Clinical trial results:
Multicenter, randomized, open-label, clinical study on the agreement of Scintimun® Granulocyte and labeled 99mTc-White Blood Cells in diagnosing infection/inflammation by immunoscintigraphy in peripheral bone and joints with suspected osteomyelitis.

Summary

EudraCT number	2006-000514-21
Trial protocol	NL HU DE CZ
Global end of trial date	05 January 2008

Results information

Result version number	v1 (current)
This version publication date	16 December 2018
First version publication date	16 December 2018

Trial information

Trial identification

Sponsor protocol code	AG-PH3

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	CIS bio international
Sponsor organisation address	BP 32, GIF SUR YVETTE, France, 91192
Public contact	Medical information, CIS bio international, florence.chossat@curiumpharma.com
Scientific contact	Medical information, CIS bio international, +33 0169857108, florence.chossat@curiumpharma.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 June 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 January 2008
Global end of trial reached?	Yes
Global end of trial date	05 January 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the present study is to assess the agreement rate of Scintimun® Granulocyte and 99mTc-WBCs with regard to the diagnosis of infection/inflammation by immunoscintigraphy, based on the evaluations of three blinded and independent readers in the absence of a standard of reference (SOR) to evaluate the true status.

Protection of trial subjects:

No specific measures put in place

Background therapy: -

Evidence for comparator:

99mTc-hexamethyl propylene amine oxime (HMPAO) enables labelling of WBCs in vivo and does not need to perform cell isolation in vitro
The patient receives both treatments (cross-over study) therefore comparison with an antibody is not possible

Actual start date of recruitment	26 September 2006
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: 20
Country: Number of subjects enrolled	Czech Republic: 44
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hungary: 42
Country: Number of subjects enrolled	France: 22
Worldwide total number of subjects	130
EEA total number of subjects	130

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	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Five countries were involved. Randomisation of products injection was performed centrally.
First patient first visit : 26/09/2006
Last patient last visit : 04/01/2008

Pre-assignment

Screening details:

Patients with suspected or documented osteomyelitis in the peripheral skeleton (e.g. patients with loosening of joint prosthesis and or diabetic foot. In addition localised pain, and/or nonhealing skin ulceration, and/or fever > 37.8°C for at least 3 days, WBCs elevated, ESR elevated, suggestive RX findings. Patients with HAMA positive excluded

Period 1

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

Blinding implementation details:

The study was open-label design. However the agreement rate was based on the evaluation of three blinded and independent readers in a blinded reading.

Arms

Are arms mutually exclusive?	No
Arm title	SCINTIMUN first

Arm description:

Multicenter, open- label, randomised, intra-individual comparison.
Each patient was injected with SCINTIMUN and 99mTc-WBCs in random order with a minimum time interval of two days (a minimum of 48 hours) between the injections.
In SCINTIMUN first arm, SCINTIMUN was injected first

Arm type	Experimental
Investigational medicinal product name	besilesomab
Investigational medicinal product code	
Other name	SCINTIMUN
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous bolus use

Dosage and administration details:

Single administration of 800 MBq

Investigational medicinal product name	Exametazime
Investigational medicinal product code	
Other name	CERETEC
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous bolus use

Dosage and administration details:

Single administration of 330 MBq

Arm title	CERETEC first

Arm description:

Multicenter, open- label, randomised, intra-individual comparison.
Each patient was injected with SCINTIMUN and 99mTc-WBCs in random order with a minimum time interval of two days (a minimum of 48 hours) between the injections. In this arm CERETEC is administered first.

Arm type	Active comparator

Investigational medicinal product name	hexametazime
Investigational medicinal product code	
Other name	CERETEC
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use

Dosage and administration details:
Single administration of 330 MBq

Investigational medicinal product name	besilesomab
Investigational medicinal product code	
Other name	SCINTIMUN
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use

Dosage and administration details:
800 MBq in a single injection

Number of subjects in period 1	SCINTIMUN first	CERETEC first
Started	64	66
Completed	64	66

Baseline characteristics

Reporting groups	
Reporting group title	overall trial
Reporting group description:	
overall study population	

Reporting group values	overall trial	Total	
Number of subjects	130	130	
Age categorical			
adults less than 65 years			
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			
64			
Units: years			
median	64		
standard deviation	± 13.89	-	
Gender categorical			
Units: Subjects			
Female	51	51	
Male	79	79	

End points

End points reporting groups

Reporting group title	SCINTIMUN first

Reporting group description:

Multicenter, open- label, randomised, intra-individual comparison.
Each patient was injected with SCINTIMUN and 99mTc-WBCs in random order with a minimum time interval of two days (a minimum of 48 hours) between the injections.
In SCINTIMUN first arm, SCINTIMUN was injected first

Reporting group title	CERETEC first

Reporting group description:

Multicenter, open- label, randomised, intra-individual comparison.
Each patient was injected with SCINTIMUN and 99mTc-WBCs in random order with a minimum time interval of two days (a minimum of 48 hours) between the injections. In this arm CERETEC is administered first.

Primary: agreement rate

End point title	agreement rate

End point description:

The primary analysis was the evaluation of the agreement rate of SCINTIMUN and 99mTc-WBCs with regard to the diagnosis of infection/inflammation by scintigraphy. The primary efficacy variable was calculated as an average across the results of the 3 blinded and independent readers

End point type	Primary

End point timeframe:

overall study

End point values	SCINTIMUN first	CERETEC first		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	66		
Units: percentage	84	84		

Statistical analyses

Statistical analysis title	statistical analysis of the primary variable

Statistical analysis description:

The agreement rate was analysed using a modified adjusted Chi2-test to cover clustered data and multiple measurements per cluster. The limit of clinical relevance was set to 0.7. The agreement rate was supposed to be sufficient if its one-sided 97.5% confidence interval was positioned completely above 0.70.

Comparison groups	CERETEC first v SCINTIMUN first

Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≤ 0.025
Method	Chi-squared corrected
Parameter estimate	Mean difference (final values)
Point estimate	0.8
Confidence interval	
level	95 %
sides	1-sided
lower limit	0.7
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

overall study

Adverse event reporting additional description:

- Monitoring of the adverse events until Month 1,
- Measurement of vital signs before and after each injection,
- Measurement of laboratory parameters before and 24 hours after each injection, and at Month 1,
- HAMA test at Month 1 and Month 3.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	ceretec first
Reporting group description: -	
Reporting group title	scintimun first

Reporting group description: -

Serious adverse events	ceretec first	scintimun first	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 66 (1.52%)	0 / 64 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Cardiac disorders			
cardiopulmonary failure			
subjects affected / exposed	1 / 66 (1.52%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood and lymphatic system disorders			
hemorragic anaemia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
duodenal ulcer haemorrhage			

subjects affected / exposed	1 / 66 (1.52%)	0 / 64 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	ceretec first	scintimun first	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 66 (1.52%)	8 / 64 (12.50%)	
Investigations			
C reactive protein elevated			
subjects affected / exposed	1 / 66 (1.52%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 66 (0.00%)	2 / 64 (3.13%)	
occurrences (all)	0	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 66 (1.52%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Headache			
subjects affected / exposed	0 / 66 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Burning sensation			
subjects affected / exposed	0 / 66 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Immune system disorders			
Pruritus			
subjects affected / exposed	0 / 66 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
diarrhea			
subjects affected / exposed	1 / 66 (1.52%)	0 / 64 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			

erysipela			
subjects affected / exposed	0 / 66 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Osteomyelitis chronic			
subjects affected / exposed	0 / 66 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	0 / 66 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	0	1	
Infections and infestations			
Infection			
subjects affected / exposed	0 / 66 (0.00%)	1 / 64 (1.56%)	
occurrences (all)	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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/21321791