indicates median because data was not summarized as median time to meaningful relief was greater than (>) 480 minutes (>8 hours) for placebo group. -99999 and 99999 indicates lower and upper limits of 95% CI as CI was not estimable.

End point type	Secondary

End point timeframe:	
0 - 8 hours	

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Minutes				
median (confidence interval 95%)	99999 (-99999 to 99999)	16.4 (15.6 to 19.3)	25.7 (22.2 to 29.1)	

Statistical analyses

Statistical analysis title	Placebo vs. Ibuprofen Sodium

Statistical analysis description:	
HR and corresponding 95% CI were calculated based on the Wald statistic from the PH model.	

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [7]
Method	Proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	12.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.51
upper limit	23.46

Notes:

[7] - p-value was calculated using the PH model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	Ibuprofen Sodium vs. Ibuprofen (Advil + Motrin IB)

Statistical analysis description:	
HR and corresponding 95% CI were calculated based on the Wald statistic from the PH model with treatment, baseline categorical severity and gender used as covariates.	

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)

Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [8]
Method	Proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	2.34

Notes:

[8] - p-value was calculated using the PH model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Pain Relief Rating (PRR)

End point title	Pain Relief Rating (PRR)[9]

End point description:

PRR was evaluated at different time points during the study up to 8 hours after taking the study medication, and immediately before rescue medication was taken (if necessary). PRR was assessed on a 5-point categorical pain relief rating scale where 0=No relief to 4=Complete relief. ITT population included all randomized subjects who received study medication and provided a baseline assessment.

End point type	Secondary

End point timeframe:

0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8 hours

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Units on a scale				
arithmetic mean (standard deviation)				
0.25 hours	0.4 (± 0.6)	0.7 (± 0.8)	0.5 (± 0.7)	
0.5 hours	0.5 (± 0.7)	2 (± 1.1)	1.5 (± 1.1)	
1 hour	0.6 (± 1)	2.9 (± 1)	2.5 (± 1.1)	
1.5 hours	0.7 (± 1.1)	3.1 (± 1)	2.8 (± 1.2)	
2 hours	0.7 (± 1.2)	3.1 (± 1.1)	3 (± 1.2)	
3 hours	0.7 (± 1.2)	2.9 (± 1.2)	3 (± 1.2)	
4 hours	0.8 (± 1.3)	2.8 (± 1.2)	3 (± 1.2)	
5 hours	0.7 (± 1.3)	2.6 (± 1.3)	2.8 (± 1.3)	
6 hours	0.7 (± 1.2)	2.3 (± 1.4)	2.6 (± 1.4)	
7 hours	0.5 (± 1.1)	1.9 (± 1.4)	2.3 (± 1.5)	
8 hours	0.5 (± 1.1)	1.7 (± 1.4)	2.2 (± 1.5)	

Statistical analyses

Statistical analysis title	0.25 hours: Placebo vs. Ibuprofen Sodium
Statistical analysis description:	
Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.	
Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007 [10]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.6

Notes:

[10] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.25 hours:Ibuprofen(Sodium vs Advil + Motrin IB)
Statistical analysis description:	
Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.	
Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01 [11]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.42

Notes:

[11] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.5 hours: Placebo vs Ibuprofen Sodium
Statistical analysis description:	
Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.	
Comparison groups	Ibuprofen Sodium v Placebo

Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [12]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.84

Notes:

[12] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.5 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [13]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	0.8

Notes:

[13] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hour: Placebo vs Ibuprofen sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [14]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	2.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.84
upper limit	2.6

Notes:

[14] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hour: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [15]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.66

Notes:

[15] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hours: Placebo vs Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [16]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	2.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	2.77

Notes:

[16] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022 [17]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.6

Notes:

[17] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours: Placebo vs Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [18]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	2.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	2.79

Notes:

[18] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.369 [19]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.13

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.41

Notes:

[19] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours: Placebo vs Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [20]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	2.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.78
upper limit	2.6

Notes:

[20] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.42 [21]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.42
upper limit	0.17

Notes:

[21] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours: Placebo vs Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [22]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	2.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.58
upper limit	2.45

Notes:

[22] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.151 [23]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	0.08

Notes:

[23] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours: Placebo vs Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [24]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.88

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.43
upper limit	2.33

Notes:

[24] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.16 [25]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.09

Notes:

[25] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours: Placebo vs Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [26]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	2.1

Notes:

[26] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.055 [27]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.67
upper limit	0.01

Notes:

[27] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours: Placebo vs Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [28]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.88

Notes:

[28] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04 [29]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.37

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	-0.02

Notes:

[29] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours: Placebo vs Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [30]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.69

Notes:

[30] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015 [31]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.79
upper limit	-0.08

Notes:

[31] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Pain Intensity Difference (PID)

End point title	Pain Intensity Difference (PID)[32]

End point description:

PID was derived by subtracting the pain severity score at a given post-dosing time point (pain severity score range 0 [none] to 3 [severe]) from the baseline score (Baseline pain severity score range 2 [moderate] to 3 [severe]). Total possible score range for PID: -1 (worst) to 3 (best). ITT population included all randomized subjects who received study medication and provided a baseline assessment.

End point type	Secondary

End point timeframe:

0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8 hours

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Units on a scale				
arithmetic mean (standard deviation)				
0.25 hours	0 (± 0.4)	0.3 (± 0.5)	0.1 (± 0.5)	
0.5 hours	0 (± 0.5)	1 (± 0.7)	0.6 (± 0.8)	
1 hour	0 (± 0.7)	1.5 (± 0.9)	1.3 (± 0.9)	
1.5 hour	0 (± 0.8)	1.7 (± 0.9)	1.5 (± 0.9)	
2 hours	0 (± 0.9)	1.8 (± 0.9)	1.7 (± 0.9)	
3 hours	0 (± 0.9)	1.6 (± 0.9)	1.7 (± 1)	
4 hours	0.1 (± 1)	1.5 (± 0.9)	1.7 (± 1)	
5hours	0 (± 1)	1.4 (± 1)	1.6 (± 1)	
6 hours	0 (± 0.9)	1.2 (± 1)	1.5 (± 1.1)	
7 hours	0 (± 0.9)	0.9 (± 1)	1.2 (± 1.1)	
8 hours	0 (± 0.8)	0.8 (± 1)	1.1 (± 1.1)	

Statistical analyses

Statistical analysis title	0.25 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [33]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.46

Notes:

[33] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.25 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [34]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	0.34

Notes:

[34] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.5 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [35]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.19

Notes:

[35] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.5 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [36]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.55

Notes:

[36] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hour: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [37]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	1.75

Notes:

[37] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hour: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017 [38]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.25

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.04
upper limit	0.45

Notes:

[38] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [39]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.39
upper limit	1.96

Notes:

[39] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015 [40]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.46

Notes:

[40] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [41]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.41
upper limit	1.98

Notes:

[41] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.362 [42]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	0.3

Notes:

[42] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [43]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.56

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	1.86

Notes:

[43] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.472 [44]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.14

Notes:

[44] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [45]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.7

Notes:

[45] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.134 [46]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.05

Notes:

[46] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [47]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.63

Notes:

[47] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.135 [48]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.17

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	0.05

Notes:

[48] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [49]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.5

Notes:

[49] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036 [50]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	-0.02

Notes:

[50] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [51]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.26

Notes:

[51] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.064 [52]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.01

Notes:

[52] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [53]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.85

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.18

Notes:

[53] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.074 [54]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.02

Notes:

[54] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Sum of Pain Relief Rating and Pain Intensity Difference (PRID)

End point title	Sum of Pain Relief Rating and Pain Intensity Difference

End point description:

PRID was sum of PID and PRR at each post-dosing time point. The overall possible score range, for PRID was -1 (worst) to 7 (best). PID was derived by subtracting the pain severity score at a given post-dosing time point (pain severity score range 0 [none] to 3 [severe]) from the baseline score (Baseline pain severity score range 2 [moderate] to 3 [severe]). Total possible score range for PID: -1 (worst) to 3 (best). PRR was assessed on 5-point categorical pain relief rating scale (0=No relief to 4=Complete relief). ITT population included all randomized subjects who received study medication and provided a baseline assessment.

End point type	Secondary

End point timeframe:

0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8 hours

Notes:

[55] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Units on a scale				
arithmetic mean (standard deviation)				
0.25 hours	0.4 (± 0.9)	1.1 (± 1.2)	0.6 (± 1.1)	
0.5 hours	0.6 (± 1.2)	3 (± 1.7)	2.1 (± 1.8)	
1 hour	0.7 (± 1.6)	4.4 (± 1.8)	3.8 (± 2)	
1.5 hours	0.7 (± 1.8)	4.8 (± 1.8)	4.3 (± 2)	
2 hours	0.8 (± 2)	4.9 (± 1.8)	4.7 (± 2)	
3 hours	0.7 (± 2)	4.5 (± 2)	4.7 (± 2.1)	
4 hours	0.9 (± 2.3)	4.3 (± 2.1)	4.8 (± 2.2)	
5 hours	0.8 (± 2.1)	4 (± 2.2)	4.4 (± 2.2)	
6 hours	0.6 (± 2)	3.5 (± 2.2)	4.1 (± 2.4)	
7 hours	0.5 (± 1.9)	2.9 (± 2.3)	3.5 (± 2.5)	
8 hours	0.5 (± 1.8)	2.6 (± 2.3)	3.2 (± 2.5)	

Statistical analyses

Statistical analysis title	0.25 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [56]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	1.04

Notes:

[56] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.25 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)

Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [57]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	0.75

Notes:

[57] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.5 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [58]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	2.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.82
upper limit	3.01

Notes:

[58] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.5 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [59]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.34

Notes:

[59] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hour: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [60]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	3.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.03
upper limit	4.33

Notes:

[60] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hour:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008 [61]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	1.11

Notes:

[61] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [62]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	4.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.4
upper limit	4.72

Notes:

[62] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017 [63]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	1.06

Notes:

[63] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [64]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	4.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.42
upper limit	4.75

Notes:

[64] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.359 [65]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.7

Notes:

[65] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [66]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	3.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.06
upper limit	4.45

Notes:

[66] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.436 [67]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	3

Notes:

[67] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [68]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.66
upper limit	4.14

Notes:

[68] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.139 [69]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	0.13

Notes:

[69] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [70]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.44
upper limit	3.95

Notes:

[70] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.144 [71]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	0.14

Notes:

[71] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [72]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.01
upper limit	3.58

Notes:

[72] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.043 [73]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.15
upper limit	-0.02

Notes:

[73] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [74]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	2.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.53
upper limit	3.12

Notes:

[74] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044 [75]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.16
upper limit	-0.02

Notes:

[75] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [76]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	2.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.25
upper limit	2.85

Notes:

[76] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.027 [77]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.23
upper limit	-0.08

Notes:

[77] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Time-weighted Sum of Pain Intensity Difference (SPID)

End point title	Time-weighted Sum of Pain Intensity Difference (SPID)[78]

End point description:

SPID: time-weighted sum of PID over 2, 3, 6 and 8 hours. SPID scores range was -2 (worst) to 6 (best) for SPID 0-2, -3 (worst) to 9
(best) for SPID 0-3, -6 (worst) to 18 (best) for SPID 0-6, -8 (worst) to 24 (best) for SPID 0-8. PID: baseline pain severity score minus
pain severity score at a given time point (pain severity score range 0=none to 3=severe; baseline score range 2=moderate to
3=severe). Total score range for PID: -1(worst) to 3 (best). ITT population included all randomized subjects who received study
medication and provided a baseline assessment.

End point type	Secondary

End point timeframe:

0-2, 0-3, 0-6, 0-8 hours

Notes:

[78] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Units on a scale				
arithmetic mean (standard deviation)				
SPID 0-2	0.1 (± 1.3)	2.8 (± 1.4)	2.4 (± 1.5)	
SPID 0-3	0.1 (± 2.1)	4.4 (± 2.2)	4.1 (± 2.3)	
SPID 0-6	0.2 (± 4.8)	8.5 (± 4.7)	8.9 (± 5)	
SPID 0-8	0.1 (± 6.4)	10.2 (± 6.3)	11.1 (± 6.7)	

Statistical analyses

Statistical analysis title	SPID 0-2 : Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.001 [79]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	2.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.27
upper limit	3.18

Notes:

[79] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPID 0-2 :Ibuprofen (Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007 [80]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.78

Notes:

[80] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPID 0-3 :Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and corresponding 95% CI were calculated based on

LS mean from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [81]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	4.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.6
upper limit	4.98

Notes:

[81] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPID 0-3 :Ibuprofen (Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.144 [82]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.87

Notes:

[82] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPID 0-6 :Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen Sodium - placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [83]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	8.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	6.66
upper limit	9.66

Notes:

[83] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPID 0-6 :Ibuprofen (Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.679 [84]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.31
upper limit	0.85

Notes:

[84] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPID 0-8 :Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [85]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	9.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.92
upper limit	11.96

Notes:

[85] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPID 0-8 :Ibuprofen (Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.367 [86]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.12
upper limit	0.79

Notes:

[86] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Time-weighted Sum of Pain Relief Rating (TOTPAR)

End point title	Time-weighted Sum of Pain Relief Rating (TOTPAR)[87]

End point description:

TOTPAR: time-weighted sum of PRR scores over 2, 3, 6 and 8 hours. TOTPAR score range was 0 (worst) to 8 (best) for TOTPAR 0-2,
0 (worst) to 12 (best) for TOTPAR 0-3, 0 (worst) to 24 (best) for TOTPAR 0-6, 0 (worst) to 32 (best) for TOTPAR 0-8. PRR was
evaluated at different time points during the study up to 8 hours, and immediately after taking rescue medication (if necessary).
PRR was assessed on a 5-point categorical pain relief rating scale wherein 0=No relief to 4=Complete relief. ITT population included all randomized subjects who received study medication and provided a baseline assessment.

End point type	Secondary

End point timeframe:

0-2, 0-3, 0-6, 0-8 hours

Notes:

[87] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Units on a scale				
arithmetic mean (standard deviation)				
TOTPAR 0-2	1.3 (± 1.8)	5.2 (± 1.7)	4.6 (± 1.9)	
TOTPAR 0-3	2 (± 2.9)	8.1 (± 2.7)	7.6 (± 2.8)	
TOTPAR 0-6	4.2 (± 6.5)	15.9 (± 6.1)	16.1 (± 6.1)	
TOTPAR 0-8	5.2 (± 8.4)	19.5 (± 8.5)	20.6 (± 8.5)	

Statistical analyses

Statistical analysis title	TOTPAR 0-2 : Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [88]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	3.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.32
upper limit	4.59

Notes:

[88] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	TOTPAR 0-2 :Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS means from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009 [89]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	1.07

Notes:

[89] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	TOTPAR 0-3 :Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and corresponding 95% CI were calculated based on

LS means from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [90]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	6.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.18
upper limit	7.12

Notes:

[90] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	TOTPAR 0-3 :Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS means from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.166 [91]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	1.2

Notes:

[91] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	TOTPAR 0-6 :Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and corresponding 95% CI were calculated based on LS means from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [92]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	11.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	9.54
upper limit	13.81

Notes:

[92] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	TOTPAR 0-6 :Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS means from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.703 [93]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.84
upper limit	1.24

Notes:

[93] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	TOTPAR 0-8:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and corresponding 95% CI were calculated based on LS means from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [94]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	14.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.36
upper limit	17.18

Notes:

[94] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	TOTPAR 0-8:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS means from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.303 [95]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	1

Notes:

[95] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Time-weighted Sum of Pain Relief Rating and Pain Intensity Difference (SPRID)

End point title	Time-weighted Sum of Pain Relief Rating and Pain Intensity Difference (SPRID)[96]

End point description:

SPRID: time-weighted sum of PRID over 2, 3, 6 and 8 hours. SPRID score range:-2 (worst) to 14(best) for SPRID 0-2, -3(worst) to
21(best) for SPRID 0-3, -6(worst) to 42(best) for SPRID 0-6, -8(worst) to 56(best) for SPRID 0-8. PRID: sum of PID and PRR at each
time point. Total score range for PRID: -1=worst to 7=best. PID: baseline pain severity score minus pain severity score at given time (score range 0=none to 3=severe; baseline score range 2=moderate to 3=severe). Total score range for PID: -1(worst) to 3(best), PRR: scored on 5-point pain relief rating scale (0=No relief to 4=Complete relief). ITT population included all randomized subjects who received study medication and provided a baseline assessment.

End point type	Secondary

End point timeframe:

0-2, 0-3, 0-6, 0-8 hours

Notes:

[96] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Units on a scale				
arithmetic mean (standard deviation)				
SPRID 0-2	1.3 (± 2.9)	8 (± 3)	7 (± 3.3)	
SPRID 0-3	2.1 (± 4.8)	12.6 (± 4.7)	11.8 (± 4.9)	
SPRID 0-6	4.4 (± 10.8)	24.3 (± 10.4)	25 (± 10.6)	
SPRID 0-8	5.4 (± 14.1)	29.8 (± 14.2)	31.7 (± 14.6)	

Statistical analyses

Statistical analysis title	SPRID 0-2: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - Placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [97]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	6.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.6
upper limit	7.76

Notes:

[97] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPRID 0-2: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007 [98]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.84

Notes:

[98] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPRID 0-3: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and corresponding 95% CI were calculated based on

LS mean from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [99]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	10.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.79
upper limit	12.08

Notes:

[99] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPRID 0-3: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.152 [100]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	2.05

Notes:

[100] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPRID 0-6: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [101]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	19.83

Confidence interval	
level	95 %
sides	2-sided
lower limit	16.23
upper limit	23.43

Notes:

[101] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPRID 0-6: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69 [102]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.12
upper limit	2.07

Notes:

[102] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	SPRID 0-8: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and corresponding 95% CI were calculated based on LS mean from the ANOVA model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.323 [103]
Method	ANOVA
Parameter estimate	LS mean difference
Point estimate	-1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.29
upper limit	1.75

Notes:

[103] - p-value was calculated using ANOVA model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Cumulative Percentage of Subjects With Meaningful Relief

End point title	Cumulative Percentage of Subjects With Meaningful Relief[104]

End point description:

Percentage of subjects with meaningful relief evaluated by stopping the stopwatch labelled 'meaningful relief' at the moment the subject first began to experience meaningful relief. Stopwatch was active up to 8 hours after dosing or until stopped by the
subject, or rescue medication was administered. ITT population included all randomized subjects who received study medication
and provided a baseline assessment.

End point type	Secondary

End point timeframe:

0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8 hours

Notes:

[104] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Percentage of subjects				
number (not applicable)				
0.25 hours	0	1.1	0.6	
0.5 hours	4.2	28.4	16.8	
1 hour	12.5	73.7	52.6	
1.5 hours	14.6	87.4	69.9	
2 hours	18.8	91.6	79.8	
3 hours	20.8	94.7	86.7	
4 hours	20.8	94.7	87.9	
5 hours	20.8	94.7	87.9	
6 hours	20.8	94.7	87.9	
7 hours	20.8	95.8	87.9	
8 hours	22.9	95.8	88.4	

Statistical analyses

Statistical analysis title	0.25 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on Cochran-Mantel-Haenszel (CMH) adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.49 [105]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	1.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.97
upper limit	3

Notes:

[105] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.25 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.623 [106]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.88
upper limit	2.95

Notes:

[106] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.5 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [107]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	24.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.51
upper limit	35.22

Notes:

[107] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.5 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023 [108]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	11.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	22.48

Notes:

[108] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [109]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	61.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	48.99
upper limit	73.7

Notes:

[109] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [110]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	21.25

Confidence interval	
level	95 %
sides	2-sided
lower limit	9.58
upper limit	32.92

Notes:

[110] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [111]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.59
upper limit	83.71

Notes:

[111] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [112]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	17.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.83
upper limit	27.06

Notes:

[112] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [113]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.14
upper limit	84.11

Notes:

[113] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.013 [114]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	11.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.47
upper limit	19.93

Notes:

[114] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [115]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	73.58

Confidence interval	
level	95 %
sides	2-sided
lower limit	61.83
upper limit	85.33

Notes:

[115] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.041 [116]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	8.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	14.75

Notes:

[116] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [117]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	73.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.83
upper limit	85.33

Notes:

[117] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.073 [118]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	6.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	13.36

Notes:

[118] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [119]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	73.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.83
upper limit	85.33

Notes:

[119] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.073 [120]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	6.79

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	13.36

Notes:

[120] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [121]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	73.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.83
upper limit	85.33

Notes:

[121] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.073 [122]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	6.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	13.36

Notes:

[122] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [123]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	74.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	63.14
upper limit	86.27

Notes:

[123] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035 [124]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	7.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.57
upper limit	14.1

Notes:

[124] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [125]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.61

Confidence interval	
level	95 %
sides	2-sided
lower limit	61.05
upper limit	84.17

Notes:

[125] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047 [126]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	7.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	13.48

Notes:

[126] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Cumulative Percentage of Subjects With Confirmed First Perceptible Relief

End point title	Cumulative Percentage of Subjects With Confirmed First Perceptible Relief[127]

End point description:

Percentage of subjects with first perceptible relief was evaluated by stopping a stopwatch labelled 'first perceptible relief' at the
moment the subject first began to experience any relief. Stopwatch was active up to 8 hours after dosing or until stopped by the
subject, or rescue medication was administered. The first perceptible relief was considered confirmed if the subject also stopped
the second stopwatch indicating meaningful relief. ITT population included all randomized subjects who received study medication and provided a baseline assessment.

End point type	Secondary

End point timeframe:

0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8 hours

Notes:

[127] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Percentage of subjects				
number (not applicable)				
0.25 hours	6.3	26.3	12.1	
0.5 hours	14.6	84.2	60.7	
1 hour	20.8	94.7	84.4	
1.5 hours	22.9	95.8	87.3	
2 hours	22.9	95.8	87.9	
3 hours	22.9	95.8	88.4	
4 hours	22.9	95.8	88.4	
5 hours	22.9	95.8	88.4	
6 hours	22.9	95.8	88.4	
7 hours	22.9	95.8	88.4	
8 hours	22.9	95.8	88.4	

Statistical analyses

Statistical analysis title	0.25 hours: Placebo vs. Ibuprofen Sodium
Statistical analysis description:	
Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.	
Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [128]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	20.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.79
upper limit	31.24

Notes:

[128] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.25 hours: Ibuprofen(Sodium vs Advil + Motrin IB)
Statistical analysis description:	
Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.	
Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)

Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003 [129]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	14.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.26
upper limit	24.43

Notes:

[129] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.5 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [130]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	69.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	57.67
upper limit	81.4

Notes:

[130] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.5 hours: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [131]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	23.45

Confidence interval	
level	95 %
sides	2-sided
lower limit	13.16
upper limit	33.75

Notes:

[131] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [132]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	73.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	62.77
upper limit	84.67

Notes:

[132] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hour: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014 [133]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	10.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.21
upper limit	17.08

Notes:

[133] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hour: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [134]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.05
upper limit	84.17

Notes:

[134] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hour: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.028 [135]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	8.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.02
upper limit	14.68

Notes:

[135] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hour: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [136]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.61

Confidence interval	
level	95 %
sides	2-sided
lower limit	61.05
upper limit	84.17

Notes:

[136] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hour: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036 [137]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	7.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.54
upper limit	14.08

Notes:

[137] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hour: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [138]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.05
upper limit	84.17

Notes:

[138] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hour: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047 [139]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	7.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	13.48

Notes:

[139] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hour: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [140]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.05
upper limit	84.17

Notes:

[140] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hour: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047 [141]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	7.28

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	13.48

Notes:

[141] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hour: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [142]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.05
upper limit	84.17

Notes:

[142] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hour: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047 [143]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	7.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	13.48

Notes:

[143] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hour: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [144]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.05
upper limit	84.17

Notes:

[144] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hour: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047 [145]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	7.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	13.48

Notes:

[145] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hour: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [146]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.61

Confidence interval	
level	95 %
sides	2-sided
lower limit	61.05
upper limit	84.17

Notes:

[146] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hour: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047 [147]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	7.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	13.48

Notes:

[147] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hour: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [148]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	72.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.05
upper limit	84.17

Notes:

[148] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hour: Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium - Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.047 [149]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	7.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	13.48

Notes:

[149] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Time to Treatment Failure

End point title	Time to Treatment Failure[150]

End point description:

Median time of dropping out of the subjects from the study due to lack of efficacy or rescue medication, whichever came first. ITT
population included all randomized subjects who received study medication and provided a baseline assessment. 99999 here
indicates median because data was not summarized as median time to meaningful relief was >8 hours for ibuprofen sodium group and >8 hours for ibuprofen (Advil + Motrin IB) group. -99999 and 99999 indicates lower and upper limits of 95% CI as CI was not estimable.

End point type	Secondary

End point timeframe:

0 to 8 hours

Notes:

[150] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Hours				
median (confidence interval 95%)	1.7 (1.6 to 2.1)	99999 (-99999 to 99999)	99999 (-99999 to 99999)	

Statistical analyses

Statistical analysis title	Placebo vs. Ibuprofen Sodium

Statistical analysis description:

HR and corresponding 95% CI were calculated based on the Wald statistic from the PH model.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [151]
Method	Proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08
upper limit	0.22

Notes:

[151] - p-value was calculated using PH model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	Ibuprofen Sodium vs. Ibuprofen (Advil + Motrin IB)

Statistical analysis description:

HR and corresponding 95% CI were calculated based on the Wald statistic from the PH model.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.281 [152]
Method	Proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	2.22

Notes:

[152] - p-value was calculated using PH model with treatment, baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Cumulative Percentage of Subjects With Treatment Failure

End point title	Cumulative Percentage of Subjects With Treatment Failure[153]

End point description:

Percentage of Subjects who withdrew from the study due to lack of efficacy or received rescue medication. ITT population included all randomized Subjects who received study medication and provided a baseline assessment.

End point type	Secondary

End point timeframe:

0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8 hours

Notes:

[153] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with

Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Percentage of subjects				
number (not applicable)				
0.25 hours	0	0	0	
0.5 hours	0	0	0	
1 hour	0	0	0	
1.5 hours	25	1.1	2.3	
2 hours	54.2	2.1	5.8	
3 hours	70.8	4.2	8.1	
4 hours	70.8	9.5	8.1	
5 hours	70.8	10.5	10.4	
6 hours	72.9	13.7	12.1	
7 hours	77.1	20	16.2	
8 hours	79.2	26.3	20.2	

Statistical analyses

Statistical analysis title	1.5 hours: Placebo vs. Ibuprofen Sodium
Statistical analysis description:	
Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.	
Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [154]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-23.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.67
upper limit	-11.2
Notes:	
[154] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).	

Statistical analysis title	1.5 hours: Ibuprofen(Sodium vs Advil + Motrin IB)
Statistical analysis description:	
Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.	
Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)

Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.483 [155]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.12
upper limit	1.7

Notes:

[155] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours: Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [156]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-51.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-65.63
upper limit	38.22

Notes:

[156] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.174 [157]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-3.61

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.97
upper limit	0.75

Notes:

[157] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [158]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-66.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-79.8
upper limit	-53.35

Notes:

[158] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.24 [159]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-3.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.38
upper limit	1.89

Notes:

[159] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [160]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-61.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-75.21
upper limit	-47.5

Notes:

[160] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.668 [161]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.47
upper limit	8.52

Notes:

[161] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [162]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-60.31

Confidence interval	
level	95 %
sides	2-sided
lower limit	-74.28
upper limit	-46.34

Notes:

[162] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.98 [163]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.44
upper limit	7.63

Notes:

[163] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [164]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-59.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-73.05
upper limit	-45.5

Notes:

[164] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.711 [165]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.68
upper limit	9.81

Notes:

[165] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [166]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-56.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-70.84
upper limit	-42.85

Notes:

[166] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

7 hours: Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.445 [167]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	3.72

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.94
upper limit	13.38

Notes:

[167] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [168]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-52.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-66.77
upper limit	-38.81

Notes:

[168] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.256 [169]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	6.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.75
upper limit	16.84

Notes:

[169] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Cumulative Percentage of Subjects With Complete Relief

End point title	Cumulative Percentage of Subjects With Complete Relief[170]

End point description:

Complete relief was defined as a PRR of 4. PRR was assessed on a 5-point categorical pain relief rating scale where 0=No relief to
4=Complete relief. ITT population included all randomized subjects who received study medication and provided a baseline
assessment.

End point type	Secondary

End point timeframe:

0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8 hours

Notes:

[170] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: Percentage of subjects				
number (not applicable)				
0.25 hours	0	0	0	
0.5 hours	0	6.3	3.5	
1 hour	0	27.4	20.8	
1.5 hours	0	41.1	32.4	
2 hours	0	48.4	43.9	
3 hours	0	52.6	54.9	
4 hours	6.3	54.7	61.8	
5 hours	6.3	54.7	63	
6 hours	6.3	54.7	63.6	
7 hours	6.3	54.7	64.2	
8 hours	6.3	54.7	64.2	

Statistical analyses

Statistical analysis title	0.5 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium - placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.078 [171]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	6.34

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.34
upper limit	11.34

Notes:

[171] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	0.5 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.303 [172]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	2.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.01
upper limit	8.49

Notes:

[172] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [173]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	27.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.14
upper limit	36.34

Notes:

[173] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.217 [174]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	6.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.31
upper limit	17.63

Notes:

[174] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [175]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	41.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.2
upper limit	51.12

Notes:

[175] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	1.5 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.149 [176]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	8.86

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.33
upper limit	21.04

Notes:

[176] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [177]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	48.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	38.49
upper limit	58.73

Notes:

[177] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	2 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.477 [178]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	4.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.03
upper limit	17.13

Notes:

[178] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [179]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	52.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	42.63
upper limit	62.99

Notes:

[179] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	3 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.739 [180]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-2.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.77
upper limit	10.5

Notes:

[180] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [181]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	48.53

Confidence interval	
level	95 %
sides	2-sided
lower limit	36.29
upper limit	60.77

Notes:

[181] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	4 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.28 [182]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.24
upper limit	5.65

Notes:

[182] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [183]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	48.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	36.29
upper limit	60.77

Notes:

[183] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	5 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.202 [184]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-8.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.44
upper limit	4.41

Notes:

[184] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [185]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	48.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	36.29
upper limit	60.77

Notes:

[185] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	6 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.17 [186]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-8.61

Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.02
upper limit	3.8

Notes:

[186] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [187]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	48.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	36.29
upper limit	60.77

Notes:

[187] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	7 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14 [188]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-9.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.62
upper limit	3.16

Notes:

[188] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours:Placebo vs. Ibuprofen Sodium

Statistical analysis description:

Treatment difference (Ibuprofen sodium – placebo) and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [189]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	48.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	36.29
upper limit	60.77

Notes:

[189] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	8 hours:Ibuprofen(Sodium vs Advil + Motrin IB)

Statistical analysis description:

Treatment difference [Ibuprofen sodium – Ibuprofen (Advil + Motrin IB)] and its associated 95% CI was calculated based on CMH adjusted proportions and the corresponding standard error.

Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14 [190]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in proportion
Point estimate	-9.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.62
upper limit	3.16

Notes:

[190] - p-value was calculated using CMH test which was adjusted for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Secondary: Subject Global Evaluation of Study Medication

End point title	Subject Global Evaluation of Study Medication[191]

End point description:

Subject global evaluation of study medication was performed at the 8-hour time point or immediately before taking the rescue
medication. It was scored on a 6-point categorical scale where 0 = Very poor, 1 = Poor, 2 = Fair, 3 = Good, 4 = Very Good, and 5 =
Excellent. ITT population included all randomized subjects who received study medication and provided a baseline assessment.

End point type	Secondary

End point timeframe:

8 hours

Notes:

[191] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical comparison between the two standard ibuprofen tablets (Advil vs Motrin) is not an objective of this study, so pooled data of Ibuprofen (Advil + Motrin IB) was compared with Placebo and Ibuprofen Sodium.

End point values	Placebo	Ibuprofen Sodium	Ibuprofen (Advil + Motrin IB)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	48	95	173	
Units: subjects				
arithmetic mean (standard deviation)	1.1 (± 1.3)	3.8 (± 1)	3.7 (± 1.2)	

Statistical analyses

Statistical analysis title	Placebo vs. Ibuprofen Sodium
Statistical analysis description:	
Treatment difference (Ibuprofen sodium - placebo) and the associated CI were calculated based on the weighted Gamma statistic.	
Comparison groups	Placebo v Ibuprofen Sodium
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [192]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Mean difference (final values)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	0.98

Notes:

[192] - p-value was calculated using CMH test with modified ridit scores, controlling for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Statistical analysis title	Ibuprofen Sodium vs. Ibuprofen (Advil + Motrin IB)
Statistical analysis description:	
HR and corresponding 95% CI were calculated based on the Wald statistic from the PH model.	
Comparison groups	Ibuprofen Sodium v Ibuprofen (Advil + Motrin IB)
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.667 [193]
Method	Proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.24

Notes:

[193] - p-value was calculated using CMH test with modified ridit scores, controlling for baseline PSR and gender terms. Statistical testing was done at 5% significance level (2-sided).

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
Baseline up to 8 hours (End of study)	
Adverse event reporting additional description:	
EU BR specific AE tables were generated separately as per EU format using latest coding.	
Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Single oral dose of 2 placebo tablets.	
Reporting group title	Ibuprofen Sodium
Reporting group description:	
Single oral dose of 2 ibuprofen sodium 256 mg tablets, equivalent to 400 mg ibuprofen.	
Reporting group title	Ibuprofen (Advil)
Reporting group description:	
Single oral dose of 2 ibuprofen (Advil) 200 mg tablets (total dose of 400 mg ibuprofen).	
Reporting group title	Ibuprofen (Motrin IB)
Reporting group description:	
Single oral dose of 2 ibuprofen [Motrin ibuprofen (IB)] 200 mg tablets (total dose of 400 mg ibuprofen).	

Serious adverse events	Placebo	Ibuprofen Sodium	Ibuprofen (Advil)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	0 / 86 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Ibuprofen (Motrin IB)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 87 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Placebo	Ibuprofen Sodium	Ibuprofen (Advil)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 48 (16.67%)	10 / 95 (10.53%)	12 / 86 (13.95%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 48 (2.08%)	1 / 95 (1.05%)	3 / 86 (3.49%)
occurrences (all)	1	1	3
Headache			
subjects affected / exposed	1 / 48 (2.08%)	1 / 95 (1.05%)	4 / 86 (4.65%)
occurrences (all)	1	1	4
Lethargy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 48 (2.08%)	0 / 95 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Feeling cold			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Feeling hot			
subjects affected / exposed	2 / 48 (4.17%)	1 / 95 (1.05%)	0 / 86 (0.00%)
occurrences (all)	2	1	0

Pyrexia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 95 (1.05%)	0 / 86 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 48 (2.08%)	0 / 95 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Gastric disorder			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	5 / 48 (10.42%)	7 / 95 (7.37%)	6 / 86 (6.98%)
occurrences (all)	5	7	6
Vomiting			
subjects affected / exposed	2 / 48 (4.17%)	2 / 95 (2.11%)	3 / 86 (3.49%)
occurrences (all)	2	2	3
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	0 / 86 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 48 (0.00%)	0 / 95 (0.00%)	1 / 86 (1.16%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 48 (2.08%)	0 / 95 (0.00%)	0 / 86 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Ibuprofen (Motrin		

	IB)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 87 (11.49%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	2 / 87 (2.30%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 87 (3.45%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	3 / 87 (3.45%)		
occurrences (all)	3		
Lethargy			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences (all)	1		
Chest discomfort			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		
Feeling cold			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		
Feeling hot			
subjects affected / exposed	2 / 87 (2.30%)		
occurrences (all)	2		

Pyrexia			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences (all)	1		
Gastric disorder			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	3 / 87 (3.45%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	2 / 87 (2.30%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol?   No

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Interruptions (globally)

Were there any global interruptions to the trial?   No

Limitations and caveats

 None reported