



Clinical trial results:

Study of T- and B-cell immunity after vaccination with a virosomebased influenza vaccine (Inflexal V) in patients who have undergone hematopoietic allogeneic stem cell transplantation.

Summary

EudraCT number	2013-003403-19
Trial protocol	SE
Global end of trial date	28 July 2014

Results information

Result version number	v1 (current)
This version publication date	27 November 2021
First version publication date	27 November 2021

Trial information

Trial identification

Sponsor protocol code	HCK1
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Karolinska University Hospital
Sponsor organisation address	Halsovagen 17, Stockholm, Sweden, SE-14186
Public contact	Dept. of Hematology, Karolinska University Hospital, 46 858582507, per.ljungman@ki.se
Scientific contact	Dept. of Hematology, Karolinska University Hospital, 46 858582507, per.ljungman@ki.se

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	31 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 July 2014
Global end of trial reached?	Yes
Global end of trial date	28 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Analyze T-cell and B-cell immune response after influenzavaccination with Inflexal V.

Protection of trial subjects:

Nothing in addition to routine monitoring of AE, SAE, and SUSAR.

Background therapy:

Patients had undergone allogeneic stem cell transplantation as an inclusion criterion into the trial.

Evidence for comparator:

The study product was a licensed virosomal influenza vaccine (Inflexal V). There was no comparator since it was an open exploratory study

Actual start date of recruitment	23 October 2013
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	Sweden: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	22
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment occurred from Oct 23, 2013 to Jan 03, 2014.

Pre-assignment

Screening details:

During this time 25 patients were included of whom 24 patients received the study vaccine. One patient was not vaccinated due to development of thrombocytopenia. The planned recruitment was 30 patients. The main reason that we did not reach the target recruitment was that patients received routine influenza vaccine by their local physicians.

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	Experimental arm
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Arm description:

This was a single arm open trial so this was the only arm in the study

Arm type	Experimental
Investigational medicinal product name	Inflexal V virosomal influenza vaccine
Investigational medicinal product code	Market Authorization number 20335
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

One single dose given intramuscularly

Number of subjects in period 1	Experimental arm
Started	24
Completed	24

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	24	24	
Age categorical			
All vaccinated subjects			
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)	22	22	
From 65-84 years	2	2	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	12	12	
Male	12	12	
Type of transplant conditioning			
Myeloablative vs. reduced intensity			
Units: Subjects			
Myeloablative	9	9	
Reduced intensity	15	15	
Time from transplantation to vaccination			
Units: Subjects			
< 6 months	12	12	
> 6 months	12	12	

Subject analysis sets

Subject analysis set title	Vaccinated patients
Subject analysis set type	Per protocol

Subject analysis set description:

All vaccinated patients

Reporting group values	Vaccinated patients		
Number of subjects	24		
Age categorical			
All vaccinated subjects			
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	22 2		
Gender categorical Units: Subjects			
Female	12		
Male	12		
Type of transplant conditioning			
Myeloablative vs. reduced intensity			
Units: Subjects			
Myeloablative	9		
Reduced intensity	15		
Time from transplantation to vaccination Units: Subjects			
< 6 months	12		
> 6 months	12		

End points

End points reporting groups

Reporting group title	Experimental arm
Reporting group description: This was a single arm open trial so this was the only arm in the study	
Subject analysis set title	Vaccinated patients
Subject analysis set type	Per protocol
Subject analysis set description: All vaccinated patients	

Primary: Serologic titer increase

End point title	Serologic titer increase ^[1]
End point description: No. of subjects achieving a four-fold rise in HI titers after vaccination.	
End point type	Primary
End point timeframe: Four weeks after vaccination	
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 was a one arm study looking at the response. There was no statistical analysis planned	

End point values	Vaccinated patients			
Subject group type	Subject analysis set			
Number of subjects analysed	21 ^[2]			
Units: No. of subjects	5			

Notes:

[2] - Three patients had no sample at 4 weeks after vaccination

Statistical analyses

No statistical analyses for this end point

Primary: Increase in influenza-specific T cells

End point title	Increase in influenza-specific T cells ^[3]
End point description: No. of patients doubling the number of influenza-specific T cells producing gamma-interferon after vaccination.	
End point type	Primary
End point timeframe: Four weeks after vaccination	
Notes: [3] - 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 was a one arm study looking at the response. There was no statistical analysis planned	

End point values	Vaccinated patients			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Number of subjects	10			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Four weeks after vaccination

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	4
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Reporting groups

Reporting group title	Experimental arm
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Reporting group description:

This was a single arm open trial so this was the only arm in the study

Serious adverse events	Experimental arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 24 (25.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Cardiac failure congestive	Additional description: Assessed as due to previous chemotherapy. Contributed to death.		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Diarrhoea	Additional description: Two patients developed diarrhoea due to pre-existing graft-vs-host disease		
subjects affected / exposed	2 / 24 (8.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonia	Additional description: Hospitalization		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection	Additional description: Hospitalization necessary. One influenza B. One of unknown cause		

subjects affected / exposed	2 / 24 (8.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Herpes zoster	Additional description: Hospitalized		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocarditis bacterial	Additional description: Contributed to death. Detected at autopsy. Same patient as the patient having cardiac failure		
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Experimental arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 24 (20.83%)		
General disorders and administration site conditions			
Local reactions	Additional description: At the vaccination site		
subjects affected / exposed	5 / 24 (20.83%)		
occurrences (all)	5		
Gastrointestinal disorders			
Nausea and vomiting			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Rhinitis			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		

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.

Small number of patients

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25817044>