



## Clinical trial results:

**A multicenter, single-arm study to assess the efficacy, safety, and tolerability of the BiTE® antibody blinatumomab in adult patients with minimal residual disease (MRD) of B-precursor acute lympho-blastic leukemia (Blast Successor Trial)**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-000733-76 |
| Trial protocol           | DE             |
| Global end of trial date | 31 July 2023   |

### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 02 August 2024 |
| First version publication date | 02 August 2024 |

### Trial information

#### Trial identification

|                       |                     |
|-----------------------|---------------------|
| Sponsor protocol code | GMALL-MOLACT1-BLINA |
|-----------------------|---------------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03109093 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Goethe University   |
| Sponsor organisation address | Theodor-Stern-Kai 7, Frankfurt , Germany, 60590   |
| Public contact               | GMALL-Studienzentrale, Universitätsklinik Frankfurt, Med. Klinik II, +49 (0)6963016365, gmall@em.uni-frankfurt.de |
| Scientific contact           | GMALL-Studienzentrale, Universitätsklinik Frankfurt, Med. Klinik II, +49 (0)6963016365, gmall@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                       | 20 March 2023 |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 20 March 2023 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 31 July 2023  |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of blinatumomab to induce complete MRD response in patients regardless of prior SCT

Protection of trial subjects:

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 not 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 also used for patient data in the patient files and eCRFs.

Clinical information was not released without written permission given by the subject/legal representative within the informed consent, except as necessary for monitoring by regulatory authorities or the Sponsor of the clinical study. The principal investigator also complied with all applicable national privacy regulations.

Background therapy:

No pre-phase chemotherapy was planned as patients had only minimal residual disease.

Evidence for comparator:

N.A.

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 16 January 2017 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 83 |
| Worldwide total number of subjects   | 83          |
| EEA total number of subjects         | 83          |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23 months)  | 0 |

|                           |    |
|---------------------------|----|
| Children (2-11 years)     | 0  |
| Adolescents (12-17 years) | 0  |
| Adults (18-64 years)      | 75 |
| From 65 to 84 years       | 8  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

04-04-2017 First Patient In, 11-10-2019 last Patient out.

### Pre-assignment

Screening details:

Screening was conducted to verify that the inclusion criteria for the study were met, with particular attention to the presence of minimal residual disease(MRD).

### 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 |
|-----------|--------------|

Arm description:

Patients received one to four consecutive cycles of blinatumomab. A cycle consists of a continuous intravenous infusion at a dose of 28 µg/d over four weeks followed by an infusion free interval of two weeks.

|  |  |
|--|--|
| Arm type                               | open-label single-arm study                    |
| Investigational medicinal product name | Blinatumomab                                   |
| Investigational medicinal product code |  |
| Other name                             | BLINCYTO®, BiTE®                               |
| Pharmaceutical forms                   | Powder and solution for solution for injection |
| Routes of administration               | Infusion                                       |

Dosage and administration details:

Patients received one to four consecutive cycles of blinatumomab. A cycle consists of a continuous intravenous infusion at a dose of 28 µg/d over four weeks followed by an infusion free interval of two weeks. Blinatumomab were administered as a continuous intravenous (CIV) infusion at a constant flow rate over four weeks followed by a two-week infusion free interval.

|                                       |              |
|---------------------------------------|--------------|
| <b>Number of subjects in period 1</b> | Blinatumomab |
| Started                               | 83           |
| Completed                             | 83           |

## Baseline characteristics

### Reporting groups

|   |               |
|---|---------------|
| Reporting group title   | Overall trial |
| Reporting group description:<br>This study incorporated multiple interim analyses for futility, efficacy, and unblinded sample-size reestimation. |               |

| Reporting group values                                | Overall trial | Total |  |
|---|---------------|-------|--|
| Number of subjects                                    | 83            | 83    |  |
| Age categorical<br>Units: Subjects                    |               |       |  |
| In utero  | 0             | 0     |  |
| Preterm newborn infants<br>(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)                                  | 75            | 75    |  |
| From 65-84 years                                      | 8             | 8     |  |
| 85 years and over                                     | 0             | 0     |  |
| Gender categorical<br>Units: Subjects                 |               |       |  |
| Female  | 38            | 38    |  |
| Male  | 45            | 45    |  |

### Subject analysis sets

|  |                    |
|--|--------------------|
| Subject analysis set title   | Evaluable patients |
| Subject analysis set type  | Full analysis      |
| Subject analysis set description:<br>All patients who received any infusion of the investigation drug and for whom at least one evaluable response assessment is available after start of treatment or patients who died before the first evaluation time-point. Patients for whom no sufficient MRD assessment by PCR is established due to technical reasons will be excluded from the analysis of the primary endpoint. |                    |

| Reporting group values                                | Evaluable patients |  |  |
|---|--------------------|--|--|
| Number of subjects                                    | 83                 |  |  |
| Age categorical<br>Units: Subjects                    |                    |  |  |
| In utero  | 0                  |  |  |
| Preterm newborn infants<br>(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)                                  | 75                 |  |  |

|                   |   |  |  |
|-------------------|---|--|--|
| From 65-84 years  | 8 |  |  |
| 85 years and over | 0 |  |  |

|                    |    |  |  |
|--------------------|----|--|--|
| Gender categorical |    |  |  |
| Units: Subjects    |    |  |  |
| Female             | 38 |  |  |
| Male               | 45 |  |  |

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## End points

### End points reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | Blinatumomab |
|-----------------------|--------------|

Reporting group description:

Patients received one to four consecutive cycles of blinatumomab. A cycle consists of a continuous intravenous infusion at a dose of 28 µg/d over four weeks followed by an infusion free interval of two weeks.

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Evaluable patients |
|----------------------------|--------------------|

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

Subject analysis set description:

All patients who received any infusion of the investigation drug and for whom at least one evaluable response assessment is available after start of treatment or patients who died before the first evaluation time-point. Patients for whom no sufficient MRD assessment by PCR is established due to technical reasons will be excluded from the analysis of the primary endpoint.

### Primary: Complete MRD response after one cycle of treatment

|                 |   |
|-----------------|---|
| End point title | Complete MRD response after one cycle of treatment <sup>[1]</sup> |
|-----------------|---|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

After 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            | Evaluable patients   |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 83                   |  |  |  |
| Units: Percent              | 71                   |  |  |  |

### 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 | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

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

### 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                       | 27 / 83 (32.53%)                  |  |  |
| number of deaths (all causes)                     | 24                                |  |  |
| number of deaths resulting from adverse events    | 0                                 |  |  |
| Investigations                                    |                                   |  |  |
| CRP   |                                   |  |  |
| subjects affected / exposed                       | 1 / 83 (1.20%)                    |  |  |
| occurrences causally related to treatment / all   | 0 / 1                             |  |  |
| deaths causally related to treatment / all        | 0 / 0                             |  |  |
| Neutropenia                                       |                                   |  |  |
| subjects affected / exposed                       | 1 / 83 (1.20%)                    |  |  |
| occurrences causally related to treatment / all   | 1 / 1                             |  |  |
| deaths causally related to treatment / all        | 0 / 0                             |  |  |
| Neutrophil count decreased                        |                                   |  |  |
| subjects affected / exposed                       | 1 / 83 (1.20%)                    |  |  |
| occurrences causally related to treatment / all   | 1 / 1                             |  |  |
| deaths causally related to treatment / all        | 0 / 0                             |  |  |
| White blood cell decreased                        |                                   |  |  |
| subjects affected / exposed                       | 1 / 83 (1.20%)                    |  |  |
| occurrences causally related to treatment / all   | 1 / 1                             |  |  |
| deaths causally related to treatment / all        | 0 / 0                             |  |  |
| Injury, poisoning and procedural                  |                                   |  |  |



|   |                |  |  |
|---|----------------|--|--|
| complications   |                |  |  |
| Injury, poisoning and procedural complications - Other, specify |                |  |  |
| subjects affected / exposed                                     | 3 / 83 (3.61%) |  |  |
| occurrences causally related to treatment / all                 | 3 / 3          |  |  |
| deaths causally related to treatment / all                      | 0 / 0          |  |  |
| Nervous system disorders  |                |  |  |
| Cognitive disturbance   |                |  |  |
| subjects affected / exposed                                     | 1 / 83 (1.20%) |  |  |
| occurrences causally related to treatment / all                 | 1 / 1          |  |  |
| deaths causally related to treatment / all                      | 0 / 0          |  |  |
| Dysphasia   |                |  |  |
| subjects affected / exposed                                     | 4 / 83 (4.82%) |  |  |
| occurrences causally related to treatment / all                 | 5 / 5          |  |  |
| deaths causally related to treatment / all                      | 0 / 0          |  |  |
| Encephalopathy  |                |  |  |
| subjects affected / exposed                                     | 1 / 83 (1.20%) |  |  |
| occurrences causally related to treatment / all                 | 1 / 1          |  |  |
| deaths causally related to treatment / all                      | 0 / 0          |  |  |
| Nervous system disorders - Other, specify                       |                |  |  |
| subjects affected / exposed                                     | 1 / 83 (1.20%) |  |  |
| occurrences causally related to treatment / all                 | 1 / 1          |  |  |
| deaths causally related to treatment / all                      | 0 / 0          |  |  |
| Seizure   |                |  |  |
| subjects affected / exposed                                     | 1 / 83 (1.20%) |  |  |
| occurrences causally related to treatment / all                 | 1 / 1          |  |  |
| deaths causally related to treatment / all                      | 0 / 0          |  |  |
| Tremor  |                |  |  |
| subjects affected / exposed                                     | 3 / 83 (3.61%) |  |  |
| occurrences causally related to treatment / all                 | 3 / 3          |  |  |
| deaths causally related to treatment / all                      | 0 / 0          |  |  |
| General disorders and administration site conditions            |                |  |  |
| Fever   |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 2 / 83 (2.41%) |  |  |
| occurrences causally related to treatment / all | 1 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Immune system disorders                         |                |  |  |
| Allergic reaction                               |                |  |  |
| subjects affected / exposed                     | 1 / 83 (1.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Pneumothorax                                    |                |  |  |
| subjects affected / exposed                     | 1 / 83 (1.20%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Bronchial infection                             |                |  |  |
| subjects affected / exposed                     | 1 / 83 (1.20%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Catheter related infection                      |                |  |  |
| subjects affected / exposed                     | 2 / 83 (2.41%) |  |  |
| occurrences causally related to treatment / all | 2 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations - Other, specify    |                |  |  |
| subjects affected / exposed                     | 3 / 83 (3.61%) |  |  |
| occurrences causally related to treatment / all | 1 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Tumor lysis syndrome                            |                |  |  |
| subjects affected / exposed                     | 1 / 83 (1.20%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

| <b>Non-serious adverse events</b>                               | All patients with study treatment |  |  |
|---|-----------------------------------|--|--|
| Total subjects affected by non-serious adverse events           |                                   |  |  |
| subjects affected / exposed                                     | 80 / 83 (96.39%)                  |  |  |
| Investigations  |                                   |  |  |
| Alanine aminotransferase increased                              |                                   |  |  |
| subjects affected / exposed                                     | 15 / 83 (18.07%)                  |  |  |
| occurrences (all)   | 19                                |  |  |
| AST, GOT increased  |                                   |  |  |
| subjects affected / exposed                                     | 11 / 83 (13.25%)                  |  |  |
| occurrences (all)   | 13                                |  |  |
| Immunoglobulin deficiency                                       |                                   |  |  |
| subjects affected / exposed                                     | 7 / 83 (8.43%)                    |  |  |
| occurrences (all)   | 14                                |  |  |
| Investigations - Other, specify                                 |                                   |  |  |
| subjects affected / exposed                                     | 8 / 83 (9.64%)                    |  |  |
| occurrences (all)   | 8                                 |  |  |
| Lipase increased  |                                   |  |  |
| subjects affected / exposed                                     | 9 / 83 (10.84%)                   |  |  |
| occurrences (all)   | 11                                |  |  |
| Lymphocyte count decreased                                      |                                   |  |  |
| subjects affected / exposed                                     | 38 / 83 (45.78%)                  |  |  |
| occurrences (all)   | 64                                |  |  |
| Neutrophil count decreased                                      |                                   |  |  |
| subjects affected / exposed                                     | 32 / 83 (38.55%)                  |  |  |
| occurrences (all)   | 41                                |  |  |
| Platelet count decreased  |                                   |  |  |
| subjects affected / exposed                                     | 24 / 83 (28.92%)                  |  |  |
| occurrences (all)   | 35                                |  |  |
| White blood cell count decreased                                |                                   |  |  |
| subjects affected / exposed                                     | 37 / 83 (44.58%)                  |  |  |
| occurrences (all)   | 60                                |  |  |
| Injury, poisoning and procedural complications                  |                                   |  |  |
| Injury, poisoning and procedural complications - Other, specify |                                   |  |  |
| subjects affected / exposed                                     | 4 / 83 (4.82%)                    |  |  |
| occurrences (all)   | 4                                 |  |  |

|  |  |  |  |
|--|--|--|--|
| Nervous system disorders<br>Dysphasia (Aphasia)<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Peripheral sensory neuropathy<br>subjects affected / exposed<br>occurrences (all)<br><br>Tremor<br>subjects affected / exposed<br>occurrences (all) | 5 / 83 (6.02%)<br>6<br><br>21 / 83 (25.30%)<br>21<br><br>5 / 83 (6.02%)<br>5<br><br>16 / 83 (19.28%)<br>19 |  |  |
| Blood and lymphatic system disorders<br>Anaemia/Hemoglobin<br>subjects affected / exposed<br>occurrences (all)   | 25 / 83 (30.12%)<br>39   |  |  |
| General disorders and administration site conditions<br>Chills<br>subjects affected / exposed<br>occurrences (all)<br><br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br><br>Fever/Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 4 / 83 (4.82%)<br>4<br><br>8 / 83 (9.64%)<br>12<br><br>52 / 83 (62.65%)<br>66                              |  |  |
| Immune system disorders<br>Cytokine release syndrome<br>subjects affected / exposed<br>occurrences (all)   | 9 / 83 (10.84%)<br>9   |  |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Mucositis oral   | 4 / 83 (4.82%)<br>4  |  |  |

|   |   |  |  |
|---|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                             | <p>4 / 83 (4.82%)</p> <p>4</p> <p>10 / 83 (12.05%)</p> <p>10</p> <p>6 / 83 (7.23%)</p> <p>6</p> |  |  |
| <p>Skin and subcutaneous tissue disorders</p> <p>Skin and subcutaneous tissue disorders - Other, specify</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>7 / 83 (8.43%)</p> <p>7</p>  |  |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Bone pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                              | <p>6 / 83 (7.23%)</p> <p>6</p> <p>8 / 83 (9.64%)</p> <p>8</p>                                   |  |  |
| <p>Infections and infestations</p> <p>Infections and infestations - Other, specify</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>5 / 83 (6.02%)</p> <p>5</p> <p>4 / 83 (4.82%)</p> <p>4</p>                                   |  |  |
| <p>Metabolism and nutrition disorders</p> <p>Hyperglycaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypokalaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                   | <p>18 / 83 (21.69%)</p> <p>28</p> <p>10 / 83 (12.05%)</p> <p>11</p>                             |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 06 April 2016    | Protocol Version 1.1(Approval Date: 21.04.2016)<br>The aim of this amendment was to clarify specific protocol sections, for example the Rationale for Dose Selection and Hospitalisation, to correct typing errors and to facilitate the study management in the participating centers.  |
| 17 May 2016      | Protocol Version 1.2(Approval Date 30.09.2016): The purpose of this amendment was to correct typing errors and clarify specific sections of the protocol. Additional a clarification regarding study drug treatment in pregnant persons was added, indicating that treatment should be discontinued in such patients.  |
| 08 November 2016 | Protocol Version 1.3(Approval Date 28.12.2016): The purpose of this amendment was to correct typing errors and clarify specific sections of the protocol. Furthermore, additional precautions were specified regarding adverse events related to pancreatitis. Details regarding the new patient groups and inclusion criteria have been added. With regard to the approval of Blinatumomab in MRD positive ALL with MRD levels above 10 <sup>-3</sup> by the EMA, this patient group will no longer be included in the trial, as patients may receive Blinatumomab within marketing authorization. Of course, patients with MRD between 10 <sup>-4</sup> and 10 <sup>-3</sup> will still be included. The study aims to expand experience with Blinatumomab in patients with presence of MRD below 10 <sup>-4</sup> (non quantifiable or quantifiable) as well as with positive MRD non quantifiable, as data have shown an inferior outcome for these patients groups. |
| 23 August 2018   | Protocol Version 1.4(Approval Date 19.09.2018):The purpose of this amendment was to correct typing errors and clarify specific sections of the protocol. The section "2.4.2 Phase II Trial in MRD positive B-Precursor ALL" was clarified, and the adverse neurologic events, and the "Handling of toxicities" as well. Contact number and adress of Protocol Commission members was actualized.   |
| 23 July 2019     | Protocol Version 2.0(Approval Date 06.09.2019): The purpose of this amendment was to correct typing errors and clarify specific sections of the protocol. Treatment Interruption/Dose Modification due to Adverse Events Headline Neurologic events of CTCAE grade 2 were added. The duration of study was extended to 36 months recruitment period; evaluation of primary end point to 42 months, estimated End of Study after 60 months.   |
| 04 March 2020    | Protocol Version 2.1(Approval Date 27.03.2020)Duration of the study adopted to prolonged recruitment phase, recruitment period to 48 Months and 72 Months to final analysis. Clarifications at the sections: treatment assignment, treatment interruption/dose modification due to adverse events, bone marrow aspiration / biopsy, D43/D1 of Subsequent Cycle.  |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported