



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 |
|-----------------------|------|

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 |
|------------------|------------------|

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

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|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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|-----------------|-------|
| Dictionary name | CTCAE |
|-----------------|-------|

| | |
|--------------------|---|
| Dictionary version | 4 |
|--------------------|---|

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

| 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.

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| Small number of patients |
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Notes:

Online references

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