Clinical trial results:
Evaluation of the effect of the oral administration of perindopril orodispersible at a dose of 0.150 mg/kg/day onthe muscular and myocardial function in early stage Duchenne muscular dystrophy. Double blind two years study, randomised versus placebo.

Summary

EudraCT number	2008-003856-32
Trial protocol	FR
Global end of trial date	19 October 2011

Results information

Result version number	v1 (current)
This version publication date	06 July 2016
First version publication date	31 July 2015

Trial information

Trial identification

Sponsor protocol code	CL3-90652-004

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Institut de Recherches Internationales Servier
Sponsor organisation address	50 rue Carnot, Suresnes Cedex, France, 92284
Public contact	Clinical studies department, Institut de Recherches Internationales Servier 50 rue Carnot 92284 Suresnes Cedex, +33 155724366, clinicaltrials@servier.com
Scientific contact	Clinical studies department, Institut de Recherches Internationales Servier 50 rue Carnot 92284 Suresnes Cedex, +33 155724366, clinicaltrials@servier.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	19 October 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 October 2011
Global end of trial reached?	Yes
Global end of trial date	19 October 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to assess the benefit versus placebo of the administration of perindopril on peripheral muscular function

Protection of trial subjects:

the patient will be remove of the study if : the parents or the child choose to, the ACE tolerance is too low, the start of an other treatment is needed or the cardiac functions decrease (LVEF <55%).

Background therapy:

No background therapy

Evidence for comparator:

No reference treatment was identified

Actual start date of recruitment	11 March 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	40

Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In all, 16 centres located in France, were opened and 14 centres included at least one patient.Children under 7 years.Confirmed DMD diagnosis: Either by the absence of dystrophin in the muscle biopsy. Or by the genetic study of the dystrophin gene in confirmed familial cases .

Pre-assignment

Screening details:

No screening

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, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Perindopril

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Perindopril
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

0.150 mg/kg/day per os - once a day

Arm title	Placebo

Arm description: -

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

Dosage and administration details:

1 tablet per day

Number of subjects in period 1	Perindopril	Placebo
Started	20	20
Completed	15	18
Not completed	5	2
Non Medical Reason	2	-
Protocol deviation	3	2

Baseline characteristics

Reporting groups	
Reporting group title	Perindopril
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Perindopril	Placebo	Total
Number of subjects	20	20	40
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	20	20	40
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	5.33	5.3	
standard deviation	± 1.23	± 1.17	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	20	20	40
Disease Duration Units: Months			
arithmetic mean	24.8	18.5	
standard deviation	± 19.1	± 12.4	-
Weight Units: Kg			
arithmetic mean	19.1	18.69	
standard deviation	± 3.96	± 2.43	-

End points

End points reporting groups

Reporting group title	Perindopril
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: 6 minute walking distance

End point title	6 minute walking distance
End point description:	
Change Last value under treatment minus Baseline value	
End point type	Primary
End point timeframe:	
On the period M000-M024.	

End point values	Perindopril	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19[1]	20[2]		
Units: meters				
arithmetic mean (standard deviation)	-44.9 (± 132.7)	-84.1 (± 134.3)		

Notes:

[1] - FAS

[2] - FAS

Statistical analyses

Statistical analysis title	Between group comparison using an ANCOVA
Comparison groups	Perindopril v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	60.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.96
upper limit	151.74
Variability estimate	Standard error of the mean
Dispersion value	44.95

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Over the course of the study (M0-M24)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups	
Reporting group title	Perindopril
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Perindopril	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 19 (31.58%)	3 / 20 (15.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
accidental drug intake by child			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hypotonia			

subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Myopathy			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Ear infection			
subjects affected / exposed	3 / 19 (15.79%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			

subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Perindopril	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 19 (89.47%)	17 / 20 (85.00%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 19 (26.32%)	0 / 20 (0.00%)	
occurrences (all)	6	0	
joint sprain			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Fatigue			

subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Gastroenteritis			
subjects affected / exposed	5 / 19 (26.32%)	2 / 20 (10.00%)	
occurrences (all)	7	2	
Constipation			
subjects affected / exposed	3 / 19 (15.79%)	1 / 20 (5.00%)	
occurrences (all)	3	1	
Vomiting			
subjects affected / exposed	2 / 19 (10.53%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Respiratory, thoracic and mediastinal disorders			
Bronchitis			
subjects affected / exposed	3 / 19 (15.79%)	5 / 20 (25.00%)	
occurrences (all)	4	8	
Rhinitis			
subjects affected / exposed	1 / 19 (5.26%)	6 / 20 (30.00%)	
occurrences (all)	1	6	
Nasopharyngitis			
subjects affected / exposed	2 / 19 (10.53%)	3 / 20 (15.00%)	
occurrences (all)	6	3	
Oropharyngeal pain			
subjects affected / exposed	3 / 19 (15.79%)	2 / 20 (10.00%)	
occurrences (all)	6	3	
Cough			
subjects affected / exposed	2 / 19 (10.53%)	1 / 20 (5.00%)	
occurrences (all)	6	1	
Tracheitis			
subjects affected / exposed	1 / 19 (5.26%)	2 / 20 (10.00%)	
occurrences (all)	1	7	
Renal and urinary disorders			

Enuresis			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Myopathy			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Pain in extremity			
subjects affected / exposed	2 / 19 (10.53%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Ear infection			
subjects affected / exposed	6 / 19 (31.58%)	3 / 20 (15.00%)	
occurrences (all)	8	3	
Pharyngitis			
subjects affected / exposed	1 / 19 (5.26%)	6 / 20 (30.00%)	
occurrences (all)	1	6	
Tonsillitis			
subjects affected / exposed	1 / 19 (5.26%)	3 / 20 (15.00%)	
occurrences (all)	2	5	
H1N1 influenza			
subjects affected / exposed	1 / 19 (5.26%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Influenza			
subjects affected / exposed	0 / 19 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	0 / 19 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	

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

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

The section NSAE is filled with all emergent NSAEs on treatment. This decision has been taken by the sponsor to be in accordance with the existing ICH E3 Clinical Study Report.

Notes: