Clinical trial results:
Extracorporeal Photopheresis Treatment in steroid refractory acute and chronic Graft versus Host Disease

Summary

EudraCT number	2015-001550-14
Trial protocol	DK
Global end of trial date	16 October 2016

Results information

Result version number	v1 (current)
This version publication date	07 March 2018
First version publication date	07 March 2018

Trial information

Trial identification

Sponsor protocol code	ECP-GVHD1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bispebjerg hospital
Sponsor organisation address	Bispebjerg bakke 23, Copenhagen, Denmark, 2400
Public contact	Marietta Nygaard, Bispebjerg hospital, 0045 60626201, marietta.nygaard@regionh.dk
Scientific contact	Marietta Nygaard, Bispebjerg hospital, 0045 21494386, marietta.nygaard@regionh.dk

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	12 February 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 October 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of treatment with extracorporeal photopheresis in acute and chronic GVHD.

Protection of trial subjects:

There were no specific measures to protect subjects, as they received the usual treatment in the department.

Background therapy:

Given the nature of the disease Graft versus Host Disease and the preceeding bone marrow transplantation, the patients usually recieved many other treatments. This was usually transfusions of red blood cells or platelets, or infection prophylaxis and almost all patients also received one or more immunosuppressive drugs. The latter drugs were given to treat graft versus host disease, but was always administerered at the discretion of the treating physiscian. These drugs may very well have interfered with the effect of extracorporeal photopheresis.

Evidence for comparator:

We used no comparators

Actual start date of recruitment	07 July 2015
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	Denmark: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	16

From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients referred to extracoporeal photopheresis between 07.07.2015 (first patient enrolled) and 16.09.2016 (trial ended prior to plan) were enrolled.

Pre-assignment

Screening details:

Inclusion criteria were not very strict as it was an observational trial with no control group. All patients referred to extracorporeal photopheresis were screened by sponsor/investigator (MN) and all were enrolled.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	chronic

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Uvadex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for emulsion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dependent on amount of collected blood

Arm title	Acute

Arm description:

PAtietns with acute GvHD

Arm type	Experimental
Investigational medicinal product name	Uvadex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for emulsion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dependent on amount of collected blood

Number of subjects in period 1	chronic	Acute
Started	10	13
Completed	10	13

Baseline characteristics

Reporting groups	
Reporting group title	overall trial
Reporting group description:	
All patients treated with extracorporeal photopheresis	

Reporting group values	overall trial	Total	
Number of subjects	23	23	
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)	16	16	
From 65-84 years	7	7	
85 years and over	0	0	
Age continuous Units: years			
median	55		
full range (min-max)	31 to 75	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	17	17	

Subject analysis sets	
Subject analysis set title	Chronic GvHD
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients with chronic GvHD	
Subject analysis set title	Acute GvHD
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients with acute GvHD	

Reporting group values	Chronic GvHD	Acute GvHD	
Number of subjects	10	13	
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)	7	9	
From 65-84 years	3	4	
85 years and over	0	0	
Age continuous			
Units: years			
median			
full range (min-max)			
Gender categorical			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	chronic
Reporting group description: -	
Reporting group title	Acute
Reporting group description: PAtietns with acute GvHD	
Subject analysis set title	Chronic GvHD
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients with chronic GvHD	
Subject analysis set title	Acute GvHD
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients with acute GvHD	

Primary: Best or overall response

End point title	Best or overall response
End point description: The overall (cGvHD) or best response (AGvHD) during treatment with ECP	
End point type	Primary
End point timeframe: overall trial	

End point values	Chronic GvHD	Acute GvHD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	13		
Units: number of patients				
Complete remission	1	10		
Very Good Partial Remission	0	1		
Partial Remission	6	0		
No Change	2	0		
Progressive Disease	1	2		

Statistical analyses

Statistical analysis title	None
Statistical analysis description: No statistical analysis were made because the groups are not comparable. They are two different diseases.	
Comparison groups	Chronic GvHD v Acute GvHD

Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05 [2]
Method	No comparison made

Notes:

[1] - No comparisons can be made.

[2] - No comparisons made

Secondary: Survival at one year after start of treatment

End point title	Survival at one year after start of treatment

End point description:

Number of patients alive one year from start of treatment

End point type	Secondary

End point timeframe:

1 year from start of treatment

End point values	Chronic GvHD	Acute GvHD		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: Number of patients alive				
Alive	10	7		
Dead	0	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From start of trial and until first amendment, where the reporting of adverse events were changed.

Adverse event reporting additional description:

Given the nature of the graft versus host disease and the circumstances under which the patients receive treatment, there are expected to be many serious events during the treatment course, these are not expected to be related to the ECP treatment but rather to the bone marrow transplantation and/or the concurrent immunosuppressive drugs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

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: In the amendment it is specified, why the reporting of adverse events is difficult, due to the nature of the studied diseases and the competing uncontrolled therapies. It was never an aim of this study to examine safety.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2015	Change of the reporting of Adverse events because the patients were influenced by many other drugs and circumstances causing abnormal testings, infections and other complications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 October 2016	The trial was ended pre-term	-

Notes:

Limitations and caveats

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

The trial was never finished because it turned out to be impossible to perfom it meaningfully

Notes: