



Clinical trial results:

Rivaroxaban and PCC: Prothrombin Complex Concentrate in patients with bleeding complications related to Rivaroxaban

Summary

EudraCT number	2013-004484-31
Trial protocol	AT
Global end of trial date	21 October 2016

Results information

Result version number	v1 (current)
This version publication date	10 September 2021
First version publication date	10 September 2021

Trial information

Trial identification

Sponsor protocol code	Riva-PCC
-----------------------	----------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Innsbruck
Sponsor organisation address	Anichstr. 35, Innsbruck, Austria, 6020
Public contact	Projektmanagement, Medizinische Universität Innsbruck / Univ.-Klinik für Allg. u.I Chirurg. Intensivmedizin, 0043 51250424635, bettina.schenk@i-med.ac.at
Scientific contact	Projektmanagement, Medizinische Universität Innsbruck / Univ.-Klinik für Allg. u.I Chirurg. Intensivmedizin, 0043 51250424635, bettina.schenk@i-med.ac.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	26 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 October 2016
Global end of trial reached?	Yes
Global end of trial date	21 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assessment of effective reversal of Rivaroxaban (Xarelto) with Prothrombin Complex Concentrate (Beriplex)

Protection of trial subjects:

Blood samples were drawn from an already implemented line, if applicable.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 August 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	Austria: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	2
From 65 to 84 years	10
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at the medical University of Innsbruck, Austria from 19.08.2014 (first patient first visit) until 21.10.2016 (last patient last visit).

Pre-assignment

Screening details:

Patients were screened according to the in- and exclusion criteria.

Period 1

Period 1 title	Visit 2
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Patients after PCC treatment
------------------	------------------------------

Arm description:

Thrombin generation after treatment with Prothrombin Complex Concentrate (PCC)

Arm type	Experimental
Investigational medicinal product name	Prothrombin Complex Concentrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 IU per kg Body Weight. If bleeding did not stop, the dose was repeated.

Number of subjects in period 1	Patients after PCC treatment
Started	14
Completed	14

Period 2

Period 2 title	Overall Trial
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Treatment with PCC
Arm description: All patients included received 25 IU/kg Body Weight Prothrombin Complex Concentrate (PCC). If bleeding did not stop, the dose was repeated.	
Arm type	Treatment
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Treatment with PCC
Started	14
Completed	14

Baseline characteristics

Reporting groups

Reporting group title	Visit 2
-----------------------	---------

Reporting group description: -

Reporting group values	Visit 2	Total	
Number of subjects	14	14	
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)	10	10	
From 65-84 years	2	2	
85 years and over	2	2	
Age continuous			
Units: years			
median	80		
full range (min-max)	47 to 96	-	
Gender categorical			
Units: Subjects			
Female	5	5	
Male	9	9	

End points

End points reporting groups

Reporting group title	Patients after PCC treatment
Reporting group description: Thrombin generation after treatment with Prothrombin Complex Concentrate (PCC)	
Reporting group title	Treatment with PCC
Reporting group description: All patients included received 25 IU/kg Body Weight Prothrombin Complex Concentrate (PCC). If bleeding did not stop, the dose was repeated.	
Subject analysis set title	Period 2: 1 hour after IMP administration
Subject analysis set type	Full analysis
Subject analysis set description: all study participants	

Primary: difference in thrombin generation between V1 and V2

End point title	difference in thrombin generation between V1 and V2
End point description:	
End point type	Primary
End point timeframe: V1 - prior to treatment with PCC V2 - 10 minutes after the end of PCC administration	

End point values	Treatment with PCC	Patients after PCC treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14 ^[1]	14 ^[2]		
Units: milliextinction(s)				
arithmetic mean (standard deviation)	316 (± 75)	524 (± 94)		

Notes:

[1] - Before treatment with PCC (Baseline)

[2] - After treatment with PCC (Visit 2)

Statistical analyses

Statistical analysis title	Statistical assessment of primary endpoint
Comparison groups	Treatment with PCC v Patients after PCC treatment
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other ^[3]
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Notes:

[3] - Intra-Population analysis (before treatment versus after treatment)

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

inclusion until +7 days

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	20
--------------------	----

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

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: Since these were critically ill patients the non-serious AEs are too many to list here. In total 10 Serious Adverse Events were reported (Abdominal sepsis, Septic shock, multiple organ failure, sepsis, lower respiratory tract and lung infections, Stroke, Heart failure (NOS), Haemorrhage intracranial, Metastases to central nervous system, Peripheral artery stent insertion.) Three patients died within 30 days after treatment and no death was related to the IMP.

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/29344007>