



Clinical trial results:

Prevention of severe GVHD after allogeneic hematopoietic stem cell transplantation, applied as consolidation immunotherapy in patients with hematological malignancies. A prospective randomized phase III trial.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2008-003540-11 |
| Trial protocol | NL BE |
| Global end of trial date | 07 January 2021 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 25 December 2022 |
| First version publication date | 25 December 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | HO96GVHD |
|-----------------------|----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | HOVON |
| Sponsor organisation address | De Boelelaan 1117, Amsterdam, Netherlands, |
| Public contact | HOVON Data Center, HOVON, hdc@erasmusmc.nl |
| Scientific contact | HOVON Data Center, HOVON, hdc@erasmusmc.nl |

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 | 05 July 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 02 July 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 January 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Objectives:

- to increase the proportion of patients with non severe GVHD within 180 days post-allo-SCT,
 - to reduce the progression rate and
 - to improve the progression free survival
- using a time restricted immunosuppressive regimen or a short-course post-transplant GVHD prophylaxis consisting of high-dose cyclophosphamide as compared to a prolonged, standard immunosuppressive regimen.

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 14 April 2010 |
| 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 | Netherlands: 491 |
| Country: Number of subjects enrolled | Belgium: 3 |
| Worldwide total number of subjects | 494 |
| EEA total number of subjects | 494 |

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) | 418 |
| From 65 to 84 years | 76 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All subjects gave written informed consent and were screened according to the inclusion- and exclusion criteria.

Period 1

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

Arms

| | |
|------------------------------|-------|
| Are arms mutually exclusive? | Yes |
| Arm title | Arm A |

Arm description:

Standard immunosuppression with Cyclosporin A and Myfortic.

| | |
|--|------------------------------------|
| Arm type | Standard treatment |
| Investigational medicinal product name | Cyclosporine A |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, soft, Powder for infusion |
| Routes of administration | Infusion , Oral use |

Dosage and administration details:

Cyclosporine A (CyA) immunosuppression: 9 mg/kg p.o. (in 2 doses) OR 3 mg/kg i.v. (in 2 doses) from day -5/-3 (depending on local procedures) till day 180.

| | |
|--|----------|
| Investigational medicinal product name | Myfortic |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Myfortic immunosuppression: (2x 16 mg/kg p.o.) from day 0 till day 84. Myfortic will be given with a maximum of 2160 mg/day.

| | |
|------------------|-------|
| Arm title | Arm B |
|------------------|-------|

Arm description:

Time-restricted immunosuppression with Cyclosporin A and Myfortic.

| | |
|--|------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Cyclosporine A |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, soft, Powder for infusion |
| Routes of administration | Infusion , Oral use |

Dosage and administration details:

Cyclosporine A time-restricted immunosuppression: 9 mg/kg p.o. (in 2 doses) OR 3 mg/kg i.v. (in 2 doses) from day -5/-3 (depending on local procedures) till day 84.

| | |
|--|----------|
| Investigational medicinal product name | Myfortic |
| Investigational medicinal product code | |
| Other name | |

| | |
|--------------------------|----------|
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Myfortic time-restricted immunosuppression:(2x 16 mg/kg p.o.) from day 0 till day 28. Myfortic will be given with a maximum of 2160 mg/day.

| | |
|------------------|-------|
| Arm title | Arm C |
|------------------|-------|

Arm description:

Post-transplant cyclophosphamide

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

Dosage and administration details:

Cyclophosphamide during conditioning: 14.5 mg/kg i.v. (day -6 and -5).

Cyclophosphamide during post-transplant immunosuppression: 50 mg/kg i.v. (day +3 and +4)

| | |
|--|---------------------|
| Investigational medicinal product name | Fludarabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Fludarabine during conditioning: 30 mg/m² i.v. (day -6 to -2) 5 days.

| | |
|--|------------------------------------|
| Investigational medicinal product name | Cyclosporine A |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, soft, Powder for infusion |
| Routes of administration | Infusion , Oral use |

Dosage and administration details:

Cyclosporine A during post-transplant immunosuppression: 9 mg/kg p.o. (in 2 doses) OR 3 mg/kg i.v. (in 2 doses) during day +5 till +70.

| Number of subjects in period 1 | Arm A | Arm B | Arm C |
|---------------------------------------|-------|-------|-------|
| Started | 195 | 194 | 105 |
| Completed | 35 | 38 | 40 |
| Not completed | 160 | 156 | 65 |
| Adverse Reaction | 82 | 84 | 39 |
| Other | 21 | 15 | 7 |
| At patients request | 1 | - | - |
| Lack of efficacy | 56 | 57 | 19 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Overall period |
|-----------------------|----------------|

Reporting group description: -

| Reporting group values | Overall period | Total | |
|---|----------------|-------|--|
| Number of subjects | 494 | 494 | |
| 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) | 418 | 418 | |
| From 65-84 years | 76 | 76 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 56 | | |
| full range (min-max) | 18 to 71 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 201 | 201 | |
| Male | 293 | 293 | |

End points

End points reporting groups

| | |
|--|-------|
| Reporting group title | Arm A |
| Reporting group description: Standard immunosuppression with Cyclosporin A and Myfortic. | |
| Reporting group title | Arm B |
| Reporting group description: Time-restricted immunosuppression with Cyclosporin A and Myfortic. | |
| Reporting group title | Arm C |
| Reporting group description: Post-transplant cyclophosphamide | |

Primary: Primary endpoint

| | |
|---|---------------------------------|
| End point title | Primary endpoint ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| See publication | |
| 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: Statistical analysis has been uploaded in the chart section. | |

| End point values | Arm A | Arm B | Arm C | |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 184 | 185 | 99 | |
| Units: Whole | 184 | 185 | 99 | |

| | |
|-----------------------------------|--|
| Attachments (see zip file) | Statistical data section from publication/HO96_Statistical data List of reported non-SAE's/nonsaedata96-28Nov2022.pdf List of reported SAE's/saedata96-28Nov2022.pdf |
|-----------------------------------|--|

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs CTCAE grade ≥ 2 have to be reported (with the exception of progression). However, GVHD of all grades has to be reported on the GVHD forms.

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

Dictionary used

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

| | |
|--------------------|-----|
| Dictionary version | 3.0 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Control group (standard immunosuppression) |
|-----------------------|--|

Reporting group description: -

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Time-restricted immunosuppression |
|-----------------------|-----------------------------------|

Reporting group description: -

| | |
|-----------------------|----------------------------------|
| Reporting group title | Post-transplant cyclophosphamide |
|-----------------------|----------------------------------|

Reporting group description: -

| Serious adverse events | Control group (standard immunosuppression) | Time-restricted immunosuppression | Post-transplant cyclophosphamide |
|---|---|-----------------------------------|----------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 58 / 184 (31.52%) | 70 / 185 (37.84%) | 26 / 99 (26.26%) |
| number of deaths (all causes) | 92 | 97 | 43 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasms benign, malignant and unspecified | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 1 / 184 (0.54%) | 2 / 185 (1.08%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| Vascular disorders | | | |
| Vascular disorders | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 2 / 184 (1.09%) | 3 / 185 (1.62%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 1 / 4 | 1 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 1 / 2 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General disorders and administration site conditions | Additional description: All combined, see SAE chart for details | | |

| | | | |
|---|---|------------------|----------------|
| subjects affected / exposed | 6 / 184 (3.26%) | 6 / 185 (3.24%) | 4 / 99 (4.04%) |
| occurrences causally related to treatment / all | 2 / 6 | 1 / 6 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Immune system disorders | | | |
| Immune system disorders | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 13 / 184 (7.07%) | 14 / 185 (7.57%) | 6 / 99 (6.06%) |
| occurrences causally related to treatment / all | 3 / 15 | 3 / 14 | 0 / 6 |
| deaths causally related to treatment / all | 1 / 3 | 0 / 2 | 0 / 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory, thoracic and mediastinal disorders | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 2 / 184 (1.09%) | 2 / 185 (1.08%) | 4 / 99 (4.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 3 |
| Psychiatric disorders | | | |
| Psychiatric disorders | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 0 / 184 (0.00%) | 0 / 185 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Investigations | | | |
| Investigations | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 10 / 184 (5.43%) | 8 / 185 (4.32%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 12 / 12 | 7 / 8 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Injury, poisoning and procedural complications | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 2 / 184 (1.09%) | 1 / 185 (0.54%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac disorders | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 4 / 184 (2.17%) | 1 / 185 (0.54%) | 3 / 99 (3.03%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |

| | | | |
|--|---|------------------|----------------|
| Nervous system disorders subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: All combined, see SAE chart for details | | |
| | 4 / 184 (2.17%) | 10 / 185 (5.41%) | 0 / 99 (0.00%) |
| | 3 / 4 | 8 / 10 | 0 / 0 |
| | 0 / 0 | 1 / 1 | 0 / 0 |
| Blood and lymphatic system disorders Blood and lymphatic disorders subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: All combined, see SAE chart for details | | |
| | 4 / 184 (2.17%) | 9 / 185 (4.86%) | 3 / 99 (3.03%) |
| | 4 / 6 | 5 / 9 | 3 / 3 |
| | 0 / 0 | 0 / 0 | 1 / 1 |
| Gastrointestinal disorders Gastrointestinal disorders subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: All combined, see SAE chart for details | | |
| | 17 / 184 (9.24%) | 15 / 185 (8.11%) | 3 / 99 (3.03%) |
| | 14 / 20 | 10 / 16 | 1 / 4 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders Hepatobiliary disorders subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: All combined, see SAE chart for details | | |
| | 2 / 184 (1.09%) | 2 / 185 (1.08%) | 0 / 99 (0.00%) |
| | 0 / 2 | 1 / 2 | 0 / 0 |
| | 0 / 0 | 1 / 1 | 0 / 0 |
| Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: All combined, see SAE chart for details | | |
| | 1 / 184 (0.54%) | 0 / 185 (0.00%) | 0 / 99 (0.00%) |
| | 0 / 1 | 0 / 0 | 0 / 0 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders Renal and urinary disorders subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: All combined, see SAE chart for details | | |
| | 1 / 184 (0.54%) | 2 / 185 (1.08%) | 2 / 99 (2.02%) |
| | 1 / 1 | 0 / 2 | 2 / 2 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations Infections and infestations subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: All combined, see SAE chart for details | | |
| | 11 / 184 (5.98%) | 12 / 185 (6.49%) | 1 / 99 (1.01%) |
| | 1 / 12 | 2 / 14 | 0 / 1 |
| | 0 / 2 | 2 / 3 | 0 / 0 |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---|-----------------|----------------|
| Metabolism and nutrition disorders | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 5 / 184 (2.72%) | 3 / 185 (1.62%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 2 / 5 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Control group (standard immunosuppression) | Time-restricted immunosuppression | Post-transplant cyclophosphamide |
|---|---|-----------------------------------|----------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 149 / 184 (80.98%) | 165 / 185 (89.19%) | 89 / 99 (89.90%) |
| Vascular disorders | | | |
| Vascular | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 9 / 184 (4.89%) | 7 / 185 (3.78%) | 4 / 99 (4.04%) |
| occurrences (all) | 12 | 8 | 4 |
| Surgical and medical procedures | | | |
| Surgery/intra-operative injury | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 1 / 184 (0.54%) | 0 / 185 (0.00%) | 0 / 99 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Constitutional symptoms | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 27 / 184 (14.67%) | 33 / 185 (17.84%) | 6 / 99 (6.06%) |
| occurrences (all) | 35 | 37 | 7 |
| Pain | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 14 / 184 (7.61%) | 19 / 185 (10.27%) | 10 / 99 (10.10%) |
| occurrences (all) | 14 | 20 | 11 |
| Death | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 0 / 184 (0.00%) | 1 / 185 (0.54%) | 0 / 99 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Secondary malignancy | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 0 / 184 (0.00%) | 1 / 185 (0.54%) | 0 / 99 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Syndromes | Additional description: All combined, see SAE chart for details | | |
| subjects affected / exposed | 0 / 184 (0.00%) | 2 / 185 (1.08%) | 1 / 99 (1.01%) |
| occurrences (all) | 0 | 3 | 1 |
| Immune system disorders | | | |

| | | | |
|--|---|-------------------|------------------|
| Allergy/immunology subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 2 / 184 (1.09%) | 0 / 185 (0.00%) | 3 / 99 (3.03%) |
| | 2 | 0 | 5 |
| Reproductive system and breast disorders Sexual/reproductive function subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 0 / 184 (0.00%) | 1 / 185 (0.54%) | 1 / 99 (1.01%) |
| | 0 | 1 | 1 |
| Respiratory, thoracic and mediastinal disorders Pulmonary/upper respiratory subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 8 / 184 (4.35%) | 12 / 185 (6.49%) | 8 / 99 (8.08%) |
| | 9 | 15 | 11 |
| Cardiac disorders Cardiac arrhythmia subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 4 / 184 (2.17%) | 4 / 185 (2.16%) | 3 / 99 (3.03%) |
| | 4 | 4 | 3 |
| | Additional description: All combined, see SAE chart for details | | |
| Cardiac general subjects affected / exposed occurrences (all) | 42 / 184 (22.83%) | 43 / 185 (23.24%) | 24 / 99 (24.24%) |
| | 45 | 46 | 24 |
| Nervous system disorders Neurology subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 26 / 184 (14.13%) | 22 / 185 (11.89%) | 11 / 99 (11.11%) |
| | 31 | 28 | 13 |
| Blood and lymphatic system disorders Blood/bone marrow subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 51 / 184 (27.72%) | 42 / 185 (22.70%) | 9 / 99 (9.09%) |
| | 90 | 92 | 15 |
| | Additional description: All combined, see SAE chart for details | | |
| | 3 / 184 (1.63%) | 2 / 185 (1.08%) | 1 / 99 (1.01%) |
| | 3 | 3 | 1 |
| | Additional description: All combined, see SAE chart for details | | |
| Hemorrhage/bleeding subjects affected / exposed occurrences (all) | 4 / 184 (2.17%) | 4 / 185 (2.16%) | 1 / 99 (1.01%) |
| | 5 | 4 | 1 |
| Lymphatics subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 4 / 184 (2.17%) | 8 / 185 (4.32%) | 2 / 99 (2.02%) |
| | 4 | 8 | 2 |
| Ear and labyrinth disorders | | | |

| | | | |
|--|--|---------------------------|-------------------------|
| Auditory/ear subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 3 / 184 (1.63%) 3 | 1 / 185 (0.54%) 1 | 1 / 99 (1.01%) 1 |
| Eye disorders Ocular/visual subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 6 / 184 (3.26%) 7 | 6 / 185 (3.24%) 6 | 6 / 99 (6.06%) 6 |
| Gastrointestinal disorders Gastrointestinal subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 53 / 184 (28.80%) 65 | 50 / 185 (27.03%) 70 | 27 / 99 (27.27%) 29 |
| Hepatobiliary disorders Hepatobiliary/pancreas subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 4 / 184 (2.17%) 4 | 1 / 185 (0.54%) 2 | 0 / 99 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Dermatology/skin subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 10 / 184 (5.43%) 10 | 21 / 185 (11.35%) 25 | 10 / 99 (10.10%) 12 |
| Renal and urinary disorders Renal/genitourinary subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 11 / 184 (5.98%) 12 | 11 / 185 (5.95%) 11 | 4 / 99 (4.04%) 6 |
| Endocrine disorders Endocrine subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 3 / 184 (1.63%) 3 | 7 / 185 (3.78%) 7 | 2 / 99 (2.02%) 2 |
| Musculoskeletal and connective tissue disorders Musculoskeletal/soft tissue subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 6 / 184 (3.26%) 7 | 6 / 185 (3.24%) 6 | 7 / 99 (7.07%) 7 |
| Infections and infestations Infection subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 87 / 184 (47.28%) 202 | 104 / 185 (56.22%) 226 | 71 / 99 (71.72%) 154 |
| Metabolism and nutrition disorders | | | |

| | | | |
|--|---|-------------------|------------------|
| Metabolic/laboratory subjects affected / exposed occurrences (all) | Additional description: All combined, see SAE chart for details | | |
| | 74 / 184 (40.22%) | 72 / 185 (38.92%) | 40 / 99 (40.40%) |
| | 185 | 156 | 75 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 13 October 2010 | The study objective and statistical analysis of quality of life assessment are changed; Reporting of pregnancies is added; The grading of acute GvHD is corrected. |
| 17 May 2011 | Change of principal investigator; The registration of patients receiving a T-cell depleted allogeneic SCT was added; An extra inclusion criterion for the second randomization was added; dose adjustment of cyclosporin A was added; deletion of a off protocol reason (infusion of donor lymphocytes); |
| 13 March 2012 | Change of principal investigator; Deletion of the section 'severe GvHD; The registration of patients receiving a T-cell depleted allogeneic SCT and that will be treated with immunosuppression according to local hospital policy is deleted from protocol. It was added in version 3, but has not been implemented; correction with regards to reporting of GvHD; Information requested at registering patient is corrected from "patient's initials or code" into "local patient code (optional)". |
| 17 July 2013 | Addition of an additional treatment arm with a short-course post-transplant GVHD prophylaxis consisting of high-dose cyclophosphamide. (introduction, objectives, study design, treatment, statistical considerations); Changed inclusion criterion regarding age; Changes in reason for going off protocol treatment with regards to development of GVHD; Added is the use of a Summary of Product Characteristics (SPC) for an authorized medicinal product in the definition of SUSAR. |
| 22 April 2014 | <ul style="list-style-type: none">• Arm 3 Post transplant cyclophosphamide: Cyclosporine A treatment is extended to +70 days• Arm 3: Added option of cyclosporine A p.o. dose.• Arm 1 and 2: Date start cyclosporine A is changed to day -5 –day -3 (depending on local procedures).• Period of reporting adverse events is corrected (in accordance to earlier amendment• Exemptions of SAE reporting are clarified• Exemption of SAE reporting of chronic GvHD is limited to chronic GvHD not requiring systemic treatment.• Added is a monitoring of overall mortality to detect possible differences in relapse rate between arm 1 and arm 3. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported