EU Clinical Trials Register

Clinical trial results:
Tick borne diseases in norwegian general practice. A randomized, controlled trial for treatment of erythema migrans in norwegian general practice. A comparison of phneoxymetylpenicillin, amoxicillin and doxycycline.

Summary

EudraCT number	2010-023747-15
Trial protocol	NO
Global end of trial date	10 December 2014

Results information

Result version number	v1 (current)
This version publication date	22 February 2020
First version publication date	22 February 2020
Summary attachment (see zip file)	Paper (Eliassen_Comparison_EM_CMI_2018.pdf)

Trial information

Trial identification

Sponsor protocol code	070411

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01368341
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Oslo
Sponsor organisation address	HELSAM/ASP, Oslo, Norway, 0318
Public contact	Antibiotic centre of Primary Care, University of Oslo, +47 22 85 06 55, post@antibiotikasenteret.no
Scientific contact	Antibiotic centre of Primary Care, University of Oslo, +47 22 85 06 55, post@antibiotikasenteret.no

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	02 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 December 2013
Global end of trial reached?	Yes
Global end of trial date	10 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Compare three antibiotic regimes for treatment of erythema migrans (EM).

Main objective is duration of Erythema migrans (EM). On day 1 duration until first the consulation is registered. Day 1-14 the EM is registered in a patient diary. On day 14 the doctor is asked whether the EM has disseapeared. If not the patient is followed by phone from the researchers. On day 90 they are additionally asked for how long it lasted.

Protection of trial subjects:

All patients received active treatment for their EM

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 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	Norway: 188
Worldwide total number of subjects	188
EEA total number of subjects	188

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)	130
From 65 to 84 years	55
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

All patients aged at least 18 years with clinical diagnosis of erythema migrans ("a macular rash expanding from the site of the tick bite") were eligible for inclusion.

Pre-assignment

Screening details:

Please see screening details elsewhere

Period 1

Period 1 title	2011-2013 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

Patients were given a neutral carton of medication to be opened after the first consultation. The carton contained information about the trial and the study medication, and whom to contact in case of any adverse event. The original medication package from the manufacturer, with the original product information, was included. Patients therefore knew which study drug they were given, but their GP and the researchers did not. Randomisation lists were available after the complete follow up.

Arms

Are arms mutually exclusive?	Yes
Arm title	Phenoxymethylpenicillin

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Phenoxymethylpenicillin
Investigational medicinal product code	J01CE02
Other name	Weifapenin Weifa 650 mg
Pharmaceutical forms	Tablet
Routes of administration	Gastroenteral use

Dosage and administration details:

650 mg, two tablets three times daily

Arm title	Amoxicillin

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Amoxicillin
Investigational medicinal product code	J01CA04
Other name	Amoxicillin Mylan 500 mg
Pharmaceutical forms	Capsule
Routes of administration	Gastroenteral use

Dosage and administration details:

one capsule three times daily

Arm title	Doxycycline

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	Doxycycline
Investigational medicinal product code	J01AA02
Other name	Doxycyklin Hexal 100 mg
Pharmaceutical forms	Tablet
Routes of administration	Gastroenteral use

Dosage and administration details:

one tablet twice daily

Number of subjects in period 1	Phenoxymethylpenicillin	Amoxicillin	Doxycycline
Started	56	64	68
Completed	47	56	58
Not completed	9	8	10
Lost to follow-up	9	8	10

Baseline characteristics

Reporting groups

Reporting group title	2011-2013

Reporting group description: -

Reporting group values	2011-2013	Total	
Number of subjects	188	188	
Age categorical			
Patients included were 18-85 years of age			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	130	130	
From 65-84 years	55	55	
85 years and over	3	3	
Gender categorical			
Units: Subjects			
Female	113	113	
Male	75	75	

End points

End points reporting groups

Reporting group title	Phenoxymethylpenicillin
Reporting group description: -	
Reporting group title	Amoxicillin
Reporting group description: -	
Reporting group title	Doxycycline
Reporting group description: -	

Primary: Duration of EM after treatment

End point title	Duration of EM after treatment

End point description:

xx

End point type	Primary

End point timeframe:

Patients were followed for 1 year. We found a wide range of duration of EM: 3-293 days. As the median duration were 13-14 days in all Groups, duration was verified in half of the patients at the day 14 Control. The rest were followed regularly until time

End point values	Phenoxymethyl penicillin	Amoxicillin	Doxycycline	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56[1]	64	68	
Units: Days	56	64	68	

Notes:

[1] - One lost to follow-up by day 14, but the main end point of EM duration was registered.

Attachments (see zip file)	Duration EM/20180207_CLM-17-13016_Figure 2a.tif

Statistical analyses

Statistical analysis title	Kaplan-Meier

Statistical analysis description:

The primary outcome is shown in a Kaplan-Meier plot and tested using the log-rank test.

Comparison groups	Phenoxymethylpenicillin v Amoxicillin v Doxycycline
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	≤ 0.05
Method	Logrank

Secondary: concomittant symptoms

End point title	concomittant symptoms

End point description:

Tiredness
Headache
Joint pain
Neck stiffness
Fever
Palpitations
Myalgia
Sore throat
Tender skin
Dizziness
Nausea
Chest pain
Diarrhea
Chills
Hot flushes
Coughing
(Multiple EMs)

End point type	Secondary

End point timeframe:

During treatment day 1-14

End point values	Phenoxymethyl penicillin	Amoxicillin	Doxycycline	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	64	67	
Units: concomittant symptoms	17	17	17	

Statistical analyses

Statistical analysis title	ANOVA

Statistical analysis description:

means were compared using ANOVA,
and categorical data were analyzed using c-square tests. Multiple
pair-wise comparisons were carried out if the c-square test rejected
the null hypothesis of equality of the proportions. The method
is also called post-hoc c-square test of proportions.

Comparison groups	Phenoxymethylpenicillin v Amoxicillin v Doxycycline
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANOVA
Parameter estimate	Mean difference (final values)

Secondary: Side effects

End point title	Side effects

End point description:	
Diarrhea Nausea Skin rash Other	
End point type	Secondary
End point timeframe:	
During treatment days 1-14	

End point values	Phenoxymethyl penicillin	Amoxicillin	Doxycycline	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	55	64	67	
Units: Number	55	64	67	

Statistical analyses

Statistical analysis title	ANOVA
Statistical analysis description:	
means were compared using ANOVA, and categorical data were analyzed using c-square tests. Multiple pair-wise comparisons were carried out if the c-square test rejected the null hypothesis of equality of the proportions	
Comparison groups	Phenoxymethylpenicillin v Amoxicillin v Doxycycline
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	equivalence[2]
P-value	< 0.05
Method	ANOVA

Notes:

[2] - means were compared using ANOVA,
and categorical data were analyzed using c-square tests. Multiple
pair-wise comparisons were carried out if the c-square test rejected
the null hypothesis of equality of the proportions

Adverse events

Adverse events information

Timeframe for reporting adverse events: Patients were followed for 1 year	
Assessment type	Non-systematic

Dictionary used

Dictionary name	Reported
Dictionary version	1

Reporting groups

Reporting group title	Phenoxymethylpenicillin
Reporting group description: -	
Reporting group title	Amoxicillin
Reporting group description: -	
Reporting group title	Doxycycline
Reporting group description: -	

Serious adverse events	Phenoxymethylpenicillin	Amoxicillin	Doxycycline
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 56 (0.00%)	0 / 64 (0.00%)	0 / 68 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Phenoxymethylpenicillin	Amoxicillin	Doxycycline
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 56 (0.00%)	1 / 64 (1.56%)	1 / 68 (1.47%)
Gastrointestinal disorders			
Diarrea			
subjects affected / exposed	0 / 56 (0.00%)	1 / 64 (1.56%)	0 / 68 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Sunburn			
subjects affected / exposed	0 / 56 (0.00%)	0 / 64 (0.00%)	1 / 68 (1.47%)
occurrences (all)	0	0	1

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