Clinical trial results:
A pilot study to test the feasibility, safety and efficacy of the addition of the BiTE antibody Blinatumomab to the Interfant-06 backbone in infants with MLL-rearranged acute lymphoblastic leukemia. A collaborative study of the Interfant network.

Summary

EudraCT number	2016-004674-17
Trial protocol	NL AT BE DK DE CZ FR IT
Global end of trial date	07 March 2024
Results information	
Result version number	v2 (current)
This version publication date	08 February 2026
First version publication date	23 March 2025
Version creation reason	• New data added to full data set final results

Trial information

Trial identification	
Sponsor protocol code	NL59901.078.17
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Trialregister: NL5993 (= NTR6359)

Notes:

Sponsors	
Sponsor organisation name	Princess Máxima Center for Pediatric Oncology
Sponsor organisation address	Heidelberglaan 25, Utrecht, Netherlands, 3584 CS
Public contact	Secretariat TDC, Princess Máxima Center for Pediatric Oncology, 0031 889727272, trialmanagement@prinsesmaximacentrum.nl
Scientific contact	I.M. van der Sluis, Princess Máxima Center for Pediatric Oncology, 0031 889727272, trialmanagement@prinsesmaximacentrum.nl

Notes:

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 October 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety of 1 course of blinatumomab added to the Interfant-06 backbone in infants with newly diagnosed ALL.

Protection of trial subjects:

The interests of the trial subjects are safeguarded by informing the parents verbally and in writing (informed consent), by the possibility of consulting an independent physician, by the possibility of withdrawing from the study without giving reasons, and by following the NVK "Directive on Resistance" and by the monitors involved, monitoring that the trial is conducted, recorded and reported in accordance with the protocol, ICH-GCP and the applicable regulatory requirement(s).

Background therapy:

Chemotherapy according to the Interfant-06 protocol (= Induction (IA), IB, MARMA, OCTADAD and Maintenance).

Evidence for comparator:

Clinical studies show that blinatumomab is effective and well tolerated in children and adults with ALL who are already pre-treated with intensive chemotherapy.

Actual start date of recruitment	31 July 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 3
Worldwide total number of subjects	30
EEA total number of subjects	22

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)	30
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study initiation date/first subject first visit: 31 July 2018
Last Patient in: 05 July 2021
Study completion date/last subject last visit: 07 March 2024
30 subjects enrolled

Pre-assignment

Screening details:

Newly diagnosed infants with ALL, who are treated according to the Interfant-06 protocol, stratified into the medium or high risk group, and have M1 or M2 marrow at the end of induction (~day 33 bone marrow).

Period 1

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

Arms

Arm title	Blinatumomab

Arm description:

1 course of blinatumomab 15 µg/m2/day as a 4 week continuous infusion

Arm type	Experimental
Investigational medicinal product name	Blinatumomab
Investigational medicinal product code	AMG103
Other name	Blincyto
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

1 course of blinatumomab 15 µg/m2/day as a 4 week continuous infusion

Number of subjects in period 1	Blinatumomab
Started	30
interim analysis	30
Completed	30

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	30	30	
Age categorical			
Age at diagnosis			
Units: Subjects			
< 3 months	8	8	
3 - 6 months	11	11	
6 - 9 months	6	6	
9 - 12 months	5	5	
Gender categorical			
Units: Subjects			
Female	18	18	
Male	12	12	
Risk Group			
Units: Subjects			
Medium Risk	21	21	
High Risk	9	9	
WBC			
Units: Subjects			
< 100 x 10^9/L	7	7	
≥ 100 x 10^9/L, <300 x 10^9/L	11	11	
≥ 300 x 10^9/L	12	12	
Not known	0	0	
Immunophenotype			
Units: Subjects			
B-lineage – CD10 negative	24	24	
B-lineage – CD10 positive	5	5	
B-lineage – CD10 not known	1	1	
Not known	0	0	
CNS-Involvement			
Units: Subjects			
CNS1	9	9	
CNS2	13	13	
CNS3	3	3	
Not evaluable	5	5	
KMT2A-rearrangement			
Units: Subjects			
t(4;11)	15	15	
t(9;11)	3	3	
t(11;19)	6	6	
Other partner	3	3	
Partner not known	3	3	

Prednisone Response Units: Subjects			
Prednisone Good Response	23	23	
Prednisone Poor Response	7	7	
Not known	0	0	
End of Induction MRD Units: Subjects			
<5x10^-4	18	18	
≥5x10^-4	12	12	

End points

End points reporting groups

Reporting group title	Blinatumomab
Reporting group description:	
1 course of blinatumomab 15 µg/m2/day as a 4 week continuous infusion	
Subject analysis set title	Primary - Safety of blinatumomab
Subject analysis set type	Full analysis
Subject analysis set description:	
Incidence of clinically relevant toxicities defined as any toxicity that is possibly or definitely attributable to blinatumomab AND results in permanent discontinuation of blinatumomab or death.	
Subject analysis set title	Secondary - Toxicity
Subject analysis set type	Full analysis
Subject analysis set description:	
Incidence and severity of serious adverse events till start of protocol IB, independently to relationship with blinatumomab	
Subject analysis set title	Secondary - Interruptions due to Blinatumomab
Subject analysis set type	Full analysis
Subject analysis set description:	
Number of treatment interruptions due to toxicity occurring during blinatumomab	
Subject analysis set title	Secondary - Patients with full course of Blinatumomab
Subject analysis set type	Full analysis
Subject analysis set description:	
Proportion of patients that receive a full course (4 weeks) of blinatumomab	
Subject analysis set title	Secondary - MRD response TP2, TPBlina1, TPBlina2
Subject analysis set type	Full analysis
Subject analysis set description:	
MRD response at the following time-points: TP2 d33 (end of induction), TPblina1 d15 (after initial 15 days of blinatumomab) and TPblina2 d29 (after the complete course of blinatumomab)	
Subject analysis set title	Secondary - MRD response TP4
Subject analysis set type	Full analysis
Subject analysis set description:	
MRD response at the following time-point: TP4 (end of Protocol IB)	
Subject analysis set title	Secondary - MRD response in MR patients before OCTADAD
Subject analysis set type	Full analysis
Subject analysis set description:	
Proportion of MR patients with MRD >= 5x10-4 before OCTADAD (indication for SCT)	
Subject analysis set title	Secondary - cCR/CR and post-induction EFS/long term EFS/OS
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
cCR/CR and 6 months post-induction EFS and the long-term EFS and OS	
Subject analysis set title	Secondary - MRD response at TP2
Subject analysis set type	Full analysis
Subject analysis set description:	
MRD response at the following time-point: TP2 d33 (end of induction)	
Subject analysis set title	Secondary - MRD response at TP4
Subject analysis set type	Full analysis
Subject analysis set description:	
MRD response at the following time-point: TP4 (end of Protocol IB)	
Subject analysis set title	Secondary - MRD response TPBlina1
Subject analysis set type	Full analysis

Subject analysis set description:

MRD response at the following time-point: TPblina1 d15 (after initial 15 days of blinatumomab)

Subject analysis set title	Secondary - MRD response TPBlina2
Subject analysis set type	Full analysis

Subject analysis set description:

MRD response at the following time-point: TPblina2 d29 (after the complete course of blinatumomab)

Subject analysis set title	Secondary - Pharmacokinetics
Subject analysis set type	Full analysis

Subject analysis set description:

Steady state concentration (Css)

Subject analysis set title	Secondary - Key Safety Parameters
Subject analysis set type	Full analysis

Subject analysis set description:

Incidence and severity of key safety parameters till start of maintenance and during long-term follow-up

Primary: Safety

End point title	Safety[1]

End point description:

Incidence of clinically relevant toxicities defined as any toxicity that is possibly or definitely attributable to blinatumomab AND results in permanent discontinuation of blinatumomab OR death.

End point type	Primary

End point timeframe:

From start of blinatumomab till start of chemotherapy according to protocol IB.

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: Descriptive analysis. No comparison due to only one arm in the study

End point values	Blinatumomab	Primary - Safety of blinatumomab		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	30	30		
Units: toxic effects				
permanent discontinuation of blinatumomab	0	0		
death	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity - SAEs

End point title	Toxicity - SAEs

End point description:

Incidence and severity of serious adverse events till start of protocol IB, independently to relationship with blinatumomab

End point type	Secondary

End point timeframe:

From start of blinatumomab until start of protocol IB

End point values	Secondary - Toxicity			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: toxic events				
No. of adverse events of any grade	61			
No. of adverse events of CTCAE grade3	16			
No. of serious adverse events	10			

Statistical analyses

No statistical analyses for this end point

Secondary: MRD response - TP2, TPBlina1 and TPBlina2

End point title	MRD response - TP2, TPBlina1 and TPBlina2

End point description:

MRD response at the following time-points: TP2 d33 (end of induction), TPblina1 d15 (after initial 15 days of blinatumomab) and TPblina2 d29 (after the complete course of blinatumomab)

End point type	Secondary

End point timeframe:

From start to end of Blinatumomab course

End point values	Secondary - MRD response at TP2	Secondary - MRD response TPBlina1	Secondary - MRD response TPBlina2	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	30	30	30	
Units: MRD				
MRD Negative	8	16	16	
MRD < 5x10-4	10	11	12	
MRD ≥ 5 x10-4	12	3	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity - treatment interruptions

End point title	Toxicity - treatment interruptions

End point description: Number of treatment interruptions due to toxicity occurring during blinatumomab	
End point type	Secondary
End point timeframe: Blinatumomab course	

End point values	Secondary - Interruptions due to Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: Number of times				
Blinatumomab Discontinuation	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicity - Patients who received full course of Blinatumomab

End point title	Toxicity - Patients who received full course of Blinatumomab
End point description: Proportion of patients that receive a full course (4 weeks) of blinatumomab	
End point type	Secondary
End point timeframe: During Blinatumomab course	

End point values	Secondary - Patients with full course of Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: Number of patients				
Patients who received full blinatumomab course	30			

Statistical analyses

No statistical analyses for this end point

Secondary: MRD response - TP2 and TP4

End point title	MRD response - TP2 and TP4

End point description:	
MRD response at the following time-points: TP2 d33 (end of induction) and TP4 (end of Protocol IB)	
End point type	Secondary
End point timeframe:	
From Blinatumomab until the end of Protocol Ib	

End point values	Secondary - MRD response at TP2	Secondary - MRD response at TP4		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	28		
Units: Number of patients				
MRD Negative	8	15		
MRD Positive < 5x10-4	10	11		
MRD Positive ≥ 5x10-4	12	2		

Statistical analyses

No statistical analyses for this end point

Secondary: MRD Response before OCTADAD/HSCT

End point title	MRD Response before OCTADAD/HSCT
End point description:	
Proportion of MR patients with MRD ≥ 5x10^-4 before OCTADAD (indication for SCT)	
End point type	Secondary
End point timeframe:	
Before the start of OCTADAD	

End point values	Secondary - MRD response in MR patients before OCTADAD			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Number of patients				
MRD before OCTADAD/HSCT ≥ 5x10-4	0			

Statistical analyses

No statistical analyses for this end point

Secondary: cCR/CR and 6 months post-induction EFS and long term EFS and OS

End point title	cCR/CR and 6 months post-induction EFS and long term EFS and OS

End point description:

cCR/CR and 6 months post-induction EFS and the long-term EFS and OS

End point type	Secondary

End point timeframe:

From enrollment until 16 October 2024

End point values	Secondary - cCR/CR and post-induction EFS/long term EFS/OS			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: Number of events				
Relapse	4			
Death	2			
Progressive disease	0			
Secondary malignancy	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of infection

End point title	Incidence of infection

End point description:

End point type	Secondary

End point timeframe:

From Blinatumomab course until the end of treatment (End of Maintenance)

End point values	Secondary - Key Safety Parameters			
Subject group type	Subject analysis set			
Number of subjects analysed	30[2]			
Units: Number of infections	95			

Notes:

[2] - Overall only 26 out of 30 patients had reported infections

Statistical analyses

No statistical analyses for this end point

Secondary: Severity of Infection

End point title	Severity of Infection

End point description:

Common Terminology Criteria for Adverse Events (CTCAE) grading v 4.03

End point type	Secondary

End point timeframe:

From blinatumomab course until the end of treatment (end of Maintenance)

End point values	Secondary - Key Safety Parameters			
Subject group type	Subject analysis set			
Number of subjects analysed	26[3]			
Units: Number of infections				
CTCAE grade 1	17			
CTCAE grade 2	34			
CTCAE grade 3	43			
CTCAE grade 4	1			
CTCAE grade 5	0			

Notes:

[3] - 26 out of 30 pts had infections since start of Blin till the end of Maintenance (end of treatment)

Statistical analyses

No statistical analyses for this end point

Secondary: Steady State Concentrations of Blinatumomab (Css)

End point title	Steady State Concentrations of Blinatumomab (Css)

End point description:

End point type	Secondary

End point timeframe:

During the course of blinatumomab

End point values	Secondary - Pharmacokinetics			
Subject group type	Subject analysis set			
Number of subjects analysed	26[4]			
Units: pg/mL/day				
arithmetic mean (standard deviation)	706 (± 194)			

Notes:
[4] - Only 26 out of 30 patients had available samples for Css assessment

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of blinatumomab till start of chemotherapy according to protocol IB.

Adverse event reporting additional description:

As for the Interfant-06 study, AEs occurring in each treatment phase are reported with the Toxicity Form.
During blinatumomab until start protocol IB all AEs grades are reported with the exception of non-reportable AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	(S)AEs from start of blinatumomab until start of protocol IB

Reporting group description:

Patients who had the same adverse event multiple times were counted once, and the highest grade is reported.
If a patient had episodes in different adverse event categories, it is counted in each category.
CTCAE denotes Common Terminology Criteria for Adverse Events. Only AEs with CTCAE grade >= 3 are mentioned here.
Fever of grade 1 occurred twice in one patient.

Serious adverse events	(S)AEs from start of blinatumomab until start of protocol IB		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 30 (30.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypertension	Additional description: Grade 3		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fever	Additional description: Grade 1		
subjects affected / exposed	3 / 30 (10.00%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting	Additional description: Grade 3		

subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Line infection	Additional description: Grade 3		
subjects affected / exposed	2 / 30 (6.67%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Upper Respiratory infection	Additional description: Grade 4		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin infection	Additional description: Grade 3		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	(S)AEs from start of blinatumomab until start of protocol IB		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 30 (53.33%)		
Vascular disorders			
Hypertension	Additional description: Adverse events of CTCAE grade ≥3		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anemia	Additional description: Adverse events of CTCAE grade ≥3		
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	10		
Febrile neutropenia	Additional description: Adverse events of CTCAE grade ≥3		
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Decreased neutrophil count	Additional description: Adverse events of CTCAE grade ≥3		

subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Decreased white-cell count	Additional description: Adverse events of CTCAE grade ≥3		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	2		
Hepatobiliary disorders			
Increased alanine aminotransferase level	Additional description: Adverse events of CTCAE grade ≥3		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Increased γ-glutamyltransferase level	Additional description: Adverse events of CTCAE grade ≥3		
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Infections and infestations			
Pharyngitis	Additional description: Adverse events of CTCAE grade ≥3		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypoproteinemia	Additional description: Adverse events of CTCAE grade ≥3		
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2019	Protocol amendment no. 1: Editorial changes and changes for clarification; Corrections and changes in contact details; Change in Principal investigator(s) DCOG (NL) and Sponsor representative; Additional information about blinatumomab approvals for new indication; Change of estimated study duration and timelines; Correction of exclusion criteria before start (-d3) of blinatumomab; Correction MRD measurement.
09 April 2021	Amendment no. 2: Investigator's Brochure with relevant RSI update

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/41505662

http://www.ncbi.nlm.nih.gov/pubmed/37099340