



## Clinical trial results:

### A Two-Stage Phase II Study of Autologous TriMix-DC Therapeutic Vaccine in Combination with Ipilimumab in Patients with Previously Treated Unresectable Stage III or IV Melanoma.

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2010-023058-35 |
| Trial protocol           | BE             |
| Global end of trial date | 01 June 2015   |

#### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v2 (current)  |
| This version publication date     | 02 October 2021   |
| First version publication date    | 09 April 2021   |
| Version creation reason           | • Correction of full data set<br>End date of trial 31DEC2016              |
| Summary attachment (see zip file) | Wilgenhof et al JCO article (Wilgenhof et al. _JCO.2015.63.4121.full.pdf) |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | UZB-VUB-10-001 |
|-----------------------|----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01302496 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | UZ Brussel  |
| Sponsor organisation address | Laarbeeklaan 101, Jette, Belgium, 1090                            |
| Public contact               | Bart Neyns, UZ Brussel, 0032 24775447,<br>bart.neyns@uzbrussel.be |
| Scientific contact           | Bart Neyns, UZ Brussel, 0032 24775447,<br>bart.neyns@uzbrussel.be |

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                       | 01 June 2015     |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 04 November 2013 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 01 June 2015     |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

Main objective of the trial:

To estimate the anti-tumor activity of therapeutic vaccination with autologous TriMix-DC vaccine in combination with ipilimumab in patients with previously treated, therapy-refractory or -intolerant, unresectable, AJCC Stage III or Stage IV melanoma.

Protection of trial subjects:

Signed Informed consent, in this consent is explained that the patient data is anonymized. Safety data will be collected on a continuous basis and will be reviewed by the Sponsor in order to ensure that it is appropriate to continue the study

Background therapy:

NA

Evidence for comparator:

NA

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 02 May 2011      |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety, Efficacy |
| Long term follow-up duration                              | 18 Months        |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Belgium: 39 |
| Worldwide total number of subjects   | 39          |
| EEA total number of subjects         | 39          |

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) | 32 |
| From 65 to 84 years  | 7  |
| 85 years and over    | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Patients with histologically confirmed, unresectable, American Joint Committee on Cancer (AJCC) stage III or IV melanoma with measurable disease, who experienced treatment failure with at least one prior line of systemic treatment, were eligible.

### Pre-assignment

Screening details:

Willing and able to give written informed consent

Histologically confirmed malignant melanoma

Measurable melanoma

AJCC Stage III (unresectable) or Stage IV melanoma

Response to treatment with at least one prior regimen (non-experimental or experimental) with the exception of a CD137 agonist

### Pre-assignment period milestones

|                            |    |
|----------------------------|----|
| Number of subjects started | 39 |
|----------------------------|----|

|                              |    |
|------------------------------|----|
| Number of subjects completed | 39 |
|------------------------------|----|

### Period 1

|                |                            |
|----------------|----------------------------|
| Period 1 title | Treatment (overall period) |
|----------------|----------------------------|

|                              |     |
|------------------------------|-----|
| Is this the baseline period? | Yes |
|------------------------------|-----|

|                   |                |
|-------------------|----------------|
| Allocation method | Not applicable |
|-------------------|----------------|

|               |             |
|---------------|-------------|
| Blinding used | Not blinded |
|---------------|-------------|

### Arms

|           |                              |
|-----------|------------------------------|
| Arm title | TriMixDC-MEL plus Ipilimumab |
|-----------|------------------------------|

Arm description:

Single arm study

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |            |
|--|------------|
| Investigational medicinal product name | Ipilimumab |
|--|------------|

|  |  |
|--|--|
| Investigational medicinal product code |  |
|--|--|

|            |  |
|------------|--|
| Other name |  |
|------------|--|

|                      |   |
|----------------------|---|
| Pharmaceutical forms | Concentrate for concentrate for solution for infusion |
|----------------------|---|

|                          |                 |
|--------------------------|-----------------|
| Routes of administration | Intravenous use |
|--------------------------|-----------------|

Dosage and administration details:

Ipilimumab 10mg/kg every 3 weeks x4 followed by 1 administration Q12 weeks

|  |              |
|--|--------------|
| Investigational medicinal product name | TriMixDC-MEL |
|--|--------------|

|  |  |
|--|--|
| Investigational medicinal product code |  |
|--|--|

|            |  |
|------------|--|
| Other name |  |
|------------|--|

|                      |  |
|----------------------|--|
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
|----------------------|--|

|                          |                 |
|--------------------------|-----------------|
| Routes of administration | Intravenous use |
|--------------------------|-----------------|

Dosage and administration details:

TriMixDC-MEL suspension administered every 3 weeks

| <b>Number of subjects in period 1</b> | TriMixDC-MEL plus<br>Ipilimumab |
|---------------------------------------|---------------------------------|
| Started                               | 39                              |
| Completed                             | 39                              |

## Baseline characteristics

### Reporting groups

|                       |           |
|-----------------------|-----------|
| Reporting group title | Treatment |
|-----------------------|-----------|

Reporting group description:

Single arm study, treatment arm

| Reporting group values                                | Treatment | Total |  |
|---|-----------|-------|--|
| Number of subjects                                    | 39        | 39    |  |
| Age categorical                                       |           |       |  |
| Adults (18-64years)                                   |           |       |  |
| From 65-84years                                       |           |       |  |
| 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<br>months)           | 0         | 0     |  |
| Children (2-11 years)                                 | 0         | 0     |  |
| Adolescents (12-17 years)                             | 0         | 0     |  |
| Adults (18-64 years)                                  | 32        | 32    |  |
| From 65-84 years                                      | 7         | 7     |  |
| 85 years and over                                     | 0         | 0     |  |
| Age continuous  |           |       |  |
| Median Age 46years, (range 24-70years)                |           |       |  |
| Units: years  |           |       |  |
| median  | 46        |       |  |
| full range (min-max)                                  | 24 to 70  | -     |  |
| Gender categorical                                    |           |       |  |
| Units: Subjects                                       |           |       |  |
| Female  | 16        | 16    |  |
| Male  | 23        | 23    |  |

## End points

### End points reporting groups

|   |                              |
|---|------------------------------|
| Reporting group title                             | TriMixDC-MEL plus Ipilimumab |
| Reporting group description:                      |                              |
| Single arm study                                  |                              |
| Subject analysis set title                        | Single arm study             |
| Subject analysis set type                         | Per protocol                 |
| Subject analysis set description:                 |                              |
| Single arm study                                  |                              |
| Subject analysis set title                        | Single arm study             |
| Subject analysis set type                         | Per protocol                 |
| Subject analysis set description:                 |                              |
| Single arm study, fantom arm to resolve the query |                              |

### Primary: The 6-month disease control

|   |                             |
|---|-----------------------------|
| End point title   | The 6-month disease control |
| End point description:  |                             |
| The 6-month disease control rate was 51% (95% CI, 36% to 67%), and the overall tumor response rate was 38% (including eight complete and seven partial responses). Seven complete responses and one partial tumor response are ongoing after a median follow-up time of 36 months (range, 22 to 43 months). The most common treatment-related adverse events (all grades) consisted of local DC injection site skin reactions (100%), transient post-DC infusion chills (38%) and flu-like symptoms (84%), dermatitis (64%), hepatitis (13%), hypophysitis (15%), and diarrhea/colitis (15%). Grade 3 or 4 immune-related adverse events occurred in 36% of patients. There was no grade 5 adverse event. |                             |
| End point type  | Primary                     |
| End point timeframe:  |                             |
| The 6-month disease control rate was 51% (95% CI, 36% to 67%), and the overall tumor response rate was 38% (including eight complete and seven partial responses)   |                             |

| End point values            | TriMixDC-MEL plus Ipilimumab | Single arm study     | Single arm study     |  |
|-----------------------------|------------------------------|----------------------|----------------------|--|
| Subject group type          | Reporting group              | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed | 39 <sup>[1]</sup>            | 39                   | 39 <sup>[2]</sup>    |  |
| Units: whole                | 39                           | 39                   | 39                   |  |

Notes:

[1] - Singel arm study

[2] - fantom arm

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title  | ORR% estimate  |
| Statistical analysis description:   |  |
| A Simon two-stage design (minimax) was used to test the null hypothesis that the DCR at 6 months was <33% versus the alternative hypothesis that the DCR at 6 months was > 50%. Using an a error of .05 and a b error of .20, a DCR by irRC at 6 months of greater than seven of 19 patients was needed to continue the study and recruit a final total of 39 patients. |  |
| Comparison groups   | TriMixDC-MEL plus Ipilimumab v Single arm study v Single arm study |

|   |                      |
|---|----------------------|
| Number of subjects included in analysis | 117                  |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other <sup>[3]</sup> |
| Parameter estimate                      | ORR%                 |
| Point estimate                          | 51                   |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 36                   |
| upper limit                             | 67                   |
| Variability estimate                    | Standard deviation   |

Notes:

[3] - single arm phase II study



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Throughout the duration of the study

Clinical and blood parameters were assessed every 3 weeks. Adverse events (AEs) were graded for severity according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.0).

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

### Dictionary used

|                    |       |
|--------------------|-------|
| Dictionary name    | CTCAE |
| Dictionary version | 4     |

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Study population |
|-----------------------|------------------|

Reporting group description:

All the 39 patients that entered the study

| Serious adverse events                            | Study population |  |  |
|---|------------------|--|--|
| Total subjects affected by serious adverse events |                  |  |  |
| subjects affected / exposed                       | 0 / 39 (0.00%)   |  |  |
| number of deaths (all causes)                     | 26               |  |  |
| number of deaths resulting from adverse events    | 0                |  |  |

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

| Non-serious adverse events                            | Study population  |  |  |
|---|---|--|--|
| Total subjects affected by non-serious adverse events |   |  |  |
| subjects affected / exposed                           | 39 / 39 (100.00%)   |  |  |
| Nervous system disorders                              |   |  |  |
| Hypophysitis  | Additional description: Immune related AE; Grade II                                       |  |  |
| subjects affected / exposed                           | 6 / 39 (15.38%)   |  |  |
| occurrences (all)                                     | 6   |  |  |
| General disorders and administration site conditions  |   |  |  |
| Skin injection site reaction                          | Additional description: Dendritic cells related AE; Grade II skin injection site reaction |  |  |
| subjects affected / exposed                           | 39 / 39 (100.00%)   |  |  |
| occurrences (all)                                     | 39  |  |  |
| Flu-like symptoms                                     | Additional description: Dendritic cells related AE; Grade II (<72h post administration)   |  |  |

|   |   |  |  |
|---|---|--|--|
| subjects affected / exposed                     | 33 / 39 (84.62%)  |  |  |
| occurrences (all)                               | 33  |  |  |
| Gastrointestinal disorders                      |   |  |  |
| Colitis   | Additional description: Immune related AE; Colitis/diarrhea grade II/II |  |  |
| subjects affected / exposed                     | 8 / 39 (20.51%)   |  |  |
| occurrences (all)                               | 8   |  |  |
| Hepatobiliary disorders                         |   |  |  |
| Hepatitis                                       | Additional description: Immune related AE; Grade III/IV                 |  |  |
| subjects affected / exposed                     | 5 / 39 (12.82%)   |  |  |
| occurrences (all)                               | 5   |  |  |
| Respiratory, thoracic and mediastinal disorders |   |  |  |
| Pneumonitis                                     | Additional description: Immune related AE; Grade III                    |  |  |
| subjects affected / exposed                     | 3 / 39 (7.69%)  |  |  |
| occurrences (all)                               | 3   |  |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported