Clinical trial results:
A Multi-centre, Open-label Study Evaluating the Safety and Tolerability of Colestilan (MCI-196) in Paediatric Subjects with Chronic Kidney Disease Stages 3b to 5 and with Hyperphosphataemia not on Dialysis

Summary

EudraCT number	2012-002582-35
Trial protocol	GB DE
Global end of trial date	14 January 2015

Results information

Result version number	v1 (current)
This version publication date	19 February 2016
First version publication date	19 February 2016

Trial information

Trial identification

Sponsor protocol code	MCI-196-E16

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01818687
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mitsubishi Tanabe Pharma Corporation
Sponsor organisation address	17-10, Nihonbashi-Koamicho, Chuo-ku, Tokyo, Japan, 103-8405
Public contact	General Information, Mitsubishi Tanabe Pharma Europe Ltd , regulatory@mt-pharma-eu.com
Scientific contact	General Information, Mitsubishi Tanabe Pharma Europe Ltd, regulatory@mt-pharma-eu.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000878-PIP02-11
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	18 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 December 2014
Global end of trial reached?	Yes
Global end of trial date	14 January 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to assess safety and tolerability of colestilan in paediatric subjects (aged 2 years to <18 years) with CKD Stages 3b to 5, diagnosed with hyperphosphataemia, who were not on dialysis.

Protection of trial subjects:

1 For subjects on phosphate binders: during the wash-out period, a max of 4 weeks, subjects stopped their current phosphate binder treatment, which was likely to cause a rise in P levels. The increase in P was not dangerous for a short period of time and once the required P level was reached, the subject was randomised and treated with Colestilan (MCI-196). The level to which the P is required to rise was specified in inclusion criteria 6 and 7.
2 When specifying the amount of blood to be drawn the following guidelines were used: trial-related blood loss (including loss in the procedure) should not exceed 3% of total blood volume during a period of 4 weeks and should not exceed 1% total blood volume at any single time.
Subjects were enrolled to the study only if they could safely provide 8 ml of blood at each visit.
3 When investigating new drugs there is always a risk of unexpected side effects and occasionally allergic reactions. Subjects were closely monitored during the study.
4 Rescue treatment: Hyperphosphataemia, after the max dose of Colestilan (MCI-196) (BSAeq of 15 g/day) was reached, the subject was either withdrawn from the study or the Investigator added CBPB as rescue medication, in addition to the max dose of Colestilan (MCI-196). Adjustment of dosing of vitamin D/analogues was permitted during the study to correct hypocalcaemia. The appropriate doses of rescue treatment were decided by the Investigator based on his/her clinical experience.
5 Consent/assent process: Enough time was provided to the subject/parent/caregiver to consider participation in the study. In addition to the patient information sheet and consent/assent forms, a study flipchart was provided to all sites, which was used as a tool to help explain/discuss aspects of the study in more detail.
6 Tablet intake - it is known that tablets can be difficult to swallow, especially by very young children. The IMP was made available also in granule formulation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 June 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	United Kingdom: 2
Worldwide total number of subjects	4
EEA total number of subjects	4

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)	3
Adolescents (12-17 years)	1
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from those patients with hyperphosphataemia who were already attending the clinics for the treatment of CKD stages 3b to 5.

Pre-assignment

Screening details:

The study comprised of a screening period (1 to 4 weeks) and a wash-out period (1 to 4 weeks). A total of 14 subjects were screened. 10 subjects were withdrawn before randomisation (screen failed).

Period 1

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

Arms

Arm title	MCI-196 (All Subjects)

Arm description:

All study subjects were treated for 17 weeks. The starting daily doses of colestilan (MCI-196) was the body surface area equivalent (BSAeq) of 6 g/day in adults, (i.e., 3.47 g/m²/day), oral, divided doses with food. The colestilan dose was titrated up within 3 days of the visit, based on the serum P level and/or the judgement of the Investigator, whichever was more suitable for the best care of the subject.

Arm type	Experimental
Investigational medicinal product name	Colestilan
Investigational medicinal product code	MCI-196
Other name	
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

1 gram tablets and granules of approximately 20 mg packaged in 2 g or 3 g sachets

Number of subjects in period 1	MCI-196 (All Subjects)
Started	4
Completed	4

Baseline characteristics

Reporting groups	
Reporting group title	MCI-196 (All Subjects)

Reporting group description:

All study subjects were treated for 17 weeks. The starting daily doses of colestilan (MCI-196) was the body surface area equivalent (BSAeq) of 6 g/day in adults, (i.e., 3.47 g/m²/day), oral, divided doses with food. The colestilan dose was titrated up within 3 days of the visit, based on the serum P level and/or the judgement of the Investigator, whichever was more suitable for the best care of the subject.

Reporting group values	MCI-196 (All Subjects)	Total	
Number of subjects	4	4	
Age categorical			
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)	3	3	
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	10.3		
standard deviation	± 2.6	-	
Gender categorical			
Units: Subjects			
Female	1	1	
Male	3	3	

End points

End points reporting groups

Reporting group title	MCI-196 (All Subjects)

Reporting group description:

All study subjects were treated for 17 weeks. The starting daily doses of colestilan (MCI-196) was the body surface area equivalent (BSAeq) of 6 g/day in adults, (i.e., 3.47 g/m²/day), oral, divided doses with food. The colestilan dose was titrated up within 3 days of the visit, based on the serum P level and/or the judgement of the Investigator, whichever was more suitable for the best care of the subject.

Primary: Percentage of subjects who, due to hyperphosphataemia, require rescue treatment and/or discontinuation of therapy with colestilan (MCI-196)

End point title	Percentage of subjects who, due to hyperphosphataemia, require rescue treatment and/or discontinuation of therapy with colestilan (MCI-196)[1]

End point description:

End point type	Primary

End point timeframe:

Baseline to Week 17

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely. From the limited data collected in this study, due to small sample size, no analysis of the data was conducted nor can any reasonable conclusions be made.

End point values	MCI-196 (All Subjects)			
Subject group type	Reporting group			
Number of subjects analysed	4[2]			
Units: Percentage	0			

Notes:

[2] - This study was prematurely terminated. No statistical analyses were completed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AE) that occurred from the time written informed consent/assent was taken until the end of study or discontinuation were recorded in the source documents and reported in the CRF.

Adverse event reporting additional description:

AEs were classified as 'treatment emergent' (i.e. TEAEs or serious TEAEs) if they occurred following administration of IMP. All events reported in this database are treatment emergent.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	MCI-196 (All subjects)

Reporting group description:

All study subjects were treated for 17 weeks. The starting daily doses of colestilan (MCI-196) was the body surface area equivalent (BSAeq) of 6 g/day in adults, (i.e., 3.47 g/m²/day), oral, divided doses with food. The colestilan dose was titrated up within 3 days of the visit, based on the serum P level and/or the judgement of the Investigator, whichever was more suitable for the best care of the subject.

Serious adverse events	MCI-196 (All subjects)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	MCI-196 (All subjects)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Investigations			
Blood sodium increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Calcium ionised decreased			

subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Fibroblast growth factor 23 increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	3		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
General disorders and administration site conditions			
Drug interaction			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Granuloma			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	4		
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Abdominal pain upper			

subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Lip dry subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2 1 / 4 (25.00%) 1 1 / 4 (25.00%) 2 1 / 4 (25.00%) 1		
Skin and subcutaneous tissue disorders Miliaria subjects affected / exposed occurrences (all) Skin irritation subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1		
Endocrine disorders Hyperparathyroidism subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	 1 / 4 (25.00%) 1 1 / 4 (25.00%) 1		
Metabolism and nutrition disorders Hyperphosphataemia			

subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 3		

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? Yes

Date	Interruption	Restart date
14 January 2015	Study early termination	-

Notes:

Limitations and caveats

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

There were significant challenges to recruitment in all age groups and in this patient population. The study was terminated early due to the withdrawal of the MAA.

Notes: