



## Clinical trial results:

### Phase I/II study of peptide vaccination associated with tumoral immunomodulation with proinflammatory cytokines and imiquimod in patients with advanced metastatic melanoma

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2010-020435-40 |
| Trial protocol           | BE             |
| Global end of trial date | 20 July 2015   |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 17 March 2021 |
| First version publication date | 17 March 2021 |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | LUC 10-002 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01191034 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Cliniques universitaires Saint-Luc   |
| Sponsor organisation address | Avenue Hippocrate 10, Brussels, Belgium, 1200  |
| Public contact               | Cliniques universitaires Saint-Luc, Cliniques universitaires Saint-Luc, 0032 2 7645471, jean-francois.baurain@uclouvain.be |
| Scientific contact           | Jean-François Baurain, Jean-François Baurain, 0032 2 7645471, jean-francois.baurain@uclouvain.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:

## Results analysis stage

|  |                |
|--|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 01 August 2012 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 01 August 2012 |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 20 July 2015   |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

To determine whether peptide vaccination associated with local peritumoral treatment with a combination of interleukin-2, interferon-alpha, granulocyte-macrophage colony stimulating factor, and imiquimod, induces tumor responses.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines, and country-specific national and local laws.

Background therapy:

- Vaccinations : vaccine MAGE-3.A1 peptide or NA17.A2 peptide
- Local treatment with immunomodulatory drugs : IL-2, IFN- $\alpha$ , GM-CSF and Imiquimod

Evidence for comparator:

No applicable

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 01 October 2010 |
| 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 | Belgium: 3 |
| Worldwide total number of subjects   | 3          |
| EEA total number of subjects         | 3          |

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)                      | 1 |
| From 65 to 84 years                       | 1 |

|                   |   |
|-------------------|---|
| 85 years and over | 1 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

Dermatology consultation from AUG 2010 till MAR 2013

### Pre-assignment

Screening details:

NA

### Period 1

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

### Arms

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | Experimental arm |
|------------------|------------------|

Arm description:

The vaccine is either the MAGE-3.A1 peptide, or the NA17.A2 peptide, or both, matching the patient's HLA type and the gene expression of his tumor. If both antigens are expressed, then the patient received both peptides.

This treatment is combine subcutaneous peritumoral injections of IL-2, IFN- $\alpha$  and GMCSF, as well as topical applications of imiquimod.

|  |                                   |
|--|-----------------------------------|
| Arm type                               | Experimental                      |
| Investigational medicinal product name | MAGE-3.A1 peptide                 |
| Investigational medicinal product code |                                   |
| Other name                             |                                   |
| Pharmaceutical forms                   | Solution for injection            |
| Routes of administration               | Subcutaneous use, Intradermal use |

Dosage and administration details:

300  $\mu$ g

|  |                                   |
|--|-----------------------------------|
| Investigational medicinal product name | NA17.A2 peptide                   |
| Investigational medicinal product code |                                   |
| Other name                             |                                   |
| Pharmaceutical forms                   | Solution for injection            |
| Routes of administration               | Intradermal use, Subcutaneous use |

Dosage and administration details:

300  $\mu$ g

|  |                        |
|--|------------------------|
| Investigational medicinal product name | IL-2                   |
| Investigational medicinal product code |                        |
| Other name                             | Proleukin®             |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

IL-2 : 6000 IU peritumoral injection

|  |                        |
|--|------------------------|
| Investigational medicinal product name | IFN- $\alpha$          |
| Investigational medicinal product code |                        |
| Other name                             | IntronA®               |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

|  |                        |
|--|------------------------|
| Dosage and administration details:   |                        |
| IFN-α : 100.000 IU peritumoral injection   |                        |
| Investigational medicinal product name   | GM-CSF                 |
| Investigational medicinal product code   |                        |
| Other name   | Leukine®               |
| Pharmaceutical forms   | Solution for injection |
| Routes of administration   | Subcutaneous use       |
| Dosage and administration details:   |                        |
| GM-CSF : 300 ng peritumoral injection  |                        |
| Investigational medicinal product name   | Imiquimod cream        |
| Investigational medicinal product code   |                        |
| Other name   | Aldara                 |
| Pharmaceutical forms   | Cream                  |
| Routes of administration   | Topical use            |
| Dosage and administration details:   |                        |
| - Imiquimod cream : topical application, applied during 24h, applied on days +2 and +7 following vaccines 3 and 4. |                        |

| <b>Number of subjects in period 1</b> | Experimental arm |
|---------------------------------------|------------------|
| Started                               | 3                |
| Completed                             | 3                |

## Baseline characteristics

### Reporting groups

| Reporting group title | Overall trial |
|-----------------------|---------------|
|-----------------------|---------------|

Reporting group description:

The vaccine is either the MAGE-3.A1 peptide, or the NA17.A2 peptide, or both, matching the patient's HLA type and the gene expression of his tumor. If both antigens are expressed, then the patient received both peptides.

This treatment is combine subcutaneous peritumoral injections of IL-2, IFN-α and GMCSF, as well as topical applications of imiquimod.

| Reporting group values                                | Overall trial | Total |  |
|---|---------------|-------|--|
| Number of subjects                                    | 3             | 3     |  |
| Age categorical                                       |               |       |  |
| 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)                                  | 1             | 1     |  |
| From 65-84 years                                      | 1             | 1     |  |
| 85 years and over                                     | 1             | 1     |  |
| Age continuous  |               |       |  |
| Units: years  |               |       |  |
| arithmetic mean                                       | 71            |       |  |
| standard deviation                                    | ± 13.4        | -     |  |
| Gender categorical                                    |               |       |  |
| Units: Subjects                                       |               |       |  |
| Female  | 1             | 1     |  |
| Male  | 2             | 2     |  |

## End points

### End points reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Experimental arm |
|-----------------------|------------------|

Reporting group description:

The vaccine is either the MAGE-3.A1 peptide, or the NA17.A2 peptide, or both, matching the patient's HLA type and the gene expression of his tumor. If both antigens are expressed, then the patient received both peptides.

This treatment is combine subcutaneous peritumoral injections of IL-2, IFN- $\alpha$  and GMCSF, as well as topical applications of imiquimod.

### Primary: Tumor response

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

End point description:

To determine whether peptide vaccination associated with local peritumoral treatment with a combination of interleukin-2, interferon-alpha, granulocyte-macrophage colony stimulating factor, and imiquimod, induces tumor responses. Tumor response assessed in accordance with the Modified RECIST version 1.1

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

End point timeframe:

Week 11 day 71

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 since 3 patients included

| End point values            | Experimental arm |  |  |  |
|-----------------------------|------------------|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 3                |  |  |  |
| Units: percent              |                  |  |  |  |
| number (not applicable)     | 66               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Immunogenicity of the treatment

|                 |  |
|-----------------|--|
| End point title | Immunogenicity of the treatment <sup>[2]</sup> |
|-----------------|--|

End point description:

To document whether this association induces cytolytic T lymphocyte responses to the vaccine antigens. CTL responses assessed by comparing either the anti-MAGE-3.A1 or the anti- NA17.A2 CTLp frequency in the pre- and post-immune blood of patients vaccinated with the respective antigen.

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

End point timeframe:

At week 11, day 71

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Notes:

[2] - 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 since 3 patients included

|   |                  |  |  |  |
|---|------------------|--|--|--|
| <b>End point values</b>                 | Experimental arm |  |  |  |
| Subject group type                      | Reporting group  |  |  |  |
| Number of subjects analysed             | 3                |  |  |  |
| Units: Immune response against Antigens | 3                |  |  |  |

### Statistical analyses

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No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All Serious Adverse Events occurring at any time after the patient has signed the informed consent, the screening visit, and within 30 days of the last day on which the investigational agent was administered must be reported within 24 hours of awareness o

Adverse event reporting additional description:

Adverse Events attributes assigned by the investigator: AE diagnosis or syndrome(s); event description; dates of onset and resolution; severity; assessment of relatedness to study treatment; and action taken.

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

### Dictionary used

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

|                    |     |
|--------------------|-----|
| Dictionary version | 3.0 |
|--------------------|-----|

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Experimental arm |
|-----------------------|------------------|

Reporting group description:

The vaccine is either the MAGE-3.A1 peptide, or the NA17.A2 peptide, or both, matching the patient's HLA type and the gene expression of his tumor. If both antigens are expressed, then the patient received both peptides. This treatment is combine subcutaneous peritumoral injections of IL-2, IFN-α and GMCSF, as well as topical applications of imiquimod.

| Serious adverse events                            | Experimental arm |  |  |
|---|------------------|--|--|
| Total subjects affected by serious adverse events |                  |  |  |
| subjects affected / exposed                       | 0 / 3 (0.00%)    |  |  |
| number of deaths (all causes)                     | 0                |  |  |
| number of deaths resulting from adverse events    | 0                |  |  |

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

| Non-serious adverse events                            | Experimental arm |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 2 / 3 (66.67%)   |  |  |
| Injury, poisoning and procedural complications        |                  |  |  |
| Pain due to a fall                                    |                  |  |  |
| subjects affected / exposed                           | 1 / 3 (33.33%)   |  |  |
| occurrences (all)                                     | 1                |  |  |
| General disorders and administration site conditions  |                  |  |  |
| Oedema right leg                                      |                  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                       | 1 / 3 (33.33%) |  |  |
| occurrences (all)                                 | 1              |  |  |
| Pain right leg                                    |                |  |  |
| subjects affected / exposed                       | 1 / 3 (33.33%) |  |  |
| occurrences (all)                                 | 1              |  |  |
| Bleeding of lesions after intratumoral infections |                |  |  |
| subjects affected / exposed                       | 1 / 3 (33.33%) |  |  |
| occurrences (all)                                 | 1              |  |  |
| Pain in injected lesions                          |                |  |  |
| subjects affected / exposed                       | 1 / 3 (33.33%) |  |  |
| occurrences (all)                                 | 2              |  |  |
| Gastrointestinal disorders                        |                |  |  |
| Gastric pain                                      |                |  |  |
| subjects affected / exposed                       | 1 / 3 (33.33%) |  |  |
| occurrences (all)                                 | 1              |  |  |
| Skin and subcutaneous tissue disorders            |                |  |  |
| Erythema right leg                                |                |  |  |
| subjects affected / exposed                       | 1 / 3 (33.33%) |  |  |
| occurrences (all)                                 | 1              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                |
|------------------|--------------------------|
| 21 December 2010 | Amendment 1, version 1.1 |
| 15 March 2012    | Amendment 2, version 2.0 |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported