



Clinical trial results:

Full title of the trial: Allogeneic Stem Cell Transplantation of NiCord®, Umbilical Cord Blood-derived Ex Vivo Expanded Stem and Progenitor Cells, in Adolescents and Adult Patients with Hematological Malignancies

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-000074-19 |
| Trial protocol | ES IT NL |
| Global end of trial date | 29 June 2018 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 12 July 2019 |
| First version publication date | 12 July 2019 |
| Summary attachment (see zip file) | Synopsis (CSR_SNG01_v1.0_20JUN2019 Synopsis.pdf) |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | GCP#03.01.020 |
|-----------------------|---------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01816230 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Gamida Cell Ltd. |
| Sponsor organisation address | Beit Ofer, 5 Nahum Hafzadi, Jerusalem, Israel, 9548401 |
| Public contact | Kelly Myers, Gamida Cell Ltd, 972 26595631, kelly@gamida-cell.com |
| Scientific contact | Kelly Myers, Gamida Cell Ltd, 972 26595631, kelly@gamida-cell.com |

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 | 27 June 2018 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 June 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Assess the cumulative incidence of NiCord-derived neutrophil engraftment at 42 days following transplantation.

Assess the incidence of secondary graft failure at 180 days following transplantation of NiCord.

Protection of trial subjects:

The Data Monitoring Committee met to discuss and ensure patient safety throughout the trial. The committee reviewed the accumulated data after 3 patients entered the study and were assessed at day 100 following transplant. At this initial review, the DMC monitored in particular: any occurrence of primary or secondary graft failure, as well as any substantial decrease in donor chimerism (especially myeloid chimerism), or evidence of impending graft failure, as well as all study data in general. A subsequent DMC review took place after 3 patients received the cryopreserved NiCord product and were assessed at day 100 following transplant. Early safety assessment guidelines were used to monitor primary & secondary graft failure, non-relapse mortality at 100 days and alert the DMC.

Background therapy:

1) Myeloablative conditioning regimens: (Each transplant center used the same conditioning regimen for all patients transplanted at their center).

a) Regimen A (Day -11 to -2):

Total Body irradiation (TBI) 1350 cGy, Fludarabine: 160 mg/m², (optional: Cyclophosphamide: 120 mg/kg or Thiotepa: 10 mg/kg)

b) Regimen B (Day -7 to -3):

Thiotepa 10 mg/kg, Busulfan 9.6 mg/kg, Fludarabine 150 mg/m²

c) Regimen C (Day -5 to -2):

Clofarabine 120 mg/m², Fludarabine 40 mg/m², Busulfan AUC 90 mg*h/L

2) GvHD prophylaxis regimen consisted of Mycophenolate Mofetil (MMF) and a calcineurin inhibitor (Tacrolimus or Cyclosporine). Each transplant center used the same calcineurin inhibitor for all patients. Tacrolimus or Cyclosporine from day -3 through day +150 Target tacrolimus trough blood levels of 5-15 ng/ml. Target cyclosporine trough levels of 200-400 ng/mL by TDX method (or 100-250 ng/mL by Tandem MS or equivalent level for other CSA testing methods).

Mycophenolate Mofetil (MMF) 1 g TID IV or PO (15 mg/kg IV TID if patient weighs <50 kg) beginning day -3 to at least day +60.

3) G-CSF therapy was started on day +1 at a dose of 5 µg/kg/day continuing at least until the ANC is >1,000/µl x 2 consecutive days.

Evidence for comparator:

N/A

| | |
|---|--|
| Actual start date of recruitment | 21 May 2013 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy, Ethical reason, Regulatory reason, Scientific research |
| Long term follow-up duration | 4 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 18 |
| Country: Number of subjects enrolled | Singapore: 2 |
| Country: Number of subjects enrolled | Italy: 1 |
| Country: Number of subjects enrolled | Netherlands: 3 |
| Country: Number of subjects enrolled | Spain: 14 |
| Worldwide total number of subjects | 38 |
| EEA total number of subjects | 18 |

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) | 3 |
| Adults (18-64 years) | 35 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Recruitment began in the US in May 2013, followed by Spain, Italy, Netherlands and Singapore.

Pre-assignment

Screening details:

59 subjects assessed for eligibility. 11 ineligible (5 progressive disease, 5 medical deterioration, 1 minimal residual disease). 5 withdrew due to projected waiting time for NiCord production. 5 transplanted with unmanipulated CBU only. 2 transplanted with unmanipulated CBU + NiCord. 36 treated with NiCord.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|-----------|--------|
| Arm title | NiCord |
|-----------|--------|

Arm description:

NiCord® is a cryopreserved stem/progenitor cell based product of purified CD133+ cells composed of ex vivo expanded allogeneic UCB cells. NiCord® comprises: 1) cord blood-derived ex vivo expanded CD133+ cells (NiCord® cultured fraction (CF)); and 2) the non-cultured cell fraction (CD133-) of the same CBU (NiCord® Non-cultured Fraction (NF)). Both fractions, i.e. NiCord® CF and NiCord® NF, will be kept frozen until they are infused on the day of transplantation.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | NiCord |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Dispersion for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Dosage is administered once.

| | |
|---------------------------------------|--------|
| Number of subjects in period 1 | NiCord |
| Started | 38 |
| Completed | 38 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall trial |
| Reporting group description: - | |

| Reporting group values | Overall trial | Total | |
|---------------------------|---------------|-------|--|
| Number of subjects | 38 | 38 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adolescents (12-17 years) | 3 | 3 | |
| Adults (18-64 years) | 35 | 35 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 16 | 16 | |
| Male | 22 | 22 | |

Subject analysis sets

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Efficacy & Safety Analysis |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Any patient that received NiCord as a standalone graft.

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Additional Safety Analysis |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

included all patients who received NiCord® as a standalone, or with an unmanipulated CBU.

| Reporting group values | Efficacy & Safety Analysis | Additional Safety Analysis | |
|---------------------------|----------------------------|----------------------------|--|
| Number of subjects | 36 | 38 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adolescents (12-17 years) | 2 | 3 | |
| Adults (18-64 years) | 34 | 35 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 16 | 16 | |
| Male | 20 | 22 | |

End points

End points reporting groups

| | |
|-----------------------|--------|
| Reporting group title | NiCord |
|-----------------------|--------|

Reporting group description:

NiCord® is a cryopreserved stem/progenitor cell based product of purified CD133+ cells composed of ex vivo expanded allogeneic UCB cells. NiCord® comprises: 1) cord blood-derived ex vivo expanded CD133+ cells (NiCord® cultured fraction (CF)); and 2) the non-cultured cell fraction (CD133-) of the same CBU (NiCord® Non-cultured Fraction (NF)). Both fractions, i.e. NiCord® CF and NiCord® NF, will be kept frozen until they are infused on the day of transplantation.

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Efficacy & Safety Analysis |
|----------------------------|----------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Any patient that received NiCord as a standalone graft.

| | |
|----------------------------|----------------------------|
| Subject analysis set title | Additional Safety Analysis |
|----------------------------|----------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

included all patients who received NiCord® as a standalone, or with an unmanipulated CBU.

Primary: NiCord neutrophil engraftment

| | |
|-----------------|--|
| End point title | NiCord neutrophil engraftment ^[1] |
|-----------------|--|

End point description:

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

End point timeframe:

42 days following transplantation

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 is a single-arm study; to assess the incidence of neutrophil engraftment post transplant a cumulative incidence curve will be computed along with a 95% confidence interval at 42 days post-transplant. Death prior to engraftment will be considered as a competing risk.

| End point values | NiCord | Efficacy & Safety Analysis | | |
|-----------------------------|-----------------|----------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 36 | 36 | | |
| Units: Proportion | | | | |
| number (not applicable) | 94 | 94 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Secondary graft failure

| | |
|-----------------|--|
| End point title | Secondary graft failure ^[2] |
|-----------------|--|

End point description:

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

End point timeframe:

180 days

Notes:

[2] - 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 is a single-arm study; the cumulative incidence of secondary graft failure out of those who had initial engraftment will be described using the cumulative incidence estimator, treating death and disease relapse/progression prior to secondary graft failure as a competing event.

| End point values | NiCord | Efficacy & Safety Analysis | | |
|----------------------------------|-------------------|----------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 36 | 36 | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 2.8 (0.2 to 12.6) | 2.8 (0.2 to 12.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to neutrophil engraftment

End point titleTime to neutrophil engraftment

End point description:

End point typeSecondary

End point timeframe:

42 days

| End point values | NiCord | Efficacy & Safety Analysis | | |
|----------------------------------|-----------------|----------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 36 | 36 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 11.5 (9 to 14) | 11.5 (9 to 14) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to platelet engraftment

End point titleTime to platelet engraftment

End point description:

End point typeSecondary

End point timeframe:

180 days

| End point values | NiCord | Efficacy & Safety Analysis | | |
|----------------------------------|-------------------|----------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 34 ^[3] | 34 | | |
| Units: days | | | | |
| median (confidence interval 95%) | 34 (32 to 42) | 34 (32 to 42) | | |

Notes:

[3] - Patients who engrafted neutrophils

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet engraftment

| | |
|------------------------|----------------------|
| End point title | Platelet engraftment |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 100 days | |

| End point values | Efficacy & Safety Analysis | | | |
|-----------------------------|----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 34 | | | |
| Units: percent | | | | |
| number (not applicable) | 81 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: non-relapse mortality

| | |
|------------------------|-----------------------|
| End point title | non-relapse mortality |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 100 days | |

| End point values | Efficacy & Safety Analysis | | | |
|----------------------------------|----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 36 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 8.3 (2.1 to 20.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Acute GVHD II-IV

| | |
|------------------------|------------------|
| End point title | Acute GVHD II-IV |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 100 days | |

| End point values | Efficacy & Safety Analysis | | | |
|----------------------------------|----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 36 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 44.4 (27.7 to 59.9) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Acute GVHD III-IV

| | |
|------------------------|-------------------|
| End point title | Acute GVHD III-IV |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 100 days | |

| End point values | Efficacy & Safety Analysis | | | |
|----------------------------------|----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 36 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 11 (3 to 24) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Chronic GVHD

| | |
|------------------------|--------------|
| End point title | Chronic GVHD |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 180 days | |

| End point values | Efficacy & Safety Analysis | | | |
|----------------------------------|----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 36 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 30.6 (16.3 to 46.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Chronic GVHD

| | |
|------------------------|--------------|
| End point title | Chronic GVHD |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 1 year | |

| End point values | Efficacy & Safety Analysis | | | |
|----------------------------------|----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 36 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 41.7 (25.1 to 57.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary graft failure

| | |
|------------------------|-------------------------|
| End point title | Secondary graft failure |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 1 year | |

| End point values | Efficacy & Safety Analysis | | | |
|----------------------------------|----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 36 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 5.6 (1 to 16.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

| | |
|------------------------|------------------|
| End point title | Overall survival |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 180 days | |

| End point values | Efficacy & Safety Analysis | | | |
|----------------------------------|----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 36 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 80 (63 to 90) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

| | |
|------------------------|------------------|
| End point title | Overall survival |
| End point description: | |
| | |
| End point type | Secondary |
| End point timeframe: | |
| 1 year | |

| End point values | Efficacy & Safety Analysis | | | |
|----------------------------------|----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 36 | | | |
| Units: percent | | | | |
| number (confidence interval 95%) | 51 (33 to 67) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 1 year post-transplant

Adverse event reporting additional description:

Infections and GvHD were reported up to 1 year post-transplant.

All common events post-transplant were collected up to day 42 post-transplant. Grade 3-4 non-serious adverse events collected up to one year post-transplant.

Grade 3-5 adverse events and all grades serious adverse events have been reported to the database.

Assessment type

Systematic

Dictionary used

Dictionary name

MedDRA

Dictionary version

21

Reporting groups

Reporting group title

NiCord treated patients

Reporting group description: -

| Serious adverse events | NiCord treated patients | | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 35 / 38 (92.11%) | | |
| number of deaths (all causes) | 16 | | |
| number of deaths resulting from adverse events | 8 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Haematological malignancy | Additional description: Includes: Acute myeloid leukaemia; Leukaemia recurrent; Myelodysplastic syndrome | | |
| subjects affected / exposed | 9 / 38 (23.68%) | | |
| occurrences causally related to treatment / all | 0 / 9 | | |
| deaths causally related to treatment / all | 0 / 8 | | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|---|--|--|--|
| Asthenia | subjects affected / exposed | 1 / 38 (2.63%) | | |
| | occurrences causally related to treatment / all | 0 / 1 | | |
| | deaths causally related to treatment / all | 0 / 0 | | |
| fever | subjects affected / exposed | 1 / 38 (2.63%) | | |
| | occurrences causally related to treatment / all | 0 / 1 | | |
| | deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | | |
| Graft versus host disease | | Additional description: Includes: Acute Graft versus host disease (GvHD), GvHD, GvHD in gastrointestinal tract | | |
| | subjects affected / exposed | 11 / 38 (28.95%) | | |
| | occurrences causally related to treatment / all | 17 / 17 | | |
| | deaths causally related to treatment / all | 2 / 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | | |
| Respiratory disorder | | Additional description: Includes: Bronchospasm; Dyspnoea; Pneumonitis; Pulmonary oedema; Respiratory failure | | |
| | subjects affected / exposed | 5 / 38 (13.16%) | | |
| | occurrences causally related to treatment / all | 0 / 5 | | |
| | deaths causally related to treatment / all | 0 / 0 | | |
| pain - non-cardiac | subjects affected / exposed | 1 / 38 (2.63%) | | |
| | occurrences causally related to treatment / all | 0 / 1 | | |
| | deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | | |
| Transaminases increased | subjects affected / exposed | 1 / 38 (2.63%) | | |
| | occurrences causally related to treatment / all | 0 / 1 | | |
| | deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | | |
| Transplant failure | subjects affected / exposed | 4 / 38 (10.53%) | | |
| | occurrences causally related to treatment / all | 2 / 4 | | |
| | deaths causally related to treatment / all | 0 / 0 | | |
| Fall | | | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed | 2 / 38 (5.26%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| cardiac and vascular disorders | Additional description: Includes cardiogenic shock, atrial fibrillation, pericardial infusion | | |
| subjects affected / exposed | 3 / 38 (7.89%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Nervous system disorders | | | |
| Central nervous system events | Additional description: Includes: Cerebrovascular accident; Encephalopathy; Haemorrhage intracranial; Spinal epidural haematoma; Syncope | | |
| subjects affected / exposed | 5 / 38 (13.16%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Eye disorders | | | |
| Optic nerve disorder | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Gastrointestinal disorder | Additional description: Includes: Colitis; Diarrhoea; Gastrointestinal disorder; Stomatitis | | |
| subjects affected / exposed | 5 / 38 (13.16%) | | |
| occurrences causally related to treatment / all | 0 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Venoocclusive liver disease | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Myopathy | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Infection | | Additional description: Includes: Adenovirus; Bacteraemia; Cystitis; Cystitis viral; CMV viraemia; Device related; Enterocolitis infectious; Escherichia bacteraemia; Liver abscess; Lung infection; Pneumonia; Sepsis; URT infection, Viral haemorrhagic cystitis | |
| subjects affected / exposed | 18 / 38 (47.37%) | | |
| occurrences causally related to treatment / all | 0 / 26 | | |
| deaths causally related to treatment / all | 0 / 4 | | |
| Metabolism and nutrition disorders | | | |
| Fluid overload | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anorexia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 3 %

| Non-serious adverse events | NiCord treated patients | | |
|---|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 38 / 38 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Disease recurrence | Additional description: includes serious adverse events | | |
| subjects affected / exposed | 9 / 38 (23.68%) | | |
| occurrences (all) | 9 | | |
| General disorders and administration site conditions | | | |
| Mucosal inflammation | Additional description: includes serious adverse events | | |
| subjects affected / exposed | 9 / 38 (23.68%) | | |
| occurrences (all) | 9 | | |
| Pain | Additional description: includes serious adverse events | | |
| subjects affected / exposed | 7 / 38 (18.42%) | | |
| occurrences (all) | 9 | | |
| Oedema | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | | |
| occurrences (all) | 3 | | |
| Immune system disorders | | | |
| Graft versus host disease | Additional description: includes serious adverse events | | |
| subjects affected / exposed | 10 / 38 (26.32%) | | |
| occurrences (all) | 16 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | Additional description: includes serious adverse events | | |
| subjects affected / exposed | 3 / 38 (7.89%) | | |
| occurrences (all) | 4 | | |
| Hypoxia | Additional description: includes serious adverse events | | |
| subjects affected / exposed | 4 / 38 (10.53%) | | |
| occurrences (all) | 5 | | |
| Investigations | | | |
| Blood creatine increased | Additional description: includes serious adverse events | | |
| subjects affected / exposed | 2 / 38 (5.26%) | | |
| occurrences (all) | 2 | | |
| Hepatic enzyme increased | Additional description: includes serious adverse events | | |

| | | | |
|--|---|--|--|
| subjects affected / exposed occurrences (all) | 3 / 38 (7.89%) 3 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | Additional description: includes serious adverse events | | |
| subjects affected / exposed occurrences (all) | 2 / 38 (5.26%) 2 | | |
| Transplant failure | Additional description: includes serious adverse events | | |
| subjects affected / exposed occurrences (all) | 4 / 38 (10.53%) 4 | | |
| Cardiac disorders | | | |
| Cardiac disorder | Additional description: includes arrhythmia, atrial fibrillation, cardiogenic shock, pericardial infusion. includes serious adverse events | | |
| subjects affected / exposed occurrences (all) | 4 / 38 (10.53%) 5 | | |
| Nervous system disorders | | | |
| Somnolence | Additional description: includes serious adverse events | | |
| subjects affected / exposed occurrences (all) | 2 / 38 (5.26%) 2 | | |
| Syncope | Additional description: includes serious adverse events | | |
| subjects affected / exposed occurrences (all) | 2 / 38 (5.26%) 2 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | Additional description: includes serious adverse events | | |
| subjects affected / exposed occurrences (all) | 4 / 38 (10.53%) 4 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | Additional description: includes serious adverse events | | |
| subjects affected / exposed occurrences (all) | 3 / 38 (7.89%) 3 | | |
| Dysphagia | Additional description: includes serious adverse events | | |
| subjects affected / exposed occurrences (all) | 4 / 38 (10.53%) 5 | | |
| Nausea | Additional description: includes serious adverse events | | |
| subjects affected / exposed occurrences (all) | 11 / 38 (28.95%) 12 | | |
| Hepatobiliary disorders | | | |

| | | | |
|---|---|--|--|
| hepatobiliary disorder subjects affected / exposed occurrences (all) | Additional description: includes serious adverse events | | |
| | 2 / 38 (5.26%) | | |
| | 2 | | |
| Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all) | Additional description: includes serious adverse events | | |
| | 2 / 38 (5.26%) | | |
| | 2 | | |
| Musculoskeletal and connective tissue disorders Muscular weakness subjects affected / exposed occurrences (all) | Additional description: includes serious adverse events | | |
| | 4 / 38 (10.53%) | | |
| | 4 | | |
| Infections and infestations Bacteraemia subjects affected / exposed occurrences (all) Enterocolitis infectious subjects affected / exposed occurrences (all) Infection subjects affected / exposed occurrences (all) Sepsis subjects affected / exposed occurrences (all) | Additional description: includes serious adverse events | | |
| | 2 / 38 (5.26%) | | |
| | 3 | | |
| | Additional description: includes serious adverse events | | |
| | 2 / 38 (5.26%) | | |
| | 2 | | |
| | Additional description: includes serious adverse events | | |
| | 2 / 38 (5.26%) | | |
| | 2 | | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all) Hypoalbuminaemia subjects affected / exposed occurrences (all) Hyponatraemia | Additional description: includes serious adverse events | | |
| | 9 / 38 (23.68%) | | |
| | 10 | | |
| | Additional description: includes serious adverse events | | |
| | 6 / 38 (15.79%) | | |
| | 6 | | |
| | Additional description: includes serious adverse events | | |
| | 2 / 38 (5.26%) | | |
| | 3 | | |
| | Additional description: includes serious adverse events | | |

| | | | |
|-----------------------------|---|--|--|
| subjects affected / exposed | 2 / 38 (5.26%) | | |
| occurrences (all) | 2 | | |
| Hypophosphataemia | Additional description: includes serious adverse events | | |
| subjects affected / exposed | 2 / 38 (5.26%) | | |
| occurrences (all) | 2 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 20 February 2014 | To expand patient population and clarify eligibility criteria |
| 20 March 2014 | Change in manufacturing procedure to cryopreserved product. Modify eligibility criteria. Additional option for conditioning regimen. |
| 28 August 2014 | Add safety objective. Define childbearing potential and appropriate contraception. |
| 04 December 2014 | Modify eligibility criteria. Additional regimen specific stopping guidelines. Additional supportive and viral monitoring care guidelines. Update AE reporting guidelines. |
| 27 March 2015 | Increase number of patients for study enrollment. Modify eligibility criteria, COA release criteria, GvHD prophylaxis medication administration and assessment grading criteria. |

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/28392378>

<http://www.ncbi.nlm.nih.gov/pubmed/30523748>

<http://www.ncbi.nlm.nih.gov/pubmed/24911148>