Clinical trial results:
Phase II trial for the treatment of older patients with newly diagnosed CD19 positive, Ph/BCR-ABL negative B-precursor acute lymphoblastic leukemia with sequential dose reduced chemotherapy and Blinatumomab (EWALL-BOLD)

Summary

EudraCT number	2017-002853-13
Trial protocol	DE
Global end of trial date	06 August 2024

Results information

Result version number	v1 (current)
This version publication date	24 January 2025
First version publication date	24 January 2025

Trial information

Trial identification

Sponsor protocol code	EWALL-BOLD

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Goethe University
Sponsor organisation address	Theodor-Stern-Kai 7, Frankfurt am Main, Germany,
Public contact	Medizinische Klinik II, Goethe Universität, 0049 (0)6963016365, goekbuget@em.uni-frankfurt.de
Scientific contact	Medizinische Klinik II, Goethe Universität, 0049 (0)6963016365, goekbuget@em.uni-frankfurt.de

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	03 December 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 August 2024
Global end of trial reached?	Yes
Global end of trial date	06 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the rate of complete hematologic remission after induction therapy

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	01 June 2018
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: 52
Worldwide total number of subjects	52
EEA total number of subjects	52

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	23
From 65 to 84 years	29
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient in 06/11/2018 (MM/DD/YYYY), last patient out 08/06/2024 (MM/DD/YYYY)

Pre-assignment

Screening details:

The study was conducted in older patients with newly diagnosed B-precursor ALL. Other eligibility criteria were determined within a screening period of up to two weeks prior to the first administration of Induction I.

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:

N.A. (open-label single-arm phase II study)

Arms

Arm title	Blinatumomab - single arm

Arm description:

Patients started with a prephase treatment, which was not part of the clinical trial. During this period screening investigations were performed. Patients received then a dose reduced induction phase Iwith chemotherapy followed by one cycle of Blinatumomab as induction phase II.

Arm type	Experimental
Investigational medicinal product name	Blinatumomab
Investigational medicinal product code	
Other name	BiTE antibody blinatumomab
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients received four cycles of blinatumomab alternating with standard chemotherapy. A cycle consists of a continuous intravenous infusion at a dose of 28 µg/d in a constant flow rate over four weeks followed by a two-week infusion free interval.

Number of subjects in period 1	Blinatumomab - single arm
Started	52
Completed	47
Not completed	5
Consent withdrawn by subject	5

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	52	52	
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)	23	23	
From 65-84 years	29	29	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	19	19	
Male	33	33	

Subject analysis sets

Subject analysis set title	Efficacy set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients who received any infusion of study treatment starting with induction phase I and either died during the induction therapy or had a bone marrow evaluation after the end of induction therapy (induction I and cycle I with Blinatumomab) will be considered.

Reporting group values	Efficacy set		
Number of subjects	47		
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)	21		
From 65-84 years	26		
85 years and over	0		

Gender categorical Units: Subjects			
Female	19		
Male	28		

End points

End points reporting groups

Reporting group title	Blinatumomab - single arm

Reporting group description:

Patients started with a prephase treatment, which was not part of the clinical trial. During this period screening investigations were performed. Patients received then a dose reduced induction phase Iwith chemotherapy followed by one cycle of Blinatumomab as induction phase II.

Subject analysis set title	Efficacy set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients who received any infusion of study treatment starting with induction phase I and either died during the induction therapy or had a bone marrow evaluation after the end of induction therapy (induction I and cycle I with Blinatumomab) will be considered.

Primary: Proportion of patients achieving a complete hematologic remission after induction therapy

End point title	Proportion of patients achieving a complete hematologic remission after induction therapy[1]

End point description:

End point type	Primary

End point timeframe:

After induction therapy (one cycle of chemotherapy and one cycle of Blinatumomab)

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.

End point values	Efficacy set			
Subject group type	Subject analysis set			
Number of subjects analysed	47			
Units: percent	85			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment phase + follow-up	
Assessment type	Systematic

Dictionary used	
Dictionary name	NCI CTCAE
Dictionary version	4.0

Reporting groups	
Reporting group title	All patients with study treatment
Reporting group description:	
All patients who received any infusion of the investigational drug.	

Serious adverse events	All patients with study treatment		
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 47 (70.21%)		
number of deaths (all causes)	12		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Myelodysplastic syndrome			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Colon carcinoma			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cystic lesion in both ovaries			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thromboembolic event			

subjects affected / exposed	3 / 47 (6.38%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 1		
Surgical and medical procedures			
Port dislocation			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Suspected secondary tumor			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	4 / 47 (8.51%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Haemophagozytose (HLH)			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusion			

subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
AST/ALT increased			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Alanine aminotransferase increase			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Gastrointestinal anastomic leak			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiomyopathy			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular tachycardia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphasia			

subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	2 / 47 (4.26%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Amnestic aphasia				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Aphasia				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neurotoxicity				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Thrombocytopenia				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	5 / 47 (10.64%)			
occurrences causally related to treatment / all	5 / 6			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				

Gastroenteritis				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileal obstruction				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Elevation of Transaminase				
subjects affected / exposed	1 / 47 (2.13%)			
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	2 / 47 (4.26%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Spondylodyscitis				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Anorectal infection				

subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Breast infection				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Catheter related infection				
subjects affected / exposed	10 / 47 (21.28%)			
occurrences causally related to treatment / all	11 / 13			
deaths causally related to treatment / all	0 / 0			
Covid19 Pneumonia				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection with staphylococcus epidermis in peripheral blood cultur				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumocystitis jirovecii infection				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
SARS CoV-2 infection				
subjects affected / exposed	1 / 47 (2.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spondylodiscitis				

subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	3 / 47 (6.38%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	2 / 47 (4.26%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Upper respiratory infection			
subjects affected / exposed	2 / 47 (4.26%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperglycemia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All patients with study treatment		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 47 (97.87%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 47 (10.64%)		
occurrences (all)	6		

Hypotension			
subjects affected / exposed	7 / 47 (14.89%)		
occurrences (all)	7		
General disorders and administration site conditions			
Bleeding			
subjects affected / exposed	4 / 47 (8.51%)		
occurrences (all)	5		
Oedema face			
subjects affected / exposed	4 / 47 (8.51%)		
occurrences (all)	4		
Oedema limbs			
subjects affected / exposed	16 / 47 (34.04%)		
occurrences (all)	27		
Fatigue			
subjects affected / exposed	11 / 47 (23.40%)		
occurrences (all)	27		
fever			
subjects affected / exposed	23 / 47 (48.94%)		
occurrences (all)	49		
general disorders - other			
subjects affected / exposed	5 / 47 (10.64%)		
occurrences (all)	7		
Localised oedema			
subjects affected / exposed	4 / 47 (8.51%)		
occurrences (all)	8		
Pain			
subjects affected / exposed	9 / 47 (19.15%)		
occurrences (all)	9		
Immune system disorders			
allergic reaction			
subjects affected / exposed	4 / 47 (8.51%)		
occurrences (all)	4		
Cytokine release syndrome			
subjects affected / exposed	7 / 47 (14.89%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			

cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all) Productive cough subjects affected / exposed occurrences (all)	5 / 47 (10.64%) 7 8 / 47 (17.02%) 11 4 / 47 (8.51%) 4		
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 3 4 / 47 (8.51%) 10		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) alkaline phosphatase increased subjects affected / exposed occurrences (all) Antithrombin III decreased subjects affected / exposed occurrences (all) AST, GOT increased subjects affected / exposed occurrences (all) Blood bilirubin increased subjects affected / exposed occurrences (all) Cholesterol high subjects affected / exposed occurrences (all) Creatinine urine increased	20 / 47 (42.55%) 28 5 / 47 (10.64%) 9 21 / 47 (44.68%) 26 18 / 47 (38.30%) 26 17 / 47 (36.17%) 24 4 / 47 (8.51%) 10		

subjects affected / exposed	7 / 47 (14.89%)		
occurrences (all)	11		
Fibrinogen decreased			
subjects affected / exposed	16 / 47 (34.04%)		
occurrences (all)	24		
GGT increased			
subjects affected / exposed	10 / 47 (21.28%)		
occurrences (all)	15		
GOT/GPT increased			
subjects affected / exposed	30 / 47 (63.83%)		
occurrences (all)	71		
Investigations - other			
subjects affected / exposed	9 / 47 (19.15%)		
occurrences (all)	10		
Lipase decreased			
subjects affected / exposed	13 / 47 (27.66%)		
occurrences (all)	27		
Serum amylase increased			
subjects affected / exposed	4 / 47 (8.51%)		
occurrences (all)	6		
Weight increased			
subjects affected / exposed	7 / 47 (14.89%)		
occurrences (all)	10		
Nervous system disorders			
cognitive disturbance			
subjects affected / exposed	3 / 47 (6.38%)		
occurrences (all)	3		
Dizziness			
subjects affected / exposed	11 / 47 (23.40%)		
occurrences (all)	15		
Headache			
subjects affected / exposed	9 / 47 (19.15%)		
occurrences (all)	20		
Nervous system disorder			
subjects affected / exposed	4 / 47 (8.51%)		
occurrences (all)	7		

Paraesthesia			
subjects affected / exposed	7 / 47 (14.89%)		
occurrences (all)	15		
Peripheral sensory neuropathy			
subjects affected / exposed	4 / 47 (8.51%)		
occurrences (all)	5		
Tremor			
subjects affected / exposed	6 / 47 (12.77%)		
occurrences (all)	13		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	29 / 47 (61.70%)		
occurrences (all)	66		
Other			
subjects affected / exposed	3 / 47 (6.38%)		
occurrences (all)	8		
Febrile neutropenia			
subjects affected / exposed	7 / 47 (14.89%)		
occurrences (all)	8		
Immunoglobulins decreased			
subjects affected / exposed	19 / 47 (40.43%)		
occurrences (all)	36		
Lymphocyte count decreased			
subjects affected / exposed	24 / 47 (51.06%)		
occurrences (all)	60		
Neutrophil count decreased			
subjects affected / exposed	28 / 47 (59.57%)		
occurrences (all)	59		
Platelet count decreased			
subjects affected / exposed	32 / 47 (68.09%)		
occurrences (all)	65		
White blood cell count decreased			
subjects affected / exposed	33 / 47 (70.21%)		
occurrences (all)	78		
Eye disorders			

Dry eye subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 6		
Eye disorder subjects affected / exposed occurrences (all)	5 / 47 (10.64%) 8		
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	8 / 47 (17.02%) 11		
Constipation subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 5		
Diarrhoea subjects affected / exposed occurrences (all)	16 / 47 (34.04%) 24		
Gastroesophageal reflux disease subjects affected / exposed occurrences (all)	4 / 47 (8.51%) 4		
Gastrointestinal disorder subjects affected / exposed occurrences (all)	6 / 47 (12.77%) 8		
mucositis subjects affected / exposed occurrences (all)	15 / 47 (31.91%) 16		
Nausea subjects affected / exposed occurrences (all)	18 / 47 (38.30%) 42		
obstipation subjects affected / exposed occurrences (all)	16 / 47 (34.04%) 23		
Vomiting subjects affected / exposed occurrences (all)	8 / 47 (17.02%) 14		
Hepatobiliary disorders			

hepatobiliary disorders - other subjects affected / exposed occurrences (all)	3 / 47 (6.38%) 3		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Rash maculo-papular subjects affected / exposed occurrences (all) skin and subcutaneous tissue disorders - other subjects affected / exposed occurrences (all)	 3 / 47 (6.38%) 3 3 / 47 (6.38%) 3 8 / 47 (17.02%) 19		
Renal and urinary disorders Acute/chronic kidney injury subjects affected / exposed occurrences (all)	 8 / 47 (17.02%) 10		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all) musculoskeletal and connective tissue disorders - other subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 5 / 47 (10.64%) 5 4 / 47 (8.51%) 6 4 / 47 (8.51%) 7 3 / 47 (6.38%) 4		
Infections and infestations Infection subjects affected / exposed occurrences (all) infection and infestations - other	 23 / 47 (48.94%) 36 		

subjects affected / exposed	9 / 47 (19.15%)		
occurrences (all)	10		
Lip infection			
subjects affected / exposed	3 / 47 (6.38%)		
occurrences (all)	5		
Urinary tract infection			
subjects affected / exposed	5 / 47 (10.64%)		
occurrences (all)	7		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	26 / 47 (55.32%)		
occurrences (all)	76		
Hypertriglyceridaemia			
subjects affected / exposed	3 / 47 (6.38%)		
occurrences (all)	9		
Hypoalbuminaemia			
subjects affected / exposed	20 / 47 (42.55%)		
occurrences (all)	38		
Hyperuricaemia			
subjects affected / exposed	3 / 47 (6.38%)		
occurrences (all)	5		
Hypocalcaemia			
subjects affected / exposed	3 / 47 (6.38%)		
occurrences (all)	7		
Hypokalaemia			
subjects affected / exposed	12 / 47 (25.53%)		
occurrences (all)	17		
Hypophosphataemia			
subjects affected / exposed	4 / 47 (8.51%)		
occurrences (all)	7		
triglyceride increased			
subjects affected / exposed	14 / 47 (29.79%)		
occurrences (all)	20		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 August 2018	Protocol version 1.4 modifications: - Correction of the standard of care description accoridng to the recommendation in Germany; - Establishment a Data safety Monitoring Board; - Modification in the CSF prophylaxis: possibility to postpone the CSF prophylaxis.
20 February 2020	Modifications of Protocol version 1.5: - Inclusion criteria: a Ph/BCR-ABL-negative ALL must be present. This point was already included in the title of the study, but the addition was missing in the inclusion criteria. - Corrections in the study time points for blinatumomab cycles and tests - Screening phase: the inclusion of the patient should be carried out before Induction I and not before the first Blina cycle - IMP: Extension of the approval of blinatumomab for MRD positive ALL - End of study: the end of the trial was defined in the protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported