Clinical trial results:
AN OPEN LABEL, PHASE I/II STUDY TO INVESTIGATE THE USE OF VORAXAZE™ AS INTENDED INTERVENTION IN PATIENTS WITH CENTRAL NERVOUS SYSTEM LYMPHOMA AND WITH IMPAIRED RENAL FUNCTION BEING TREATED WITH HIGH-DOSE METHOTREXATE.
"VALIDATE"

Summary

EudraCT number	2020-004102-63
Trial protocol	DE
Global end of trial date	01 October 2024

Results information

Result version number	v1 (current)
This version publication date	10 April 2026
First version publication date	10 April 2026

Trial information

Trial identification

Sponsor protocol code	CNS-Lymphoma-Vorax-1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04841434
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Charité - Universitätsmedizin Berlin
Sponsor organisation address	Charitéplatz 1, Berlin, Germany, 10117
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 November 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 October 2024
Global end of trial reached?	Yes
Global end of trial date	01 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate tolerability of intended intervention with VoraxazeTM, in addition to LV, in patients with renal impairment or renal failure during previous HD-MTX therapy.
• To measure the efficacy of VoraxazeTM in lowering the MTX blood levels in patients who are being treated with HD-MTX and LV.
• To demonstrate the feasibility and safety of escalating doses of HD-MTX in patients with renal impairment or renal failure by use of intended intervention with VoraxazeTM, in addition to LV.
• To assess the immunological response to VoraxazeTM after repeated use and the effect of any response on the safety and efficacy of VoraxazeTM.
• To describe levels of MTX and DAMPA in plasma (and CSF in selected patients) following VoraxazeTM administration.
• To assess tolerability of HD-MTX in patients with renal impairment or renal failure in the setting of VoraxazeTM administration.
.. and further items as outlined in the protocol.

Protection of trial subjects:

The study was conducted in accordance with the ICH E6 (R2) Guideline for Good Clinical Practice (GCP), with applicable local regulations
(including European Directive 2001/20/EC, German Medicinal Products Act - AMG), and accordance the latest version of Declaration of Helsinki.

Background therapy:

HDMTX is a key component of treatment protocols for CNSL patients (pts), but impaired renal function in elderly or comorbid pts limits its use. The recombinant enzyme glucarpidase rapidly hydrolyzes MTX into non-toxic metabolites and is approved for therapeutic use in pts with delayed MTX elimination following HDMTX. We conducted a phase I/II study to assess the efficacy of prophylactic glucarpidase in HDMTX-treated pts with renal impairment or a history of delayed MTX elimination.
MTX is used either alone or as part of a combined chemotherapy protocol either in standard or high doses in the treatment of a range of cancers and other diseases. Dose escalation were be performed using three dose levels of MTX. This phase I-II trial is intented to demonstrate tolerability (i.e. absence of severe non-hematological toxicity) and efficacy of intended intervention with repeated doses of Voraxaze, in addition to leucovorin (LV), in patients with renal impairment or renal failure during previous HD-MTX therapy.

Evidence for comparator: -

Actual start date of recruitment	06 August 2021
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: 18
Worldwide total number of subjects	18
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)	0
Adults (18-64 years)	1
From 65 to 84 years	15
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

The study was conducted between August 6, 2021 and October 1, 2024 at one site in Germany.

Pre-assignment

Screening details:

Adult patients with CNS lymphomas who were undergoing active treatment were identified on the basis of the treatment records of our university hospital in accordance with the predefined inclusion criteria. The multidisciplinary lymphoma tumor board at Charité discussed the potential suitability for inclusion in the study on a consensus basis.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

The study was designed as a single-arm, open-label, prospective, monocenter, phase I/II study. VoraxazeTM used as intended intervention in patients with CNS lymphoma being treated with HD-MTX who have impaired renal function.

Arms

Are arms mutually exclusive?	Yes
Arm title	MTX Level 1

Arm description:

3.0 g/m2 Methotrexat
+ Glucarpidase (IMP)

Arm type	Experimental
Investigational medicinal product name	Glucarpidase
Investigational medicinal product code	Voraxaze
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Injection

Dosage and administration details:

-Glucarpidase was administered intravenously by bolus intravenous injection over 5 minutes at each cycle 24 hours after start of HD-MTX and Rituximab allowed as standard-of-care for patients.
-VoraxazeTM: 2000 Units in patients weighing ≤100kg and at least 20 Units per kg body weight in patients weighing >100kg is given in each HD-MTX cycle as a slow IV injection at 24 hours (+/- 2 hours) after the start of HD-MTX infusion.
- Patients were be treated at 3.0 g/m2 dose HD.MTX by injection, with 14 days between cycles (a maximum delay of 28 days is permitted in order to allow time for a patient to recover from the previous cycle). HD-MTX administered over 4 hours according to dose level, given every 14 days for up to 6 cycles.

Arm title	MTX Level 2

Arm description:

3.5 g/m2 Methotrexat
+ Glucarpidase (IMP)

Arm type	Experimental

Investigational medicinal product name	Glucarpidase
Investigational medicinal product code	Voraxaze
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Injection

Dosage and administration details:

-Glucarpidase was administered intravenously by bolus intravenous injection over 5 minutes at each cycle 24 hours after start of HD-MTX and Rituximab allowed as standard-of-care for patients.
-VoraxazeTM: 2000 Units in patients weighing ≤100kg and at least 20 Units per kg body weight in patients weighing >100kg is given in each HD-MTX cycle as a slow IV injection at 24 hours (+/- 2 hours) after the start of HD-MTX infusion.
- Patients were be treated at 3.5 g/m2 dose HD.MTX by injection, with 14 days between cycles (a maximum delay of 28 days is permitted in order to allow time for a patient to recover from the previous cycle). HD-MTX administered over 4 hours according to dose level, given every 14 days for up to 6 cycles.

Arm title	MTX Level 3

Arm description:

4.0 g/m2 Methotrexat
+ Glucarpidase (IMP)

Arm type	Experimental
Investigational medicinal product name	Glucarpidase
Investigational medicinal product code	Voraxaze
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Injection

Dosage and administration details:

-Glucarpidase was administered intravenously by bolus intravenous injection over 5 minutes at each cycle 24 hours after start of HD-MTX and Rituximab allowed as standard-of-care for patients.
-VoraxazeTM: 2000 Units in patients weighing ≤100kg and at least 20 Units per kg body weight in patients weighing >100kg is given in each HD-MTX cycle as a slow IV injection at 24 hours (+/- 2 hours) after the start of HD-MTX infusion.
- Patients were be treated at 4.0 g/m2 dose HD.MTX by injection, with 14 days between cycles (a maximum delay of 28 days is permitted in order to allow time for a patient to recover from the previous cycle). HD-MTX administered over 4 hours according to dose level, given every 14 days for up to 6 cycles.

Number of subjects in period 1	MTX Level 1	MTX Level 2	MTX Level 3
Started	6	6	6
Completed	6	6	6

Baseline characteristics

Reporting groups	
Reporting group title	MTX Level 1
Reporting group description:	
3.0 g/m2 Methotrexat + Glucarpidase (IMP)	

Reporting group title	MTX Level 2
Reporting group description:	
3.5 g/m2 Methotrexat + Glucarpidase (IMP)	
Reporting group title	MTX Level 3
Reporting group description:	
4.0 g/m2 Methotrexat + Glucarpidase (IMP)	

Reporting group values	MTX Level 1	MTX Level 2	MTX Level 3
Number of subjects	6	6	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	1
From 65-84 years	5	5	5
85 years and over	1	1	0
Age continuous Units: years			
arithmetic mean	76.5	79.00	74.33
standard deviation	± 7.01	± 5.32	± 6.02
Gender categorical Units: Subjects			
Female	3	3	1
Male	3	3	5
CNS lymphoma type			
PCNSL= Primary central nervous system lymphoma SCNSL =Secondary CNS lymphoma			
Units: Subjects			
PCNSL	5	5	6
SCNSL	1	1	0
ECOG at baseline Units: Subjects			
ECOG = 0	0	0	1
ECOG = 1	2	3	1

ECOG = 2	1	1	1
ECOG = 3	0	1	1
ECOG = 4	3	1	2
GFR at baseline			
Units: ml/min/ 1,73 m2			
arithmetic mean	75.67	66.5	64.17
standard deviation	± 7.89	± 7.72	± 13.13
Hemoglobin			
Units: g/dl			
arithmetic mean	11.41	11.68	11.3
standard deviation	± 2.94	± 1.32	± 0.84

Reporting group values	Total		
Number of subjects	18		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	1		
From 65-84 years	15		
85 years and over	2		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	7		
Male	11		
CNS lymphoma type			
PCNSL= Primary central nervous system lymphoma SCNSL =Secondary CNS lymphoma			
Units: Subjects			
PCNSL	16		
SCNSL	2		
ECOG at baseline			
Units: Subjects			
ECOG = 0	1		
ECOG = 1	6		
ECOG = 2	3		
ECOG = 3	2		
ECOG = 4	6		
GFR at baseline			
Units: ml/min/ 1,73 m2			
arithmetic mean			

standard deviation	-		
Hemoglobin Units: g/dl arithmetic mean standard deviation	-		

End points

End points reporting groups

Reporting group title	MTX Level 1
Reporting group description:	
3.0 g/m2 Methotrexat + Glucarpidase (IMP)	

Reporting group title	MTX Level 2
Reporting group description:	
3.5 g/m2 Methotrexat + Glucarpidase (IMP)	

Reporting group title	MTX Level 3
Reporting group description:	
4.0 g/m2 Methotrexat + Glucarpidase (IMP)	

Primary: Reduction of MTX plasma levels

End point title	Reduction of MTX plasma levels[1]

End point description:

Administration of glucarpidase resulted in a median reduction of MTX plasma levels within 15 minutes by 99.2% (95% CI: 98.4-99.1%). Results from serum samples analyses for anti-glucarpidase antibodies were performed, but in pts with more than two HDMTX cycles, there was no statistically significant difference in the reduction of MTX plasma levels between the first and last cycles (p=0.47). Glucarpidase treatment reduced MTX plasma levels to a median of 0.05 µmol/L (range 0.00-0.84) within 15 minutes. MTX plasma levels remained consistently below 0.6 µmol/L across all cycles at 42 hours or later after start of the HDMTX infusion.

End point type	Primary

End point timeframe:

within 15 minutes

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: Only descriptive analysis was conducted. Administration of glucarpidase resulted in a median reduction of MTX plasma levels within 15 minutes according to study protocol by 99.2% (95% CI: 98.4-99.1%). MTX plasma levels remained below 0.6 µmol/L across all cycles.

End point values	MTX Level 1	MTX Level 2	MTX Level 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: µmol/L				
arithmetic mean (standard deviation)				
Cycle 1	0.9912 (± 0.006)	0.9909 (± 0.002)	0.9942 (± 0.002)	
Cycle 2	0.9860 (± 0.008)	0.9942 (± 0.004)	0.9930 (± 0.005)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: overall time	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	5.0
Reporting groups	
Reporting group title	MTX Level 1
Reporting group description: 3.0 g/m2 Methotrexat + Glucarpidase	
Reporting group title	MTX Level 2
Reporting group description: 3.5 g/m2 Methotrexat+ Glucarpidase	
Reporting group title	MTX Level 3
Reporting group description: 4.0 g/m2 Methotrexat+ Glucarpidase	

Serious adverse events	MTX Level 1	MTX Level 2	MTX Level 3
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	3 / 6 (50.00%)	4 / 6 (66.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Ventricular fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fever			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal hemorrhage	Additional description: upper and lower		
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lung infection			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	MTX Level 1	MTX Level 2	MTX Level 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	6 / 6 (100.00%)	6 / 6 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Port dislocation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Edema limbs			
subjects affected / exposed	3 / 6 (50.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Fever			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Chills	Additional description: shivering		
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
allergic reaction			
subjects affected / exposed	2 / 6 (33.33%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	4	2	0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Intermittand confusional state			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
increased creatinine			
subjects affected / exposed	1 / 6 (16.67%)	4 / 6 (66.67%)	2 / 6 (33.33%)
occurrences (all)	2	4	2
decreased folic acid			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Loss of weight			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Thrombocyte cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lack of vitamin D3			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Tachyarrhythmia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Cerebral ischaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Seizure			

subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	3 / 6 (50.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	7	2	2
Eye disorders			
Glaucomatocyclitic crises			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Mucositis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Rash	Additional description: Exanthem		
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Hematuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hypothyroidism			

subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypopituitarism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	4 / 6 (66.67%)	2 / 6 (33.33%)	4 / 6 (66.67%)
occurrences (all)	11	3	8
Covid-19/ Lung infection			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Enteritis infectious			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	2 / 6 (33.33%)
occurrences (all)	1	2	3
Hyperuricaemia			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 August 2022	update Protocol Version 3.0 (dated 29/03/2021) to Protocol Version 4.0 (15/02/2022): - Replacement of the investigator's brochure with product information following approval of Voraxaze in the EU - Adjustment of concomitant medication from cycle 2 onwards. (Due to previous IMP-associated AEs, mandatory premedication prior to glucarpidase administration was introduced.) - Adjustment of benefit/risk assessment - Addition of information on adverse events of special interest (AESI)
18 September 2023	change: Extension of the shelf life of the medication by 1 year
23 July 2024	update Protocol Version 5.0 (03/05/2024): - Deletion of the follow-up periods 90 and 180 days after the last administration of Voraxaze TM. Now only 30 days follow-up after the last administration.

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.

The small sample size, the single-arm design, and a severely ill CNS lymphoma population limit conclusions to the pharmacological efficacy and tolerability of the IMP without meaningful results about the antineoplastic efficacy.

Notes: