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 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, bart.neyns@uzbrussel.be
Scientific contact	Bart Neyns, UZ Brussel, 0032 24775447, 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:

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:

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:

Population of trial subjects

Subjects enrolled per country

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

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)	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

Number of subjects in period 1	TriMixDC-MEL plus 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 (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)	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[1]	39	39[2]	
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[3]
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: Imune 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

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported