



Clinical trial results:

RETIC trial: Reversal of Trauma Induced Coagulopathy by using Coagulation factor concentrates or Fresh frozen Plasma

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2011-004139-29 |
| Trial protocol | AT |
| Global end of trial date | 20 February 2016 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 25 October 2020 |
| First version publication date | 25 October 2020 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | RETIC |
|-----------------------|-------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01545635 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name | Medical University Innsbruck |
| Sponsor organisation address | Christoph-Probst-Platz 1, Innrain 52 A, Innsbruck, Austria, 6020 |
| Public contact | Univ.Do. Dr. Petra Innerhofer, Medical University Innsbruck, University Hospital for Anaesthesia and Intensive Care, +43 (0)50504-28503, petra.innerhofer@tirol-kliniken.at |
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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 | 20 February 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 20 February 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 February 2016 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To assess the difference in incidence of multi organ failure (MOF) after treatment of trauma induced coagulopathy with Fresh frozen plasma (FFP) or Coagulation factor concentrates (CFC).

Protection of trial subjects:

Fibrinogen administration is calculated and aimed to maintain fibrinogen concentration and polymerization within the lower normal levels of healthy adults. In addition, ROTEM assays are performed following each therapeutic step and enable detection of hypercoagulability. Several cases of thrombembolism have been reported after PCC administration. However the majority of data refers to patients receiving huge doses and continuous administration such as needed in patients with haemophilia and antibody formation. The doses used in the present study will be low and are aimed to raise factors levels up to 50% which is the lower normal level. Furthermore patients are closely monitored by ROTEM and a shortened ExTEM CT value should warrant against overdosing. Regarding FXIII concentrate no cases of thrombembolism following FXIII administration have been reported so far. Finally the amount of blood loss (120ml total, about 2% of calculated blood volume in a 70kg patient) due to study related blood sampling should not harm the patient.

Background therapy:

TXA will be administered to all included study patients as a single bolus of 20mg/kg immediately after inclusion. Additional doses will be administered if indicated by ROTEM assays. Red blood cells will be transfused to maintain haemoglobin between 8-10mg/dl. Autologous salvaged red cells will be re-transfused irrespective of actual hemoglobin levels. Platelet concentrates (1-2 U PC) will be administered if clot firmness remains poor to maintain platelet count between 50-100 G/L or (ExTEM A10 <35mm) albeit sufficient fibrinogen polymerization (FibTEM A10 >10mm). Crystalloid fluids and 4% modified gelatin solution should be used preferently to maintain normovolemia in amounts directed by the treating anaesthetist. Because of the profound effect of HES solutions on haemostasis HES should be avoided and only used if gelatin is contraindicated (known or new allergy). The use of HES will be documented and explained. All patients receive prewarmed iv fluids. In both groups pH, Ca⁺⁺, BE and temperature are monitored and corrected as possible (targets pH>7.2, Ca⁺⁺ >1mmol/L, BE >-4, temperature >35°C).

Evidence for comparator:

We hypothesize that the exclusively use of CFC improves outcome of severely traumatized patients. The administration of CFC should effectively and timely raise coagulation factor levels, thereby limiting coagulopathic bleeding. Because volume expansion and dilution can be avoided with use of CFC the numbers of red cell and platelet transfusion should be reduced. As all types of blood components increase susceptibility to nosocomial infection and sepsis a reduction in allogeneic transfusions and avoidance of FFP should result in a lower incidence of sepsis and multi organ failure. To test the hypothesis we will conduct a prospective study in adult patients with major trauma and coagulopathy randomly receiving CFC or FFP for correcting TIC.

| | |
|-----------------------------------------------------------|---------------|
| Actual start date of recruitment | 01 March 2012 |
| 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 | Austria: 100 |
| Worldwide total number of subjects | 100 |
| EEA total number of subjects | 100 |

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) | 1 |
| Adults (18-64 years) | 88 |
| From 65 to 84 years | 11 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Adult patients (aged 18–80 years) with trauma exhibiting an Injury Severity Score (ISS) greater than 15 and clinical signs or risk of substantial haemorrhage were screened for trauma-induced coagulopathy, which was defined as abnormally low fibrin polymerisation (measured with FibTEM assay) and/or prolonged initiation of coagulation (ExCT).

Pre-assignment

Screening details:

Between March 3, 2012, and Feb 20, 2016, 292 trauma patients with an expected ISS greater than 15 were screened for eligibility, of whom 192 were found ineligible. 100 patients were enrolled and randomly assigned to receive either FFP (n=48) or CFC (n=52).

Period 1

| | |
|------------------------------|-----------------------------------|
| Period 1 title | Treatment period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Subject |

Blinding implementation details:

Enrolled patients were randomly assigned (1:1) to FFP or CFC. An independent statistician determined random codes using permuted blocks with varying block size and Stata/MP 10.1 for Windows Statistical Software. Randomisation was stratified for presence or absence of brain injury, and patients were stratified into three ISS groups (ISS 16–30, 31–50, or >50).

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | Yes |
| Arm title | CFC group |

Arm description:

We started bleeding management with CFC immediately after randomisation and during surgical or radiological interventions, and continued study-specific coagulation management during the first 24 h at the intensive care unit (ICU).

Considering that coagulopathy might reoccur, one or several treatment loops were administered during the entire study period (lasting from admission to the emergency department until 24 h at the ICU).

In total 50 patients completed the treatment period, of which 38 patients received a single dose of CFC, 10 patients received a double dose of CFC and 2 patients received a double dose of CFC and in a crossover fashion rescue medication.

| | |
|----------------------------------------|------------------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Haemocomplettan P |
| Investigational medicinal product code | |
| Other name | Blutgerinnungsfaktor 1, Human Fibrinogen |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

The used dosage of fibrinogen (50mg/kg), refer to the European Guidelines of trauma management (published 2010, 2013, 2016).

| | |
|----------------------------------------|------------------------------------------------|
| Investigational medicinal product name | Fibrogammin P 250E |
| Investigational medicinal product code | |
| Other name | FACTOR XIII |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

The FXIII concentrate were administered at 20IU/kg.

| | |
|----------------------------------------------------------------------|------------------------------------------------|
| Investigational medicinal product name | Beriplex P/N 500 I.E |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| The 4 factor-PCC and FXIII concentrate were administered at 20IU/kg. | |
| Arm title | FFP group |

Arm description:

We started bleeding management with FFP immediately after randomisation and during surgical or radiological interventions, and continued study-specific coagulation management during the first 24 h at the intensive care unit (ICU).

Considering that coagulopathy might reoccur, one or several treatment loops were administered during the entire study period (lasting from admission to the emergency department until 24 h at the ICU).

In total 44 patients completed the treatment period, of which 12 patients received a single dose of FFP, 9 patients received a double dose of FFP and 23 patients received a double dose of FFP and in a crossover fashion rescue medication.

| | |
|----------------------------------------|--------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Octaplas SD Blutgruppe A |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

For the FFP group, transfusion of FFP (Octapharma, Vienna, Austria) delivered by the local blood bank was done in a single dose of 15 mL/kg of bodyweight.

Octaplas shows activity that is comparable to that of normal fresh-frozen human plasma. The final product contains 45-70 mg/mL of plasma protein.

| Number of subjects in period 1 | CFC group | FFP group |
|---------------------------------------|-----------|-----------|
| Started | 52 | 48 |
| Completed | 50 | 44 |
| Not completed | 2 | 4 |
| age < 18 years | 1 | - |
| fatal injury | 1 | 3 |
| Protocol deviation | - | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | CFC group |
|-----------------------|-----------|

Reporting group description:

We started bleeding management with CFC immediately after randomisation and during surgical or radiological interventions, and continued study-specific coagulation management during the first 24 h at the intensive care unit (ICU).

Considering that coagulopathy might reoccur, one or several treatment loops were administered during the entire study period (lasting from admission to the emergency department until 24 h at the ICU).

In total 50 patients completed the treatment period, of which 38 patients received a single dose of CFC, 10 patients received a double dose of CFC and 2 patients received a double dose of CFC and in a crossover fashion rescue medication.

| | |
|-----------------------|-----------|
| Reporting group title | FFP group |
|-----------------------|-----------|

Reporting group description:

We started bleeding management with FFP immediately after randomisation and during surgical or radiological interventions, and continued study-specific coagulation management during the first 24 h at the intensive care unit (ICU).

Considering that coagulopathy might reoccur, one or several treatment loops were administered during the entire study period (lasting from admission to the emergency department until 24 h at the ICU).

In total 44 patients completed the treatment period, of which 12 patients received a single dose of FFP, 9 patients received a double dose of FFP and 23 patients received a double dose of FFP and in a crossover fashion rescue medication.

| Reporting group values | CFC group | FFP group | Total |
|-------------------------------------------------------|-----------|-----------|-------|
| Number of subjects | 52 | 48 | 100 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 1 | 0 | 1 |
| Adults (18-64 years) | 45 | 43 | 88 |
| From 65-84 years | 6 | 5 | 11 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 42.60 | 42.26 | |
| standard deviation | ± 16.724 | ± 16.748 | - |
| Gender categorical Units: Subjects | | | |
| Female | 12 | 13 | 25 |
| Male | 40 | 35 | 75 |

End points

End points reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | CFC group |
|-----------------------|-----------|

Reporting group description:

We started bleeding management with CFC immediately after randomisation and during surgical or radiological interventions, and continued study-specific coagulation management during the first 24 h at the intensive care unit (ICU).

Considering that coagulopathy might reoccur, one or several treatment loops were administered during the entire study period (lasting from admission to the emergency department until 24 h at the ICU).

In total 50 patients completed the treatment period, of which 38 patients received a single dose of CFC, 10 patients received a double dose of CFC and 2 patients received a double dose of CFC and in a crossover fashion rescue medication.

| | |
|-----------------------|-----------|
| Reporting group title | FFP group |
|-----------------------|-----------|

Reporting group description:

We started bleeding management with FFP immediately after randomisation and during surgical or radiological interventions, and continued study-specific coagulation management during the first 24 h at the intensive care unit (ICU).

Considering that coagulopathy might reoccur, one or several treatment loops were administered during the entire study period (lasting from admission to the emergency department until 24 h at the ICU).

In total 44 patients completed the treatment period, of which 12 patients received a single dose of FFP, 9 patients received a double dose of FFP and 23 patients received a double dose of FFP and in a crossover fashion rescue medication.

Primary: Multiple organ failure

| | |
|-----------------|------------------------|
| End point title | Multiple organ failure |
|-----------------|------------------------|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 0- day 30

| End point values | CFC group | FFP group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 44 | | |
| Units: MOF | | | | |
| number (not applicable) | 25 | 29 | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Multiple organ failure |
| Comparison groups | CFC group v FFP group |

| | |
|-----------------------------------------|-----------------|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.15 |
| Method | Fisher exact |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.78 |
| upper limit | 4.86 |

Secondary: Massive transfusions of RBC

| | |
|---------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| End point title | Massive transfusions of RBC |
| End point description: | |
| As further secondary efficacy endpoint, we also addressed frequency of massive transfusions of RBC during the first 24 h. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 0 | |

| End point values | CFC group | FFP group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 44 | | |
| Units: Number of patients | | | | |
| number (not applicable) | 6 | 13 | | |

Statistical analyses

| | |
|-----------------------------------------|-----------------------------|
| Statistical analysis title | Massive transfusions of RBC |
| Comparison groups | CFC group v FFP group |
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.042 |
| Method | Fisher exact |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.95 |
| upper limit | 10.87 |

Secondary: Frequency of transfusions of platelet concentrates

| | |
|-----------------|----------------------------------------------------|
| End point title | Frequency of transfusions of platelet concentrates |
|-----------------|----------------------------------------------------|

End point description:

As further secondary efficacy endpoint, we also addressed frequency of transfusions of platelet concentrates during the first 24 h.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 0

| End point values | CFC group | FFP group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 44 | | |
| Units: Number of patients | | | | |
| number (not applicable) | 10 | 21 | | |

Statistical analyses

| | |
|-----------------------------------|---------------------------------------------------|
| Statistical analysis title | Frequency of transfusions of platelet concentrate |
|-----------------------------------|---------------------------------------------------|

| | |
|-------------------|-----------------------|
| Comparison groups | FFP group v CFC group |
|-------------------|-----------------------|

| | |
|-----------------------------------------|----|
| Number of subjects included in analysis | 94 |
|-----------------------------------------|----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|-------------|
| Analysis type | superiority |
|---------------|-------------|

| | |
|---------|----------|
| P-value | = 0.0078 |
|---------|----------|

| | |
|--------|--------------|
| Method | Fisher exact |
|--------|--------------|

| | |
|--------------------|-----------------|
| Parameter estimate | Odds ratio (OR) |
|--------------------|-----------------|

| | |
|----------------|-----|
| Point estimate | 3.6 |
|----------------|-----|

| | |
|---------------------|--|
| Confidence interval | |
|---------------------|--|

| | |
|-------|------|
| level | 95 % |
|-------|------|

| | |
|-------|---------|
| sides | 2-sided |
|-------|---------|

| | |
|-------------|------|
| lower limit | 1.35 |
|-------------|------|

| | |
|-------------|-------|
| upper limit | 10.18 |
|-------------|-------|

Secondary: Bleeding score of 2 or 3

| | |
|-----------------|--------------------------|
| End point title | Bleeding score of 2 or 3 |
|-----------------|--------------------------|

End point description:

Bleeding score is defined as number from 0-3, dependent on severity of bleeding. A coagulopathic bleeding score of 2 or 3 after first study drug administration was more frequently observed in the FFP group.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 0

| End point values | CFC group | FFP group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 44 | | |
| Units: Patients | | | | |
| number (not applicable) | 14 | 31 | | |

Statistical analyses

| | |
|-----------------------------------------|--------------------------|
| Statistical analysis title | Bleeding score of 2 or 3 |
| Comparison groups | CFC group v FFP group |
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.004 |
| Method | Fisher exact |

| | |
|-----------------------------------------|--------------------------------------------------|
| Statistical analysis title | Bleeding score of 2 or 3 and massive transfusion |
| Comparison groups | CFC group v FFP group |
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 |
| Method | Fisher exact |

Secondary: Rescue therapy

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
| End point title | Rescue therapy |
| End point description: 20 (87%) of the 23 patients in the FFP group who required rescue medication needed rescue already in the first treatment loop, whereas three other patients in the FFP group and the two patients in the CFC group received rescue therapy in later treatment loops. | |
| End point type | Secondary |
| End point timeframe: Day 0 | |

| End point values | CFC group | FFP group | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 44 | | |
| Units: Patients | | | | |
| number (not applicable) | 2 | 23 | | |

Statistical analyses

| Statistical analysis title | Rescue medication |
|-----------------------------------------|-----------------------|
| Comparison groups | CFC group v FFP group |
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Fisher exact |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 25.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.47 |
| upper limit | 240.03 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 0- day 30

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 4.03 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | CFC group |
|-----------------------|-----------|

Reporting group description:

We started bleeding management with CFC immediately after randomisation and during surgical or radiological interventions, and continued study-specific coagulation management during the first 24 h at the intensive care unit (ICU).

Considering that coagulopathy might reoccur, one or several treatment loops were administered during the entire study period (lasting from admission to the emergency department until 24 h at the ICU).

In total 50 patients completed the treatment period, of which 38 patients received a single dose of CFC, 10 patients received a double dose of CFC and 2 patients received a double dose of CFC and rescue medication.

In these patients, rescue therapy was initiated, meaning FFP was administered to patients in the CFC group.

| | |
|-----------------------|-----------|
| Reporting group title | FFP group |
|-----------------------|-----------|

Reporting group description:

We started bleeding management with FFP immediately after randomisation and during surgical or radiological interventions, and continued study-specific coagulation management during the first 24 h at the intensive care unit (ICU).

Considering that coagulopathy might reoccur, one or several treatment loops were administered during the entire study period (lasting from admission to the emergency department until 24 h at the ICU).

In total 44 patients completed the treatment period, of which 12 patients received a single dose of FFP, 9 patients received a double dose of FFP and 23 patients received a double dose of FFP and rescue medication.

| Serious adverse events | CFC group | FFP group | |
|---------------------------------------------------|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 15 / 52 (28.85%) | 18 / 48 (37.50%) | |
| number of deaths (all causes) | 5 | 2 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Vascular disorders | | | |
| DVT | | | |
| subjects affected / exposed | 5 / 52 (9.62%) | 8 / 48 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |

| | | | |
|-------------------------------------------------|----------------|-----------------|--|
| subjects affected / exposed | 3 / 52 (5.77%) | 1 / 48 (2.08%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arterial thrombosis | | | |
| subjects affected / exposed | 2 / 52 (3.85%) | 2 / 48 (4.17%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Delir | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 2 / 48 (4.17%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute renal failure | | | |
| subjects affected / exposed | 5 / 52 (9.62%) | 7 / 48 (14.58%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | CFC group | FFP group | |
|-------------------------------------------------------|----------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 5 / 52 (9.62%) | 3 / 48 (6.25%) | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 1 / 48 (2.08%) | |
| occurrences (all) | 2 | 2 | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 48 (0.00%) | |
| occurrences (all) | 1 | 1 | |
| Nervous system disorders | | | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 52 (0.00%) | 2 / 48 (4.17%) | |
| occurrences (all) | 2 | 2 | |
| Vocal cord paralysis | | | |

| | | | |
|---------------------------------------------------------------------------------------------------------|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 52 (1.92%) 1 | 0 / 48 (0.00%) 1 | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 1 / 52 (1.92%) 1 | 0 / 48 (0.00%) 1 | |
| Skin and subcutaneous tissue disorders Exanthema subjects affected / exposed occurrences (all) | 1 / 52 (1.92%) 2 | 1 / 48 (2.08%) 2 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 14 March 2012 | substantial amendments: another trial monitor, another member in study team (a medical doctor for transfusion medicine), definition for platelet transfusion trigger (50.000-100.000) |
| 14 July 2012 | Substantial amendment of an inclusion criterium: Limit of FibTEM was changed from <7mm to <9mm |

Notes:

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/28457980>