



## Clinical trial results:

**A single arm Phase I/II study of the safety and efficacy of gene-modified WT1 TCR therapy in patients with myelodysplastic syndrome (MDS) or acute myeloid leukaemia (AML) who have failed to achieve or maintain an IWG defined response following hypomethylating agent therapy**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2014-003111-10 |
| Trial protocol           | DE BE          |
| Global end of trial date | 15 May 2018    |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 18 January 2020 |
| First version publication date | 18 January 2020 |

### Trial information

#### Trial identification

|                       |                   |
|-----------------------|-------------------|
| Sponsor protocol code | D-00272-CT2014002 |
|-----------------------|-------------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |                                                                                     |
|------------------------------|-------------------------------------------------------------------------------------|
| Sponsor organisation name    | Cell Medica Ltd.                                                                    |
| Sponsor organisation address | Canal Side Studios, 8-14 St Pancras Way, London, United Kingdom, NW1 0QG            |
| Public contact               | Clinical Trials Information, Cell Medica Ltd., 44 2075544070, info@cellmedica.co.uk |
| Scientific contact           | Clinical Trials Information, Cell Medica Ltd., 44 2075544070, info@cellmedica.co.uk |

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:

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**Results analysis stage**

|                                                      |             |
|------------------------------------------------------|-------------|
| Analysis stage                                       | Final       |
| Date of interim/final analysis                       | 15 May 2018 |
| Is this the analysis of the primary completion data? | Yes         |
| Primary completion date                              | 15 May 2018 |
| Global end of trial reached?                         | Yes         |
| Global end of trial date                             | 15 May 2018 |
| Was the trial ended prematurely?                     | Yes         |

Notes:

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**General information about the trial**

Main objective of the trial:

To examine the safety and proportion of subjects achieving one or more IWG (2006) response criteria (within 12 months) following gene-modified WT1 TCR therapy

Protection of trial subjects:

This study was conducted in accordance with the protocol, the Declaration of Helsinki (and amendments), the International Conference on Harmonisation (ICH) Guidelines on Good Clinical Practice (GCP), and applicable local regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment                          | 15 September 2015 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

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**Population of trial subjects****Subjects enrolled per country**

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | Belgium: 1        |
| Worldwide total number of subjects   | 3                 |
| EEA total number of subjects         | 3                 |

Notes:

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**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)                      | 0 |
| From 65 to 84 years                       | 3 |
| 85 years and over                         | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study was initiated at 7 centres in the UK (London, Bristol, Leeds and Cardiff), Belgium (Leuven and Bruges) and Germany (Dresden). Only 4 centres screened or recruited subjects. Three subjects failed screening.

### Pre-assignment

Screening details:

The study aimed to enrol approximately 30 subjects with MDS or AML who had received hypomethylating agent therapy, and who were either relapsed or stable. Subjects who had received hypomethylating agent therapy as part of a combination regimen could be considered for eligibility at the discretion of the Sponsor.

### Period 1

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

### Arms

|                                        |                                                                                                 |
|----------------------------------------|-------------------------------------------------------------------------------------------------|
| Arm title                              | Gene-modified WT1 TCR therapy                                                                   |
| Arm description: -                     |                                                                                                 |
| Arm type                               | Experimental                                                                                    |
| Investigational medicinal product name | Gene-modified Wilms' Tumour Antigen 1 (WT1) T cell receptor (TCR)-transduced autologous T cells |
| Investigational medicinal product code |                                                                                                 |
| Other name                             |                                                                                                 |
| Pharmaceutical forms                   | Suspension for injection                                                                        |
| Routes of administration               | Intravenous use                                                                                 |

Dosage and administration details:

A single dose of bulk WT1 TCR-transduced T cells ( $\leq 2 \times 10^7/\text{kg}$ ) was intravenously administered following protocol-specified lymphodepletive conditioning regimen. Additionally, daily IL-2 subcutaneous injections ( $1 \times 10^6$  units/m<sup>2</sup>) were administered for 5 days concomitantly to each subject, following infusion of the ATIMP.

| Number of subjects in period 1 | Gene-modified WT1 TCR therapy |
|--------------------------------|-------------------------------|
| Started                        | 3                             |
| Completed                      | 0                             |
| Not completed                  | 3                             |
| Disease progression            | 1                             |
| Death                          | 2                             |

## Baseline characteristics

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### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Main study |
|-----------------------|------------|

Reporting group description: -

| Reporting group values | Main study | Total |  |
|------------------------|------------|-------|--|
| Number of subjects     | 3          | 3     |  |
| Age categorical        |            |       |  |
| Units: Subjects        |            |       |  |
| From 65-84 years       | 3          | 3     |  |
| Gender categorical     |            |       |  |
| Units: Subjects        |            |       |  |
| Female                 | 1          | 1     |  |
| Male                   | 2          | 2     |  |
| Race                   |            |       |  |
| Units: Subjects        |            |       |  |
| White                  | 3          | 3     |  |

## End points

### End points reporting groups

|                                |                               |
|--------------------------------|-------------------------------|
| Reporting group title          | Gene-modified WT1 TCR therapy |
| Reporting group description: - |                               |

### Primary: Proportion of subjects achieving IWG response

|                 |                                                              |
|-----------------|--------------------------------------------------------------|
| End point title | Proportion of subjects achieving IWG response <sup>[1]</sup> |
|-----------------|--------------------------------------------------------------|

End point description:

The planned primary endpoint assessment was the proportion of subjects achieving one or more of the following IWG response criteria within 12 months of administration of WT1 TCR-transduced T cells: complete remission; partial remission; marrow complete remission; cytogenetic response; haematological improvement.

Haematological disease evaluation was conducted approximately 28 days after T cell infusion in all subjects, approximately 3 months after T cell infusion in 2 subjects and approximately 4 months after T cell infusion in one subject. Bone marrow disease evaluation was conducted at screening in all subjects and approximately 3 months after screening in 2 subjects.

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

End point timeframe:

12 months

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: Due to the early termination and the very small number of subjects recruited, the Sponsor decided not to complete the statistical analysis as described in the protocol.

| End point values             | Gene-modified WT1 TCR therapy |  |  |  |
|------------------------------|-------------------------------|--|--|--|
| Subject group type           | Reporting group               |  |  |  |
| Number of subjects analysed  | 3                             |  |  |  |
| Units: Subjects              |                               |  |  |  |
| Achieved IWG response        | 0                             |  |  |  |
| Did not achieve IWG response | 3                             |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

An evaluation of the incidence of AEs was made at each study visit.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

### Reporting groups

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Gene-modified WT1 TCR therapy |
|-----------------------|-------------------------------|

Reporting group description: -

| Serious adverse events                               | Gene-modified WT1 TCR therapy                                                                        |  |  |
|------------------------------------------------------|------------------------------------------------------------------------------------------------------|--|--|
| Total subjects affected by serious adverse events    |                                                                                                      |  |  |
| subjects affected / exposed                          | 3 / 3 (100.00%)                                                                                      |  |  |
| number of deaths (all causes)                        | 3                                                                                                    |  |  |
| number of deaths resulting from adverse events       | 0                                                                                                    |  |  |
| Investigations                                       |                                                                                                      |  |  |
| Platelet count decreased                             |                                                                                                      |  |  |
| subjects affected / exposed                          | 1 / 3 (33.33%)                                                                                       |  |  |
| occurrences causally related to treatment / all      | 0 / 1                                                                                                |  |  |
| deaths causally related to treatment / all           | 0 / 0                                                                                                |  |  |
| Blood and lymphatic system disorders                 |                                                                                                      |  |  |
| Febrile neutropenia                                  | Additional description: One occurrence of the event assessed as 'possibly' relatedness to study drug |  |  |
| subjects affected / exposed                          | 2 / 3 (66.67%)                                                                                       |  |  |
| occurrences causally related to treatment / all      | 1 / 2                                                                                                |  |  |
| deaths causally related to treatment / all           | 0 / 0                                                                                                |  |  |
| General disorders and administration site conditions |                                                                                                      |  |  |
| Chest pain                                           | Additional description: One occurrence of the event assessed as 'remote' relatedness to study drug   |  |  |
| subjects affected / exposed                          | 1 / 3 (33.33%)                                                                                       |  |  |
| occurrences causally related to treatment / all      | 1 / 2                                                                                                |  |  |
| deaths causally related to treatment / all           | 0 / 0                                                                                                |  |  |
| Immune system disorders                              |                                                                                                      |  |  |
| Cytokine release syndrome                            | Additional description: Event assessed as 'possibly' relatedness to study drug                       |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Dyspnoea                                        |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Bronchitis                                      |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pneumonia parainfluenzae viral                  |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Hyperglycaemia                                  |                |  |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

|                                                                     |                               |  |  |
|---------------------------------------------------------------------|-------------------------------|--|--|
| <b>Non-serious adverse events</b>                                   | Gene-modified WT1 TCR therapy |  |  |
| Total subjects affected by non-serious adverse events               |                               |  |  |
| subjects affected / exposed                                         | 3 / 3 (100.00%)               |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                               |  |  |
| Paraneoplastic syndrome                                             |                               |  |  |
| subjects affected / exposed                                         | 1 / 3 (33.33%)                |  |  |
| occurrences (all)                                                   | 1                             |  |  |
| Surgical and medical procedures                                     |                               |  |  |

|                                                                                           |                     |  |  |
|-------------------------------------------------------------------------------------------|---------------------|--|--|
| Haematoma<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 3 (33.33%)<br>1 |  |  |
| General disorders and administration site conditions                                      |                     |  |  |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)                     | 2 / 3 (66.67%)<br>2 |  |  |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)                            | 2 / 3 (66.67%)<br>2 |  |  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                               | 2 / 3 (66.67%)<br>4 |  |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 3 (33.33%)<br>1 |  |  |
| Malaise<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 3 (33.33%)<br>3 |  |  |
| Respiratory, thoracic and mediastinal disorders                                           |                     |  |  |
| Chronic obstructive pulmonary disease<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1 |  |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                              | 2 / 3 (66.67%)<br>5 |  |  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 3 (33.33%)<br>3 |  |  |
| Haemoptysis<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 3 (33.33%)<br>1 |  |  |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 3 (33.33%)<br>1 |  |  |

|                                                                                                     |                      |  |  |
|-----------------------------------------------------------------------------------------------------|----------------------|--|--|
| Pulmonary oedema<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 3 (33.33%)<br>1  |  |  |
| Respiratory distress<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 3 (33.33%)<br>1  |  |  |
| Investigations<br>C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3 (33.33%)<br>1  |  |  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 3 (33.33%)<br>1  |  |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)            | 3 / 3 (100.00%)<br>6 |  |  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 3 (33.33%)<br>2  |  |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>3  |  |  |
| Febrile neutropenia<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 3 (33.33%)<br>1  |  |  |
| Eye disorders<br>Retinal detachment<br>subjects affected / exposed<br>occurrences (all)             | 1 / 3 (33.33%)<br>1  |  |  |
| Retinal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 3 (33.33%)<br>1  |  |  |
| Gastrointestinal disorders<br>Constipation                                                          |                      |  |  |

|                                                                                                                                                                                                                                                                                                |                                                                                                                             |  |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Diarrhoea</p> <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>1 / 3 (33.33%)</p> <p>1</p> <p>2 / 3 (66.67%)</p> <p>3</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p> |  |  |
| <p>Skin and subcutaneous tissue disorders</p> <p>Hyperhidrosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Decubitus ulcer</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>      | <p>2 / 3 (66.67%)</p> <p>2</p> <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p>                                |  |  |
| <p>Renal and urinary disorders</p> <p>Acute kidney injury</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                      | <p>1 / 3 (33.33%)</p> <p>1</p>                                                                                              |  |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain in extremity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                      | <p>1 / 3 (33.33%)</p> <p>1</p> <p>1 / 3 (33.33%)</p> <p>1</p>                                                               |  |  |
| <p>Infections and infestations</p> <p>Rhinitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                 | <p>1 / 3 (33.33%)</p> <p>1</p>                                                                                              |  |  |

|                                                                                       |                     |  |  |
|---------------------------------------------------------------------------------------|---------------------|--|--|
| Oral candidiasis<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 3 (33.33%)<br>2 |  |  |
| Pneumonia parainfluenzae viral<br>subjects affected / exposed<br>occurrences (all)    | 1 / 3 (33.33%)<br>1 |  |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1 |  |  |
| Metabolism and nutrition disorders                                                    |                     |  |  |
| Fluid overload<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 3 (33.33%)<br>1 |  |  |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 3 (33.33%)<br>1 |  |  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)                      | 2 / 3 (66.67%)<br>4 |  |  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 1 / 3 (33.33%)<br>2 |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 17 October 2014   | The Protocol Amendment (Version 2.0) was developed to provide clarity and addition of the following protocol aspects:<br>1) Further rationale for provision of 2nd infusion of WT1 TCR-transduced T cells<br>2) Clarification of schedule of activities for:<br>a. Repeat infusion, including potential for repeat leukapheresis procedure.<br>b. Provision of separate consent for HLA and brief medical history screening<br>c. Full trial consent to be performed at Visit 2<br>3) Inclusion of 24-hour in-patient hospitalisation for initial 3 subjects for infusion, including criteria for discharge<br>4) Clarification that protocol amendment will be submitted to Regulatory Authorities and Ethics Committees when DSMB recommends modifications to the clinical protocol<br>5) Clarification that an internal safety review will be held with recommendations submitted to Regulatory Authorities and Ethics Committees prior to re-start of a trial where DSMB has recommended trial suspension. |
| 19 December 2014  | The Protocol Amendment (Version 3.0) was developed to revise the starting conditioning regimen from a fludarabine-cyclophosphamide-based regimen to the lower intensity regimen of fludarabine-methylprednisolone, previously stated in the protocol. The rationale for this change is for reduction in risk and improved feasibility of clinical management of the protocol-specified population with regards to potential regimen-induced toxicities, particularly significant myelosuppression and prolonged aplasia.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 24 June 2016      | The Protocol Amendment (Version 4.0) was developed to expand the patient population, add WT1 transcript analysis as an exploratory endpoint, clarify the conditioning regimen and further clarifications throughout the document.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 01 September 2017 | The Protocol Amendment (Version 5.0) changed the Sponsor from Catapult to Cell Medica Ltd.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to difficulties in recruitment of patients, enrolment into the study was terminated early.

Notes: