Clinical trial results:
The effect of vitamin D supplementation on immune response following hepatitis B vaccine in incident and prevalent hemodialysis patients with vitamin D deficiency

Summary

EudraCT number	2011-004621-26
Trial protocol	AT
Global end of trial date	12 January 2016

Results information

Result version number	v1 (current)
This version publication date	02 December 2021
First version publication date	02 December 2021

Trial information

Trial identification

Sponsor protocol code	Devitahep

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Clinical Division of Nephrology
Sponsor organisation address	Auenbruggerplatz 27, Graz, Austria,
Public contact	Sabine Horn, Medical University Graz, 0043 31638512170, sabine.horn@medunigraz.at
Scientific contact	Sabine Horn, Medical University Graz, 0043 31638512170, sabine.horn@medunigraz.at

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	15 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 January 2016
Global end of trial reached?	Yes
Global end of trial date	12 January 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial is to evaluate whether vitamin D supplementation is able to ameliorate the response of vitamin D-deficient hemodialysis patients receiving hepatitis B immunization

Protection of trial subjects:

Protection of Trial subjects was performed with clinical visits during their routinely performed hemodialysis sessions

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2012
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	Austria: 37
Worldwide total number of subjects	37
EEA total number of subjects	37

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)	14
From 65 to 84 years	22
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from two dialysis units at the Clinical Division of Nephrology, Medical University of Graz, and the Department of Internal Medicine III (Nephrology and Dialysis), Feldkirch Academic Teaching Hospital. Patients were enrolled between October 4, 2012 and April 9, 2015.

Pre-assignment

Screening details:

A total of 37 patients were randomized, 20 allocated to the cholecalciferol supplementation group, 17 to the control group. Of these, 17 patients in the supplementation group and 11 in the control group completed the study and were analyzed per protocol (CONSORT 2010 flow diagram, Figure 1).

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Supplementation group

Arm description:

Patients reveived 28000 IU cholecalciferol Weekly at the end of dialysis session to ensure adherence

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

Dosage and administration details:

Patients reveived 28000 IU cholecalciferol Weekly at the end of dialysis session to ensure adherence

Arm title	Control group

Arm description: -

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Supplementation group	Control group
Started	20	17
Completed	17	11
Not completed	3	6
Adverse event, serious fatal	1	1
Exclusion due of recovery of renal function	-	1
Exclusion due to need for kidney transplantation	-	2
kidney transplantation	2	-

end of dialysis due to comorbidities	-	1
Protocol deviation	-	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	37	37	
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)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	14	14	
From 65-84 years	22	22	
85 years and over	1	1	
Gender categorical Units: Subjects			
Female	11	11	
Male	26	26	

Subject analysis sets

Subject analysis set title	Anti-Hbs antibodies, Test group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Categorical data are presented as absolute and relative number of patients. For continuous data mean and standard deviation (SD) or median with interquartile range (1st quartile - 3rd quartile) is used, depending on its distribution. For correlation analysis we used Spearman's correlation coefficient. Categorical parameters were compared using exact Chi-squared tests, normally distributed continuous parameters were analysed with Student's T test and not normally distributed parameters with exact Mann-Whitney U test. A two-sided P value <0.05 was deemed to indicate statistical significance. All statistical analyses were performed with IBM SPSS Statistics 25 (Release 25.0.0.1 2017. Armonk (NY), USA).

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Reporting group values	Anti-Hbs antibodies, Test group	Anti-Hbs antibodies, Control group	
Number of subjects	17	11	
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)	9		
From 65-84 years	18		
85 years and over	1		
Gender categorical Units: Subjects			
Female	11		
Male	26		

End points

End points reporting groups

Reporting group title	Supplementation group
Reporting group description:	
Patients reveived 28000 IU cholecalciferol Weekly at the end of dialysis session to ensure adherence	
Reporting group title	Control group
Reporting group description: -	
Subject analysis set title	Anti-Hbs antibodies, Test group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Categorical data are presented as absolute and relative number of patients. For continuous data mean and standard deviation (SD) or median with interquartile range (1st quartile - 3rd quartile) is used, depending on its distribution. For correlation analysis we used Spearman's correlation coefficient. Categorical parameters were compared using exact Chi-squared tests, normally distributed continuous parameters were analysed with Student's T test and not normally distributed parameters with exact Mann-Whitney U test. A two-sided P value <0.05 was deemed to indicate statistical significance. All statistical analyses were performed with IBM SPSS Statistics 25 (Release 25.0.0.1 2017. Armonk (NY), USA).	
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Primary: number of patients with anti-HBs titer ≥10 IU/L

End point title	number of patients with anti-HBs titer ≥10 IU/L
End point description:	
The primary endpoint was the number of patients with an anti-HBs titer ≥10 IU/L in the two groups. This endpoint was achieved by 35.3% of the patients in the supplementation group and 27.3% in the control group (p=0.704)	
End point type	Primary
End point timeframe:	
The primary endpoint was the number of patients with an anti-HBs titer ≥10 IU/L in the two groups eight weeks after completing the vaccination course. The secondary endpoints were the number of patients with an anti-HBs titer >100 IU/L	

End point values	Anti-Hbs antibodies, Test group	Anti-Hbs antibodies, Control group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	11		
Units: Number of patients	17	11		

Statistical analyses

Statistical analysis title	Effect of vitamin D supplementation
Comparison groups	Anti-Hbs antibodies, Test group v Anti-Hbs antibodies, Control group
Number of subjects included in analysis	28
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.704
Method	Chi-squared

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
The timeframe for reporting adverse Event reporting was 24 hours	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19

Reporting groups	
Reporting group title	Supplementation group
Reporting group description:	
Patients reveived 28000 IU cholecalciferol Weekly at the end of dialysis session to ensure adherence	
Reporting group title	Control group
Reporting group description: -	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Due to the critical patient population, it was defined that only adverse events with possible relation to the study medication/study procedures, and adverse events of special interest (hypercalcemia or hyperphosphatemia) have to be documented.
Cholecalciferol supplementation was safe with no episode of hypercalcemia or hyperphosphatemia.

Serious adverse events	Supplementation group	Control group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)	0 / 17 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 20 (5.00%)	0 / 17 (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	Supplementation group	Control group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 17 (0.00%)	

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.

We used a standardized vaccination protocol with a recommended second-generation vaccine.
The small number of patients completing the study is another limitation, and our trial is a pilot study.

Notes: