



Clinical trial results:

Treatment optimization in adult patients with newly diagnosed acute lymphoblastic leukemia or lymphoblastic lymphoma by individualised, targeted and intensified treatment - a phase IV-trial with a phase III-part to evaluate safety and efficacy of nelarabine in T-ALL patients

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2013-003466-13 |
| Trial protocol | DE |
| Global end of trial date | 05 December 2024 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 18 December 2025 |
| First version publication date | 18 December 2025 |
| Summary attachment (see zip file) | GMALL 08/2013 Ergebnisbericht BfArM (GMALL08_Ergebnisbericht_BfArM_20251202.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | GMALL082013 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02881086 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Goethe University |
| Sponsor organisation address | Theodor-Stern-Kai 7, Frankfurt am Main, Germany, 60590 |
| Public contact | GMALL Studienzentrale, University Hospital Frankfurt, 0049 6963016365, gmall@em.uni-frankfurt.de |
| Scientific contact | GMALL Studienzentrale, University Hospital Frankfurt, 0049 6963016365, gmall@em.uni-frankfurt.de |

Notes:

Paediatric regulatory details

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|--|----|
| 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 | Interim |
| Date of interim/final analysis | 25 October 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 22 October 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 05 December 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To improve event free survival (EFS), remission duration (RD), disease free survival (DFS) and overall survival (OS) compared with the previous trial GMALL 07/2003

Protection of trial subjects:

The Sponsor ensured that the protocol and all appropriate documentation according to the applicable country-specific laws and regulations were reviewed and approved by the IEC/IRB's responsible for each site and/or country. The investigator or his/her designee informed the patient/legal representative of all aspects pertaining to the patient's participation in the study and that participation in the study is voluntary and that they could withdraw at any time. The patient's/legal representative's free and expressed informed consent were obtained in writing prior to the screening procedures required for entry into the study according to all applicable regulatory requirements. To maintain confidentiality, all laboratory specimens, evaluation forms, reports and other records were identified by a coded number, sex and year of birth only. Medical information about individual patients obtained in the course of this trial is confidential and was disclosed to third parties, except authorized monitors, auditors or inspectors. Confidentiality was ensured by the use of patient numbers for the identification of each patient; these patient numbers were used for patient data in the patient files and eCRFs.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 15 July 2016 |
| 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 | Germany: 1023 |
| Worldwide total number of subjects | 1023 |
| EEA total number of subjects | 1023 |

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) | 1023 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

First patient in 08/24/2016 (MM/DD/YYYY), last patient in 08/16/2022 (MM/DD/YYYY)

Pre-assignment

Screening details:

The study was conducted in patients (18 - 55 years) with newly diagnosed acute lymphoblastic leukemia or lymphoblastic lymphoma. Other eligibility criteria were determined within a screening period prior to the first study specific measure.

Period 1

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

Blinding implementation details:

Not blinded

Arms

| | |
|--|-----------------------|
| Arm title | GMALL 08/2013 trial |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Nelarabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Emulsion for infusion |
| Routes of administration | Infusion |

Dosage and administration details:

1500 mg/m² intravenous during 2 hours on Day 1, 3 and 5

| | |
|--------------------------------|---------------------|
| Number of subjects in period 1 | GMALL 08/2013 trial |
| Started | 1023 |
| Completed | 979 |
| Not completed | 44 |
| Not started | 14 |
| Not evaluable | 30 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------------|
| Reporting group title | GMALL 08/2013 trial |
|-----------------------|---------------------|

Reporting group description: -

| Reporting group values | GMALL 08/2013 trial | Total | |
|------------------------|---------------------|-------|--|
| Number of subjects | 1023 | 1023 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 1023 | 1023 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 388 | 388 | |
| Male | 635 | 635 | |

Subject analysis sets

| | |
|----------------------------|----------|
| Subject analysis set title | Patients |
|----------------------------|----------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

The evaluation of the primary endpoint is based on the full analysis set, i. e. all evaluable patients included in the study. The historic control has been accrued between 2003 and 2011 and consists of 2492 patients with available additional information age, sex, risk group, immunophenotype (line), subtype, PH status, t(4;11) status and leukocyte count. We excluded patients with subtype "unknown" from the historical control because subtype information was available for all GMALL 08/2013 patients. This leaves us with 1943 patients. There were no LBL patients in the historical control, therefore LBL patients were also excluded from the GMALL 08/2013 population for this analysis.

| Reporting group values | Patients | | |
|------------------------|----------|--|--|
| Number of subjects | 861 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 861 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 338 | | |
| Male | 523 | | |

End points

End points reporting groups

| | |
|--------------------------------|---------------------|
| Reporting group title | GMALL 08/2013 trial |
| Reporting group description: - | |
| Subject analysis set title | Patients |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The evaluation of the primary endpoint is based on the full analysis set, i. e. all evaluable patients included in the study. The historic control has been accrued between 2003 and 2011 and consists of 2492 patients with available additional information age, sex, risk group, immunophenotype (line), subtype, PH status, t(4;11) status and leukocyte count. We excluded patients with subtype "unknown" from the historical control because subtype information was available for all GMALL 08/2013 patients. This leaves us with 1943 patients. There were no LBL patients in the historical control, therefore LBL patients were also excluded from the GMALL 08/2013 population for this analysis.

Primary: Event Free Survival

| | |
|------------------------|------------------------------------|
| End point title | Event Free Survival ^[1] |
| End point description: | |
| End point type | Primary |

End point timeframe:

time from first day of study treatment (date of first administration of study medication) to relapse, treatment failure (partial remission or worse), occurrence of a second malignant tumor or death from any cause, whichever occurs first

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: The primary endpoint (EFS) was based on a historical comparative group which cannot be reported in this system, because the pts of the historical group are not part of the trial. The detailed description is found in the report to BfArM. The two-sided log-rank (chi-squared) test for the evaluation of the primary endpoint was performed. The resulting p-value is < 0.001. Consequently, the null hypothesis of equality of hazard rates can be rejected.

| | | | | |
|-----------------------------|------------------------|--|--|--|
| End point values | GMALL 08/2013 trial | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 861 | | | |
| Units: Patients | 861 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment phase

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | GMALL 08/2013 |
|-----------------------|---------------|

Reporting group description:

All patients who started therapy

| Serious adverse events | GMALL 08/2013 | | |
|---|------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 377 / 1009 (37.36%) | | |
| number of deaths (all causes) | 227 | | |
| number of deaths resulting from adverse events | 50 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Papillary thyroid carcinoma | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Brain vein thrombosis | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hygroma | | | |
| subjects affected / exposed | 2 / 1009 (0.20%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung artery embolism | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subsegmental pulmonary embolism | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thromboembolic event | | | |
| subjects affected / exposed | 9 / 1009 (0.89%) | | |
| occurrences causally related to treatment / all | 7 / 9 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 2 / 1009 (0.20%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Allergic reaction | | | |
| subjects affected / exposed | 2 / 1009 (0.20%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anaphylactic reaction to Etoposid | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anaphylaxis | | | |
| subjects affected / exposed | 6 / 1009 (0.59%) | | |
| occurrences causally related to treatment / all | 6 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|--|------------------|--|--|--|
| Hemolytic-uremic syndrome subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypophysitis subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Suspected HLH subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory, thoracic and mediastinal disorders | | | | |
| Adult respiratory distress syndrome subjects affected / exposed | 3 / 1009 (0.30%) | | | |
| occurrences causally related to treatment / all | 3 / 3 | | | |
| deaths causally related to treatment / all | 2 / 2 | | | |
| Adult respiratory distress syndrome, lung infection | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchopulmonary hemorrhage subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Hypoxia subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pleural effusion subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

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|---|------------------|--|--|
| Pneumonitis | | | |
| subjects affected / exposed | 3 / 1009 (0.30%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 3 / 1009 (0.30%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 2 / 1009 (0.20%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Delirium and psychotic Symptoms | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Depression | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epileptical attack | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychosis | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicide attempt | | | |

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|---|------------------|--|--|
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Investigations | | | |
| CPK increased | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Creatinine increased | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Abdominal soft tissue necrosis | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 2 / 1009 (0.20%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebral vasospasm | | | |

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|---|-------------------|--|--|
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Double vision | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Edema cerebral | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Incomplete cauda equina syndrome | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intracranial hemorrhage | | | |
| subjects affected / exposed | 10 / 1009 (0.99%) | | |
| occurrences causally related to treatment / all | 10 / 10 | | |
| deaths causally related to treatment / all | 2 / 2 | | |
| Ischemia cerebrovascular (suspected) | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| JC infection | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Leukoencephalopathy | | | |

| | | | | |
|---|------------------|--|--|--|
| subjects affected / exposed | 3 / 1009 (0.30%) | | | |
| occurrences causally related to treatment / all | 3 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nelarabine associated Guillain Barre Syndrom | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Polyneuropathy | | | | |
| subjects affected / exposed | 2 / 1009 (0.20%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Reduction of vigilance, coordination disorder, disorientation | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Reversible posterior leukoencephalopathy syncrome | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Seizure | | | | |
| subjects affected / exposed | 4 / 1009 (0.40%) | | | |
| occurrences causally related to treatment / all | 3 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Somnolence | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Subdural hematoma | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tetraparesis | | | | |

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|---|------------------|--|--|
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Unclear neurological symptom complex | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intracerebral hemorrhage | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prolonged Thrombopenia | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Sicca-Syndrome | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Bleeding | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |

| | | | |
|---|------------------|--|--|
| Duodenal perforation | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Enterocolitis | | | |
| subjects affected / exposed | 2 / 1009 (0.20%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Generalized mucositis | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ileus | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mallory-Weiß-Syndrome | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mucositis oral | | | |
| subjects affected / exposed | 5 / 1009 (0.50%) | | |
| occurrences causally related to treatment / all | 5 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis | | | |
| subjects affected / exposed | 8 / 1009 (0.79%) | | |
| occurrences causally related to treatment / all | 8 / 8 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sigmadivertikulosi | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |

| | | | | |
|---|-------------------|--|--|--|
| Cirrhosis of the liver | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Elevation of blood bilirubin and transaminase | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatopathy | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Liver abscess | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Liver parenchyma damage | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Steatosis | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal and urinary disorders | | | | |
| Acute kidney injury | | | | |
| subjects affected / exposed | 29 / 1009 (2.87%) | | | |
| occurrences causally related to treatment / all | 29 / 30 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Acute renal failure | | | | |
| subjects affected / exposed | 5 / 1009 (0.50%) | | | |
| occurrences causally related to treatment / all | 5 / 5 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | |
|--|------------------|--|--|
| Increased creatinine, renal failure subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prolongation of MTX-level decrease subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure subjects affected / exposed | 6 / 1009 (0.59%) | | |
| occurrences causally related to treatment / all | 4 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure/insufficiency subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal insufficiency subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aseptic necrosis of bone subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Avascular necrosis subjects affected / exposed | 3 / 1009 (0.30%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-------------------|--|--|
| Femur necrosis both sides | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteonecrosis | | | |
| subjects affected / exposed | 26 / 1009 (2.58%) | | |
| occurrences causally related to treatment / all | 26 / 27 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteonecrosis of femoral head both sides | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteonecrosis of femoral head right side | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteoporosis | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rhabdomyolyse | | | |
| subjects affected / exposed | 6 / 1009 (0.59%) | | |
| occurrences causally related to treatment / all | 6 / 9 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spondylodiscitis | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Abdominal infection | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|------------------|--|--|--|
| Appendicitis | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Appendicitis perforated | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bone infection | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Catheter related infection | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device related infection | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Disseminated Aspergillosis | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Empyem cerebral | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Encephalitis infection | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Endocarditis infective | | | | |

| | | | | |
|---|------------------|--|--|--|
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Febrile infection | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fungal infection | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fungal pneumonia or atypical pneumonia | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Generalized Mucormycosis | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic infection (Morganella morganii) | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatitis viral | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatolienal Candidiasis | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza A virus infection | | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Invasive mycosis of the lungs | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung infection | | | |
| subjects affected / exposed | 7 / 1009 (0.69%) | | |
| occurrences causally related to treatment / all | 6 / 7 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Lung infection (fungal) | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Lung infection with ARDS | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymph gland infection | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Meningitis bacterial (E. Coli) | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Meningoencephalitis (HHV6) | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Mucormycosis | | | |

| | | | | |
|---|------------------|--|--|--|
| subjects affected / exposed | 2 / 1009 (0.20%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 2 | | | |
| Necrotizing fasciitis | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PCJ-Pneumonia | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumocystis jirovecii Pneumonia | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumogenic sepsis | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 2 / 1009 (0.20%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Pneumonia with Covid-19 | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Reactivation of CMV, CMV-pneumonia | | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory infection | | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 70 / 1009 (6.94%) | | |
| occurrences causally related to treatment / all | 66 / 73 | | |
| deaths causally related to treatment / all | 24 / 27 | | |
| Sepsis 3MRGN (E-Coli) | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic cardiomyopathy | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 5 / 1009 (0.50%) | | |
| occurrences causally related to treatment / all | 5 / 6 | | |
| deaths causally related to treatment / all | 2 / 2 | | |
| Soft tissue infection | | | |
| subjects affected / exposed | 2 / 1009 (0.20%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral infection (varizella) | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral infection SARS CoV-2 | | | |
| subjects affected / exposed | 78 / 1009 (7.73%) | | |
| occurrences causally related to treatment / all | 6 / 81 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound infection | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infection (<i>Fusarium petroliphilum</i>) | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Metabolism and nutrition disorders | | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperglycemia | | | |
| subjects affected / exposed | 3 / 1009 (0.30%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoglycemia | | | |
| subjects affected / exposed | 1 / 1009 (0.10%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatremia | | | |
| subjects affected / exposed | 2 / 1009 (0.20%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| | | | |
|---|---------------------|--|--|
| Non-serious adverse events | GMALL 08/2013 | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 968 / 1009 (95.94%) | | |
| Investigations | | | |
| Blood Bilirubin increased | | | |
| subjects affected / exposed | 589 / 1009 (58.37%) | | |
| occurrences (all) | 1111 | | |

| | | | |
|--|--------------------------------|--|--|
| Fibrinogen decreased subjects affected / exposed occurrences (all) | 357 / 1009 (35.38%) 674 | | |
| Lipase increased subjects affected / exposed occurrences (all) | 136 / 1009 (13.48%) 181 | | |
| Neutrophil Count decreased subjects affected / exposed occurrences (all) | 270 / 1009 (26.76%) 409 | | |
| Platelet Count decreased subjects affected / exposed occurrences (all) | 404 / 1009 (40.04%) 1013 | | |
| White Blood Cell decreased subjects affected / exposed occurrences (all) | 301 / 1009 (29.83%) 525 | | |
| Antithrombin deficiency subjects affected / exposed occurrences (all) | 523 / 1009 (51.83%) 1513 | | |
| Immunoglobulin deficiency subjects affected / exposed occurrences (all) | 58 / 1009 (5.75%) 115 | | |
| Transaminase increased subjects affected / exposed occurrences (all) | 733 / 1009 (72.65%) 2101 | | |
| Vascular disorders Thrombosis subjects affected / exposed occurrences (all) | 106 / 1009 (10.51%) 125 | | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 53 / 1009 (5.25%) 70 | | |
| Paresthesia | | | |

| | | | |
|--|-------------------------------|--|--|
| subjects affected / exposed occurrences (all) | 65 / 1009 (6.44%) 113 | | |
| Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all) | 93 / 1009 (9.22%) 240 | | |
| Febrile Neutropenia subjects affected / exposed occurrences (all) | 108 / 1009 (10.70%) 147 | | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 194 / 1009 (19.23%) 334 | | |
| Fever subjects affected / exposed occurrences (all) | 52 / 1009 (5.15%) 66 | | |
| Immune system disorders Allergic Reaction subjects affected / exposed occurrences (all) | 106 / 1009 (10.51%) 143 | | |
| Gastrointestinal disorders Diarrhea subjects affected / exposed occurrences (all) | 64 / 1009 (6.34%) 75 | | |
| Nausea subjects affected / exposed occurrences (all) | 107 / 1009 (10.60%) 151 | | |
| Mucositis subjects affected / exposed occurrences (all) | 503 / 1009 (49.85%) 638 | | |
| Renal and urinary disorders Acute or Chronic Kidney Injury subjects affected / exposed occurrences (all) | 57 / 1009 (5.65%) 64 | | |
| Infections and infestations | | | |

| | | | |
|------------------------------------|------------------------|--|--|
| Infection | | | |
| subjects affected / exposed | 583 / 1009 (57.78%) | | |
| occurrences (all) | 1059 | | |
| Metabolism and nutrition disorders | | | |
| Hyperglycemia | | | |
| subjects affected / exposed | 86 / 1009 (8.52%) | | |
| occurrences (all) | 159 | | |
| Hypertriglyceridemia | | | |
| subjects affected / exposed | 204 / 1009 (20.22%) | | |
| occurrences (all) | 476 | | |
| Hypoalbuminemia | | | |
| subjects affected / exposed | 132 / 1009 (13.08%) | | |
| occurrences (all) | 183 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 20 June 2017 | Change in the delivery and labeling of the investigational medicinal product Nelarabine |
| 18 November 2020 | Protocol V2 Amendment 1 dated 09/04/2020 (MM/DD/YYYY), Pat.-Info dated 09/04/2020 (MM/DD/YYYY), SmPC |
| 05 April 2022 | GMP |
| 14 March 2024 | Protocol V3 Amendment 2 dated 02/27/2024 (MM/DD/YYYY), Shortening of the post-treatment observation period and an additional questionnaire for patient self-documentation of cognitive function |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

non reported

Notes: