Clinical trial results:
Role of different phosphate binders on absorption of vitamin K, metabolism of matrix -carboxy-glutamaat (Gla) proteïne (MGP).

Summary

EudraCT number	2013-003949-41
Trial protocol	NL
Global end of trial date	01 October 2018

Results information

Result version number	v1 (current)
This version publication date	09 April 2022
First version publication date	09 April 2022
Summary attachment (see zip file)	main document (main body.docx)

Trial information

Trial identification

Sponsor protocol code	36810

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	VU medical center
Sponsor organisation address	De Boelelaan 1117, Amsterdam, Netherlands, 1081HV
Public contact	Martijn Stolk, VU medical Center, 0031 204449322, m.stolk@vumc.nl
Scientific contact	Martijn Stolk, VU medical Center, 0031 204449322, m.stolk@vumc.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	23 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 October 2018
Global end of trial reached?	Yes
Global end of trial date	01 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This research will have as aim to look at progression or decrease of vascular calcification in dialysis population with use of different phosphate binders. There is a possibility that differect phosphate binders bind vitamin K in a different way in intestinal tract end thereby cause different level of calcification. Level of calcification will be measured by dp-ucMGP which is used as markers for vascular calcification. Because of the fact that ucMGP en dp-ucMGP are vitamin K dependant PIVKA-II will be measured as well.
Better insight in mechanisms of vascular calcification under different circumstance can lead to therapeutic options which inhibit calcification and benefit survival of dialysis patients

Protection of trial subjects:

The blood work during a dialysis sessions was monitored more frequently. There was no extra pain since the blood was drawn during dialysis.

Background therapy:

No additional products were used.

Evidence for comparator:

There is evidence that lanthanumcarbonate does bind fat soluble vitamins in vivo. this was the reason to compare this drug with calcium carbonate.

Actual start date of recruitment	01 January 2014
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: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	6
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In three Dutch dialysis centers (Noord West Ziekenhuisgroep location Alkmaar, Diapriva Amsterdam, Elyse clinic Amstelveen) hemodialysis patients were enrolled. Enrollment of patients started in October 2014 and the study follow up ended in September 2018

Pre-assignment

Screening details:

Clinically stable adult (age > 18 years) hemodialysis patients with a life expectancy of more than six months were screened.

Period 1

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

Blinding implementation details:

there was no blinding implemented

Arms

Are arms mutually exclusive?	Yes
Arm title	lantahnum carbonate

Arm description:

start with use of lantahnum carbonate

Arm type	Experimental
Investigational medicinal product name	lanthanum carbonate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Soluble tablet
Routes of administration	Oral use

Dosage and administration details:

three times a day 1000 mg for eight weeks

Arm title	calcium carbonate

Arm description:

start with calcium carbonate use

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

Dosage and administration details:

three times a day 1000 mg for eight weeks

Number of subjects in period 1	lantahnum carbonate	calcium carbonate
Started	6	6
Completed	6	6

Baseline characteristics

Reporting groups

Reporting group title	baseline

Reporting group description: -

Reporting group values	baseline	Total	
Number of subjects	12	12	
Age categorical 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			
65,4			
Units: years			
arithmetic mean	65		
standard deviation	± 11	-	
Gender categorical			
gender			
Units: Subjects			
Female	4	4	
Male	8	8	
baseline			
At inclusion, we captured data on age, medical history, dialysis vintage, medication, blood pressure and laboratory data. Every two weeks serum calcium, phosphate and albumin levels were measured.			
Units: depending on the variable			
arithmetic mean	1914		
standard deviation	± 651	-	

Subject analysis sets

Subject analysis set title	baseline
Subject analysis set type	Intention-to-treat

Subject analysis set description:

baseline

Reporting group values	baseline		
Number of subjects	12		

Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous			
65,4			
Units: years			
arithmetic mean	65		
standard deviation	± 11		
Gender categorical			
gender			
Units: Subjects			
Female	4		
Male	8		
baseline			
At inclusion, we captured data on age, medical history, dialysis vintage, medication, blood pressure and laboratory data. Every two weeks serum calcium, phosphate and albumin levels were measured.			
Units: depending on the variable			
arithmetic mean	1914		
standard deviation	± 651		

End points

End points reporting groups	
Reporting group title	lantahnum carbonate
Reporting group description: start with use of lantahnum carbonate	
Reporting group title	calcium carbonate
Reporting group description: start with calcium carbonate use	
Subject analysis set title	baseline
Subject analysis set type	Intention-to-treat
Subject analysis set description: baseline	

Primary: dp-uc-MGP	
End point title	dp-uc-MGP
End point description: Primary end point was the difference in dp-ucMGP and PIVKA-II after 8 weeks of treatment between LC and CC.	
End point type	Primary
End point timeframe: Primary end point was the difference in dp-ucMGP and PIVKA-II after 8 weeks of treatment between LC and CC.	

End point values	lantahnum carbonate	calcium carbonate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: dp-uc-MGP				
arithmetic mean (standard deviation)				
difference between dp-uc-MGP	20 (± 0)	5 (± 0)		

Attachments (see zip file)	baseline /Table 1.docx laboratory parameters/Table 2.docx

Statistical analyses

Statistical analysis title	difference in dp-uc-MGP between
Statistical analysis description: difference in dp-uc-MGP between the groups after 8 weeks of treatment	
Comparison groups	lantahnum carbonate v calcium carbonate

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	= 0.9 [2]
Method	lineair mixed model
Parameter estimate	Mean difference (final values)

Notes:

[1] - cross over study, the patients that completed at least one period of 8 weeks of treatment with a binder were analysed.
[2] - not significant

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
2 patients got admitted to the hospital, however the admission was not a side effect of the medication.	
Adverse event reporting additional description:	
1 patient got admitted with galbladder problems and other one with pneumonia.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	ABR formulier
Dictionary version	1

Reporting groups	
Reporting group title	lanthanumcarbonate
Reporting group description:	
One patient with gall bladder problems got admitted. The study medication was not a causative factor.	
Reporting group title	calciumcarbonate
Reporting group description:	
One patient gor admitted for pneumonia. This was not due to the use of the study medication	

Serious adverse events	lanthanumcarbonate	calciumcarbonate	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	lanthanumcarbonate	calciumcarbonate	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
Hepatobiliary disorders			
gall bladder problems	Additional description: patients was admitted for gall bladder problems, these were unrelated to the study medication		
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia	Additional description: Admittance for pneumonia. study medication was not a causative factor.		
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
occurrences (all)	0	0	

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 number of patients that completed the trial was very small.

Notes: