Clinical trial results:
Double-blind, randomised, placebo and active controlled, parallel group study to evaluate the analgesic effect of a single oral administration of four different combination doses of DKP.TRIS with TRAM.HCl in comparison with the single agents, on moderate to severe pain following impacted third mandibular molar tooth extraction

Summary

EudraCT number	2010-022798-32
Trial protocol	GB DE ES HU IT PL
Global end of trial date	14 October 2011

Results information

Result version number	v1 (current)
This version publication date	03 November 2018
First version publication date	03 November 2018

Trial information

Trial identification

Sponsor protocol code	DEX-TRA 02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01307020
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Menarini Ricerche S.p.A
Sponsor organisation address	Via Sette Santi, 1, Flrorence, Italy, 50131
Public contact	Corporate Director, Clinical Sciences, Menarini Ricerche, S.p.A, Menarini Ricerche, S.p.A, 39 05556809990, acapriati@menarini-ricerche.it
Scientific contact	Corporate Director, Clinical Sciences, Menarini Ricerche, S.p.A, Menarini Ricerche, S.p.A, 39 05556809990, acapriati@menarini-ricerche.it

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 October 2011
Global end of trial reached?	Yes
Global end of trial date	14 October 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the analgesic efficacy of DKP.TRIS and TRAM.HCl given as fixed combinations and the analgesic efficacy of each single component in comparison to placebo on moderate to severe pain following impacted third mandibular molar tooth extraction. Ibuprofen will be used as an active control to validate the pain model.

Protection of trial subjects:

If any event(s) related to the conduct of the study or the development of the IMP affected the safety of the study participants, the Sponsor and the investigator would have taken appropriate urgent safety measures to protect the subjects against any immediate hazard. The CA and IRB/EC would have been informed forthwith about these new events and the measures taken. For subjects participating in the study, Menarini Ricerche S.p.A. stipulated an insurance policy in accordance with local regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 February 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 51
Country: Number of subjects enrolled	Spain: 141
Country: Number of subjects enrolled	United Kingdom: 180
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Hungary: 129
Country: Number of subjects enrolled	Italy: 94
Worldwide total number of subjects	611
EEA total number of subjects	611

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)	0
Adults (18-64 years)	611
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient in (screening) 23 Feb 2011, last patient out 14 Oct 2011. At 16 study centres in 6 European countries (Germany, Italy, Hungary, Poland, Spain and United Kingdom).

Pre-assignment

Screening details:

The trial encompassed 3 visits: 1-Screening; 2-Dental surgery (patients who have moderate to severe pain afterwards were randomised and received study drug); 3-End of study. Overall, 745 patients were enrolled (screened), of them 611 were randomized to receive the study drug and therefore considered as started.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo, oral film-coated table, once

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo oral film-coated tablet, once

Arm title	Ibuprofen

Arm description:

Ibuprofen 400 mg, oral film-coated table, once

Arm type	Active comparator
Investigational medicinal product name	Ibuprofen 400 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Ibuprofen 400 mg, oral film-coated table, once

Arm title	TRAM.HCl 75mg

Arm description:

Tramadol Hydrochloride high dose, oral film-coated table, once

Arm type	Active comparator

Investigational medicinal product name	TRAM.HCl 75mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

TRAM.HCl 75mg, oral film-coated table, once

Arm title	TRAM.HCl 37.5mg

Arm description:

Tramadol Hydrochloride low dose, oral film-coated table, once

Arm type	Active comparator
Investigational medicinal product name	TRAM.HCl 37.5mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

TRAM.HCl 37.5mg, oral film-coated tablet, once

Arm title	DKP-TRIS 25mg

Arm description:

Dexketoprofen Trometamol high dose, oral film-coated table, once

Arm type	Active comparator
Investigational medicinal product name	DKP-TRIS 25mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

DKP-TRIS 25mg, oral film-coated tablet, once

Arm title	DKP-TRIS 12.5mg

Arm description:

Dexketoprofen Trometamol low dose, oral film-coated table, once

Arm type	Active comparator
Investigational medicinal product name	DKP-TRIS 12.5mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

DKP-TRIS 12.5mg, oral film-coated tablet, once

Arm title	DKP-TRIS 25mg - TRAM.HCl 75mg

Arm description:

Dexketoprofen Trometamol high dose + Tramadol Hydrochloride high dose, oral film-coated table, once

Arm type	Experimental
Investigational medicinal product name	DKP-TRIS 25mg - TRAM.HCl 75mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

DKP-TRIS 25mg - TRAM.HCl 75mg,oral film-coated tablet, once

Arm title	DKP-TRIS 25mg - TRAM.HCl 37.5mg
Arm description:	
Dexketoprofen Trometamol high dose + Tramadol Hydrochloride low dose, oral film-coated table, once	
Arm type	Experimental
Investigational medicinal product name	Dexketoprofen Trometamol high dose + Tramadol Hydrochloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Dexketoprofen Trometamol high dose + Tramadol Hydrochloride low dose, oral film-coated table, once

Arm title	DKP-TRIS 12.5mg - TRAM.HCl 75mg
Arm description:	
Dexketoprofen Trometamol low dose + Tramadol Hydrochloride high dose, oral film-coated table, once	
Arm type	Experimental
Investigational medicinal product name	DKP-TRIS 12.5mg - TRAM.HCl 75mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

DKP-TRIS 12.5mg - TRAM.HCl 75mg oral film-coated tablet, once

Arm title	DKP-TRIS 12.5mg - TRAM.HCl 37.5mg
Arm description:	
Dexketoprofen Trometamol low dose + Tramadol Hydrochloride low dose, oral film-coated table, once	
Arm type	Experimental
Investigational medicinal product name	DKP-TRIS 12.5mg - TRAM.HCl 37.5mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

DKP-TRIS 12.5mg - TRAM.HCl 37.5mg, oral Film-coated tablet, once

Number of subjects in period 1	Placebo	Ibuprofen	TRAM.HCl 75mg
Started	62	61	60
Completed	62	61	60
Not completed	0	0	0
Failure of eDiary	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	TRAM.HCl 37.5mg	DKP-TRIS 25mg	DKP-TRIS 12.5mg
Started	59	61	60
Completed	58	61	60
Not completed	1	0	0
Failure of eDiary	-	-	-
Lost to follow-up	1	-	-

Number of subjects in period 1	DKP-TRIS 25mg - TRAM.HCl 75mg	DKP-TRIS 25mg - TRAM.HCl 37.5mg	DKP-TRIS 12.5mg - TRAM.HCl 75mg
Started	61	63	63
Completed	60	62	62
Not completed	1	1	1
Failure of eDiary	-	-	1
Lost to follow-up	1	1	-

Number of subjects in period 1	DKP-TRIS 12.5mg - TRAM.HCl 37.5mg
Started	61
Completed	61
Not completed	0
Failure of eDiary	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo, oral film-coated table, once	
Reporting group title	Ibuprofen
Reporting group description:	
Ibuprofen 400 mg, oral film-coated table, once	
Reporting group title	TRAM.HCl 75mg
Reporting group description:	
Tramadol Hydrochloride high dose, oral film-coated table, once	
Reporting group title	TRAM.HCl 37.5mg
Reporting group description:	
Tramadol Hydrochloride low dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 25mg
Reporting group description:	
Dexketoprofen Trometamol high dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 12.5mg
Reporting group description:	
Dexketoprofen Trometamol low dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 25mg - TRAM.HCl 75mg
Reporting group description:	
Dexketoprofen Trometamol high dose + Tramadol Hydrochloride high dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 25mg - TRAM.HCl 37.5mg
Reporting group description:	
Dexketoprofen Trometamol high dose + Tramadol Hydrochloride low dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 12.5mg - TRAM.HCl 75mg
Reporting group description:	
Dexketoprofen Trometamol low dose + Tramadol Hydrochloride high dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 12.5mg - TRAM.HCl 37.5mg
Reporting group description:	
Dexketoprofen Trometamol low dose + Tramadol Hydrochloride low dose, oral film-coated table, once	

Reporting group values	Placebo	Ibuprofen	TRAM.HCl 75mg
Number of subjects	62	61	60
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age continuous			
Units: years			
arithmetic mean	26.1	26.6	27.8
standard deviation	± 6.64	± 6.48	± 7.99
Gender categorical			
Units: Subjects			
Female	33	41	28
Male	29	20	32
BMI			
Units: Kg/m^2			
arithmetic mean	22.7	22.4	24.2
standard deviation	± 2.80	± 3.04	± 3.08

Reporting group values	TRAM.HCl 37.5mg	DKP-TRIS 25mg	DKP-TRIS 12.5mg
Number of subjects	59	61	60
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	25.5	26.9	27.0
standard deviation	± 7.15	± 6.94	± 9.85
Gender categorical			
Units: Subjects			
Female	38	44	36
Male	21	17	24
BMI			
Units: Kg/m^2			
arithmetic mean	23.0	23.5	23.6
standard deviation	± 3.19	± 3.30	± 3.20

Reporting group values	DKP-TRIS 25mg - TRAM.HCl 75mg	DKP-TRIS 25mg - TRAM.HCl 37.5mg	DKP-TRIS 12.5mg - TRAM.HCl 75mg
Number of subjects	61	63	63
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			

Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	27.3	26.3	26.9
standard deviation	± 7.55	± 7.33	± 7.62
Gender categorical			
Units: Subjects			
Female	34	36	39
Male	27	27	24
BMI			
Units: Kg/m^2			
arithmetic mean	23.2	23.0	24.1
standard deviation	± 3.19	± 2.87	± 3.69

Reporting group values	DKP-TRIS 12.5mg - TRAM.HCl 37.5mg	Total	
Number of subjects	61	611	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
arithmetic mean	28.6		
standard deviation	± 7.64	-	
Gender categorical			
Units: Subjects			
Female	35	364	
Male	26	247	
BMI			
Units: Kg/m^2			
arithmetic mean	23.7		
standard deviation	± 3.39	-	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo, oral film-coated table, once	
Reporting group title	Ibuprofen
Reporting group description: Ibuprofen 400 mg, oral film-coated table, once	
Reporting group title	TRAM.HCl 75mg
Reporting group description: Tramadol Hydrochloride high dose, oral film-coated table, once	
Reporting group title	TRAM.HCl 37.5mg
Reporting group description: Tramadol Hydrochloride low dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 25mg
Reporting group description: Dexketoprofen Trometamol high dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 12.5mg
Reporting group description: Dexketoprofen Trometamol low dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 25mg - TRAM.HCl 75mg
Reporting group description: Dexketoprofen Trometamol high dose + Tramadol Hydrochloride high dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 25mg - TRAM.HCl 37.5mg
Reporting group description: Dexketoprofen Trometamol high dose + Tramadol Hydrochloride low dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 12.5mg - TRAM.HCl 75mg
Reporting group description: Dexketoprofen Trometamol low dose + Tramadol Hydrochloride high dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 12.5mg - TRAM.HCl 37.5mg
Reporting group description: Dexketoprofen Trometamol low dose + Tramadol Hydrochloride low dose, oral film-coated table, once	

Primary: Percentage of Patients Achieving at Least 50 % of the Theoretical Maximum Total Pain Relief Score at 6 Hours Post-dosing

End point title	Percentage of Patients Achieving at Least 50 % of the Theoretical Maximum Total Pain Relief Score at 6 Hours Post-dosing

End point description:

Pain relief is measured by a verbal rating scale (ranging from 0=none to 4=complete). Theoretical maximum TOTPAR at 6 hours is calculated by summing up the maximum score of analgesia which the patient can attribute at defined time points along 6 hour (maxTOTPAR6h= 24). Unit of measure is %

End point type	Primary

End point timeframe:

6 hours

End point values	Placebo	Ibuprofen	TRAM.HCl 75mg	TRAM.HCl 37.5mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	60	59	59
Units: percent of patients				
number (not applicable)	9.7	45.0	25.4	10.2

End point values	DKP-TRIS 25mg	DKP-TRIS 12.5mg	DKP-TRIS 25mg - TRAM.HCl	DKP-TRIS 25mg - TRAM.HCl
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	60	61	63
Units: percent of patients				
number (not applicable)	55.0	26.7	72.1	55.6

End point values	DKP-TRIS 12.5mg - TRAM.HCl	DKP-TRIS 12.5mg - TRAM.HCl		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	60		
Units: percent of patients				
number (not applicable)	59.7	36.7		

Statistical analyses

Statistical analysis title	% of responders (at least 50% max TOTPAR) over 6 h
Comparison groups	Placebo v Ibuprofen v TRAM.HCl 75mg v TRAM.HCl 37.5mg v DKP-TRIS 25mg v DKP-TRIS 12.5mg v DKP-TRIS 25mg - TRAM.HCl 75mg v DKP-TRIS 25mg - TRAM.HCl 37.5mg v DKP-TRIS 12.5mg - TRAM.HCl 75mg v DKP-TRIS 12.5mg - TRAM.HCl 37.5mg
Number of subjects included in analysis	606
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared

Secondary: Percentage of Patients Achieving at Least 50 % of the Theoretical Maximum Total Pain Relief Score at 4, 8 and 12 Hours Post-dosing.

End point title	Percentage of Patients Achieving at Least 50 % of the Theoretical Maximum Total Pain Relief Score at 4, 8 and 12

	Hours Post-dosing.

End point description:

Pain relief is measured by a verbal rating scale (ranging from 0=none to 4=complete). Theoretical maximum TOTPAR at 6 hours is calculated by summing up the maximum score of analgesia which the patient can attribute at defined time points along 4, 8 and 12 hours(maxTOTPAR4h= 16, maxTOTPAR8h= 32 and maxTOTPAR12h= 48, respectively) Unit of measure is %

End point type	Secondary

End point timeframe:

4, 8 and 12 hours

End point values	Placebo	Ibuprofen	TRAM.HCl 75mg	TRAM.HCl 37.5mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	60	59	59
Units: percent of patients				
number (not applicable)				
at 4 hours post-dose	6.5	56.7	23.7	11.9
at 8 hours post- dose	6.5	33.3	20.3	6.8
at 12 hours post- dose	6.5	25.0	15.3	5.1

End point values	DKP-TRIS 25mg	DKP-TRIS 12.5mg	DKP-TRIS 25mg - TRAM.HCl	DKP-TRIS 25mg - TRAM.HCl
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	60	61	63
Units: percent of patients				
number (not applicable)				
at 4 hours post-dose	65.0	40.0	78.7	65.1
at 8 hours post- dose	31.7	16.7	54.1	44.4
at 12 hours post- dose	13.3	10.0	37.7	28.6

End point values	DKP-TRIS 12.5mg - TRAM.HCl	DKP-TRIS 12.5mg - TRAM.HCl		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	60		
Units: percent of patients				
number (not applicable)				
at 4 hours post-dose	72.6	63.3		
at 8 hours post- dose	48.4	21.7		
at 12 hours post- dose	35.5	11.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Patients Using Rescue Medication at 6 Hours

End point title	Percentage of Patients Using Rescue Medication at 6 Hours

End point description:

Percentage of patients using rescue medication at 6 hours post-dosing.

End point type	Secondary

End point timeframe:

Baseline to 6 hours

End point values	Placebo	Ibuprofen	TRAM.HCl 75mg	TRAM.HCl 37.5mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	60	59	59
Units: percentage of patients				
number (not applicable)	72.6	48.3	64.4	69.5

End point values	DKP-TRIS 25mg	DKP-TRIS 12.5mg	DKP-TRIS 25mg - TRAM.HCl	DKP-TRIS 25mg - TRAM.HCl
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	60	61	63
Units: percentage of patients				
number (not applicable)	53.3	65.0	37.7	39.7

End point values	DKP-TRIS 12.5mg - TRAM.HCl	DKP-TRIS 12.5mg - TRAM.HCl		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62	60		
Units: percentage of patients				
number (not applicable)	46.8	66.7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 10 ± 3 days	
Adverse event reporting additional description: Analyzed for the Safety population (all patients who received study treatment)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo, oral film- coated table, once	
Reporting group title	Ibuprofen
Reporting group description: Ibuprofen 400 mg, oral film-coated table, once	
Reporting group title	TRAM.HCl 75mg
Reporting group description: Tramadol Hydrochloride high dose,oral film-coated table, once	
Reporting group title	TRAM.HCl 37.5mg
Reporting group description: Tramadol Hydrochloride low dose,oral film-coated table, once	
Reporting group title	DKP-TRIS 25mg
Reporting group description: Dexketoprofen Trometamol high dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 25mg - TRAM.HCl 75mg
Reporting group description: Dexketoprofen Trometamol high dose + Tramadol Hydrochloride high dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 25mg - TRAM.HCl 37.5mg
Reporting group description: Dexketoprofen Trometamol high dose + Tramadol Hydrochloride low dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 12.5mg - TRAM.HCl 75mg
Reporting group description: Dexketoprofen Trometamol low dose + Tramadol Hydrochloride high dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 12.5mg - TRAM.HCl 37.5mg
Reporting group description: Dexketoprofen Trometamol low dose + Tramadol Hydrochloride low dose, oral film-coated table, once	
Reporting group title	DKP-TRIS 12.5mg
Reporting group description: -	

Serious adverse events	Placebo	Ibuprofen	TRAM.HCl 75mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 62 (0.00%)	0 / 61 (0.00%)	1 / 60 (1.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from			

adverse events			
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 62 (0.00%)	0 / 61 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	TRAM.HCl 37.5mg	DKP-TRIS 25mg	DKP-TRIS 25mg - TRAM.HCl 75mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 59 (0.00%)	0 / 61 (0.00%)	0 / 61 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 59 (0.00%)	0 / 61 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DKP-TRIS 25mg - TRAM.HCl 37.5mg	DKP-TRIS 12.5mg - TRAM.HCl 75mg	DKP-TRIS 12.5mg - TRAM.HCl 37.5mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 61 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DKP-TRIS 12.5mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Dizziness			

subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Ibuprofen	TRAM.HCl 75mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 62 (1.61%)	5 / 61 (8.20%)	14 / 60 (23.33%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 62 (1.61%)	2 / 61 (3.28%)	4 / 60 (6.67%)
occurrences (all)	1	2	4
Headache			
subjects affected / exposed	0 / 62 (0.00%)	1 / 61 (1.64%)	2 / 60 (3.33%)
occurrences (all)	0	1	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 61 (1.64%)	3 / 60 (5.00%)
occurrences (all)	0	1	3
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 62 (0.00%)	0 / 61 (0.00%)	6 / 60 (10.00%)
occurrences (all)	0	0	7
Vomiting			
subjects affected / exposed	0 / 62 (0.00%)	2 / 61 (3.28%)	5 / 60 (8.33%)
occurrences (all)	0	2	5

Non-serious adverse events	TRAM.HCl 37.5mg	DKP-TRIS 25mg	DKP-TRIS 25mg - TRAM.HCl 75mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 59 (8.47%)	4 / 61 (6.56%)	10 / 61 (16.39%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 59 (3.39%)	0 / 61 (0.00%)	3 / 61 (4.92%)
occurrences (all)	2	0	3
Headache			

subjects affected / exposed	3 / 59 (5.08%)	0 / 61 (0.00%)	0 / 61 (0.00%)
occurrences (all)	3	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 59 (1.69%)	2 / 61 (3.28%)	3 / 61 (4.92%)
occurrences (all)	1	2	3
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 59 (1.69%)	1 / 61 (1.64%)	4 / 61 (6.56%)
occurrences (all)	1	1	4
Vomiting			
subjects affected / exposed	0 / 59 (0.00%)	2 / 61 (3.28%)	5 / 61 (8.20%)
occurrences (all)	0	2	6

Non-serious adverse events	DKP-TRIS 25mg - TRAM.HCl 37.5mg	DKP-TRIS 12.5mg - TRAM.HCl 75mg	DKP-TRIS 12.5mg - TRAM.HCl 37.5mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 63 (9.52%)	9 / 63 (14.29%)	7 / 61 (11.48%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 63 (1.59%)	5 / 63 (7.94%)	1 / 61 (1.64%)
occurrences (all)	1	5	1
Headache			
subjects affected / exposed	2 / 63 (3.17%)	1 / 63 (1.59%)	0 / 61 (0.00%)
occurrences (all)	2	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	3 / 61 (4.92%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 63 (1.59%)	4 / 63 (6.35%)	4 / 61 (6.56%)
occurrences (all)	2	4	4
Vomiting			
subjects affected / exposed	3 / 63 (4.76%)	4 / 63 (6.35%)	3 / 61 (4.92%)
occurrences (all)	3	4	4

Non-serious adverse events	DKP-TRIS 12.5mg		

Total subjects affected by non-serious adverse events subjects affected / exposed	2 / 60 (3.33%)		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 0 / 60 (0.00%) 0 0 / 60 (0.00%) 0		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	 0 / 60 (0.00%) 0		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 2 / 60 (3.33%) 2 0 / 60 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported