Clinical trial results:
A phase I- IIa open-label clinical trial, evaluating the therapeutic vaccine hVEGF26-104/RFASE in patients with advanced solid tumors

Summary

EudraCT number	2013-002663-25
Trial protocol	NL
Global end of trial date	01 January 2020

Results information

Result version number	v1 (current)
This version publication date	02 January 2021
First version publication date	02 January 2021
Summary attachment (see zip file)	Eindrapportage - wetenschappelijke publicatie 24-09-2020 (Wetenschappelijke publicatie - eindrapportage - onco.13576.pdf)

Trial information

Trial identification

Sponsor protocol code	VEGFVAX

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	VU University Medical Center
Sponsor organisation address	De Boelelaan 1117, Amsterdam, Netherlands, 1081 HV
Public contact	Secretary Medical Oncology, VU University Medical Center, 0031 0204444321, r.goedegebuure@amsterdamumc.nl
Scientific contact	Secretary Medical Oncology, VU University Medical Center, 0031 0204444321, r.goedegebuure@amsterdamumc.nl

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	24 September 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 January 2020
Global end of trial reached?	Yes
Global end of trial date	01 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part 1:
The primary objectives of the study are:
- To investigate the safety and tolerability profile of the therapeutic vaccine hVEGF26-104/RFASE.
- To determine the effective dose of hVEGF26-104/RFASE required to neutralize VEGF in serum, defined as a VEGF level below 9,0 pg/mL.

Part 2:
- To investigate the safety and VEGF neutralizing ability of hVEGF26-104/RFASE combined with irinotecan chemotherapy in a metastatic colorectal cancer expansion cohort.
- To investigate the safety and VEGF neutralizing ability of hVEGF26-104/RFASE combined with the XELOX regimen (capecitabine plus oxaliplatin) in a metastatic colorectal cancer expansion cohort.

Protection of trial subjects:

Extensively described in studie protocol and approved by Dutch ethics committee (CCMO): 3+3 dose-escalating design, admission during clinical admission with extensive safety monitoring, saftey lab, bi weekly follow-up.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2013
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	Netherlands: 27
Worldwide total number of subjects	27
EEA total number of subjects	27

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)	10
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with advanced solid malignancies with no standard treatment options available were eligible when fulfilling predefined in- and exclusion criteria

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose-level 1

Arm description:

VEGF26–104/RFASE 62.5 µg/20 mg

Arm type	Experimental
Investigational medicinal product name	hVEGF/RFASE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IM injection on day 0, 14 and 28

Arm title	Dose-level 2

Arm description:

hVEGF26–104/RFASE 125 µg/20 mg

Arm type	Experimental
Investigational medicinal product name	hVEGF/RFASE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IM injection on day 0, 14 and 28

Arm title	Dose-level 3A

Arm description:

hVEGF26–104/RFASE 250 µg/20 mg

Arm type	Experimental
Investigational medicinal product name	hVEGF/RFASE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

IM injection on day 0, 14 and 28

Arm title	Dose-level 3B
Arm description: hVEGF26–104/RFASE 250 µg/40 mg	
Arm type	Experimental
Investigational medicinal product name	hVEGF/RFASE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: IM injection on day 0, 14 and 28	
Arm title	Dose-level 4
Arm description: hVEGF26–104/RFASE 500 µg/40 mg	
Arm type	Experimental
Investigational medicinal product name	hVEGF/RFASE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: IM injection on day 0, 14 and 28	
Arm title	Dose-level 5
Arm description: hVEGF26–104/RFASE 1.000 µg/40 mg	
Arm type	Experimental
Investigational medicinal product name	hVEGF/RFASE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: IM injection on day 0, 14 and 28	

Number of subjects in period 1	Dose-level 1	Dose-level 2	Dose-level 3A
Started	4	3	4
Completed	4	3	4
Not completed	0	0	0
did not commence treatment	-	-	-

Number of subjects in period 1	Dose-level 3B	Dose-level 4	Dose-level 5
Started	4	8	4
Completed	4	7	4
Not completed	0	1	0
did not commence treatment	-	1	-

Baseline characteristics

End points

End points reporting groups

Reporting group title	Dose-level 1
Reporting group description: VEGF26–104/RFASE 62.5 µg/20 mg	
Reporting group title	Dose-level 2
Reporting group description: hVEGF26–104/RFASE 125 µg/20 mg	
Reporting group title	Dose-level 3A
Reporting group description: hVEGF26–104/RFASE 250 µg/20 mg	
Reporting group title	Dose-level 3B
Reporting group description: hVEGF26–104/RFASE 250 µg/40 mg	
Reporting group title	Dose-level 4
Reporting group description: hVEGF26–104/RFASE 500 µg/40 mg	
Reporting group title	Dose-level 5
Reporting group description: hVEGF26–104/RFASE 1.000 µg/40 mg	

Primary: Safety and tolerability

End point title	Safety and tolerability[1]
End point description:	
End point type	Primary
End point timeframe: overall clinical trial	

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: Descriptive data

End point values	Dose-level 1	Dose-level 2	Dose-level 3A	Dose-level 3B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	3	4
Units: Grade 3 or higher related adverse events	0	0	0	0

End point values	Dose-level 4	Dose-level 5		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7[2]	4		
Units: Grade 3 or higher related adverse events	0	0		

Notes:
[2] - 1 did not commence treatment

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Whole clinical trial

Adverse event reporting additional description:

Please see PMID: 33105058 DOI: 10.1002/onco.13576

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Whole clinical trial

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Please see PMID: 33105058 DOI: 10.1002/onco.13576

Serious adverse events	Whole clinical trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 26 (65.38%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pain			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
tromboembolic event			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Confusional state			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Somnolence			

subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
anemia			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Pain in extremity			

subjects affected / exposed	2 / 26 (7.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Fever			
subjects affected / exposed	3 / 26 (11.54%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 26 (3.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Whole clinical trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)		

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33105058