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) régulations/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-α, 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

Arm title	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-α 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 µg

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 µg

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-α
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.

Number of subjects in period 1	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 (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)	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-α and GMCSF,as well as topical applications of imiquimod.

Primary: Tumor response

End point title	Tumor response[1]

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[2]

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

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

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Immune response against Antigens	3			

Statistical analyses

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:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported