Clinical trial results:
Paracetamol or NSAID's in acute musculoskeletal syndromes

Summary

EudraCT number	2013-000381-11
Trial protocol	NL
Global end of trial date	01 August 2016

Results information

Result version number	v1 (current)
This version publication date	02 December 2021
First version publication date	02 December 2021
Summary attachment (see zip file)	Journal article (PanAM Ann Emerg Med.pdf)

Trial information

Trial identification

Sponsor protocol code	NL42823.018.13

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Nederlands Trial Register: NTR3982

Notes:

Sponsors

Sponsor organisation name	Amsterdam UMC location AMC
Sponsor organisation address	Meibergdreef 9, Amsterdam, Netherlands,
Public contact	Emergency Department, Academisch Medisch Centrum, 0031 0205663336, m.l.ridderikhof@amc.uva.nl
Scientific contact	Emergency Department, Academisch Medisch Centrum, 0031 0205663336, m.l.ridderikhof@amc.uva.nl

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	31 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2016
Global end of trial reached?	Yes
Global end of trial date	01 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to compare the effect in treatment of pain with three different strategies of pain management in patients presenting to an Emergency Department and to a general practice with acute musculoskeletal syndromes (defined as musculoskeletal complaints after sustaining an injury with exclusion of a fracture). The strategies of pain management which will be compared are paracetamol, diclofenac and the combination of paracetamol and diclofenac.

Protection of trial subjects:

NA

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	01 June 2013
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	Netherlands: 547
Worldwide total number of subjects	547
EEA total number of subjects	547

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)	505

From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

- Adult patients (18 years and older)
- Presenting to 2 university EDs; and urgent care center and one general practice
- Non-penetrating minor musculoskeletal injuries of an extremity
- WIthin 48 hours prior to presentation

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Paracetamol

Arm description: -

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

Dosage and administration details:

4x1000mg in a blinded fashion

Arm title	Diclofenac

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Diclofenac
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

3x50mg in a blinded fashion

Arm title	Paracetamol and Diclofenac

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Paracetamol and Diclofenac
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Paracetamol 4x1000mg and Diclofenac 3x50mg

Number of subjects in period 1	Paracetamol	Diclofenac	Paracetamol and Diclofenac
Started	182	183	182
Completed	182	183	182

Baseline characteristics

End points

End points reporting groups

Reporting group title	Paracetamol
Reporting group description: -	
Reporting group title	Diclofenac
Reporting group description: -	
Reporting group title	Paracetamol and Diclofenac
Reporting group description: -	

Primary: NRS pain score at 90 minutes

End point title	NRS pain score at 90 minutes
End point description:	
End point type	Primary
End point timeframe:	
90 minutes	

End point values	Paracetamol	Diclofenac	Paracetamol and Diclofenac	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	173	180	175	
Units: NRS pain score				
geometric mean (confidence interval 95%)	-1.23 (-1.50 to -0.95)	-1.20 (-1.44 to -0.96)	-1.18 (-1.41 to -0.94)	

Statistical analyses

Statistical analysis title	Statistical analysis plan

Statistical analysis description:

The primary outcome, between-group difference in mean NRS pain scores
Unpaired numerical data conforming to a normal distribution were analyzed using one-way analysis of variance

Comparison groups	Paracetamol v Diclofenac v Paracetamol and Diclofenac
Number of subjects included in analysis	528
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0125 [1]
Method	t-test, 1-sided

Notes:

[1] - Bonferroni adjustment

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 30 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	none specified
Dictionary version	0
Reporting groups	
Reporting group title	Adverse events in the ED

Reporting group description: -

Serious adverse events	Adverse events in the ED		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 547 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Adverse events in the ED		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	92 / 547 (16.82%)		
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 547 (0.91%)		
occurrences (all)	5		
Dizziness			
subjects affected / exposed	16 / 547 (2.93%)		
occurrences (all)	16		
Tiredness			
subjects affected / exposed	30 / 547 (5.48%)		
occurrences (all)	30		
Social circumstances			

Feeling cold			
subjects affected / exposed	1 / 547 (0.18%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	10 / 547 (1.83%)		
occurrences (all)	10		
Nausea			
subjects affected / exposed	23 / 547 (4.20%)		
occurrences (all)	23		
Vomiting			
subjects affected / exposed	1 / 547 (0.18%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	1 / 547 (0.18%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Dry mouth			
subjects affected / exposed	1 / 547 (0.18%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Itching			
subjects affected / exposed	2 / 547 (0.37%)		
occurrences (all)	2		
Sweating			
subjects affected / exposed	2 / 547 (0.37%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 September 2015	Extension of the recruitment period

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Results regarding primary outcome available here online. For complete results, see the published manuscript in Annals of Emergency Medicine (PMID 29033294)

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29033294