



## 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          | v1            |
| This version publication date  | 23 March 2025 |
| First version publication date | 23 March 2025 |

### 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                                       | Interim        |
| Date of interim/final analysis                       | 31 August 2022 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 31 August 2022 |
| 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                              | 2 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:

| <b>Subjects enrolled per age group</b>    |    |
|-------------------------------------------|----|
| 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 <sup>9</sup> /L                            | 7             | 7     |  |
| ≥ 100 x 10 <sup>9</sup> /L, <300 x 10 <sup>9</sup> /L | 11            | 11    |  |
| ≥ 300 x 10 <sup>9</sup> /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 <sup>-4</sup>      | 18 | 18 |  |
| ≥5x10 <sup>-4</sup>      | 12 | 12 |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                         |                                                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                   | Blinatumomab                                               |
| Reporting group description:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>Proportion of MR patients with MRD $\geq 5 \times 10^{-4}$ 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:<br>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:<br>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:<br>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)

### Primary: Safety

|                 |                       |
|-----------------|-----------------------|
| End point title | Safety <sup>[1]</sup> |
|-----------------|-----------------------|

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: The 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 will be described as percentage of patients and also estimated with the exposure-adjusted incidence rate, calculated as the ratio between the number of these adverse events and the total time at risk from study entry, in weeks. In addition, incidence of death will be calculated.

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

|                              |                                               |  |  |  |
|------------------------------|-----------------------------------------------|--|--|--|
| <b>End point values</b>      | 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                                                  |

|                                                |                                                       |  |  |  |
|------------------------------------------------|-------------------------------------------------------|--|--|--|
| <b>End point values</b>                        | 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 <sup>-4</sup> | 10                              | 11                              |  |  |
| MRD Positive ≥ 5x10 <sup>-4</sup> | 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:<br>Proportion of MR patients with MRD ≥ 5x10 <sup>-4</sup> before OCTADAD (indication for SCT) |                                  |
| End point type                                                                                                        | Secondary                        |
| End point timeframe:<br>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 <sup>-4</sup> | 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:<br>cCR/CR and 6 months post-induction EFS and the long-term EFS and OS |                                                                 |
| End point type                                                                                | Secondary                                                       |

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End point timeframe:

From enrollment until 31 August 2022

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|                             |                                                                        |  |  |  |
|-----------------------------|------------------------------------------------------------------------|--|--|--|
| <b>End point values</b>     | Secondary -<br>cCR/CR and<br>post-induction<br>EFS/long term<br>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

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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  $\geq 3$  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 %

|                                                       |                                                              |  |  |
|-------------------------------------------------------|--------------------------------------------------------------|--|--|
| <b>Non-serious adverse events</b>                     | (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:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

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