Clinical trial results:
Safety and tolerability of neoadjuvant nivolumab for locally advanced resectable oral cancer, combined with [18F]BMS-986192 / [18F]-FDG PET imaging and immunomonitoring for response prediction.

Summary

EudraCT number	2018-002643-28
Trial protocol	NL
Global end of trial date	06 January 2022

Results information

Result version number	v1 (current)
This version publication date	20 February 2024
First version publication date	20 February 2024

Trial information

Trial identification

Sponsor protocol code	CA209-8JD

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	BMS
Sponsor organisation address	Orteliuslaan 1000, Utrecht, Netherlands, 3258 BD
Public contact	Dr. C.W. Menke-van Houven van Oordt, Amsterdam UMC, locatie VUmc, 31 0204444321, c.menke@vumc.nl
Scientific contact	Dr. C.W. Menke-van Houven van Oordt, Amsterdam UMC, locatie VUmc, 31 0204444321, c.menke@vumc.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	04 February 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2021
Global end of trial reached?	Yes
Global end of trial date	06 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To investigate heterogeneity in tumor uptake of [18F]BMS-986192 between patients and within tumor lesions of the same patient (primary tumor and TDLN/lymph node metastases) before treatment, in relation to changes in [18F]-FDG uptake before and on treatment

2. To investigate the feasibility and safety of neoadjuvant nivolumab immunotherapy prior to surgery for locally advanced oral cancer.

Protection of trial subjects:

Yes

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2018
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: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	3
From 65 to 84 years	12

85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Between March 1, 2019 and July 31, 2021 seventeen patients were enrolled. One patient had to be excluded from the study as the tumor was considered inoperable during the diagnostic workup.

Pre-assignment

Screening details:

During the screening period (day -5 – 0) potential subjects will be evaluated to determine that they fulfill the entry requirements as set forth in in- and exclusion criteria, according to protocol.

Pre-assignment period milestones

Number of subjects started	16
Number of subjects completed	16

Period 1

Period 1 title	Accrual (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	All patients

Arm description:

all patients

Arm type	Experimental
Investigational medicinal product name	nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

480 mg

Number of subjects in period 1	All patients
Started	16
Completed	16

Baseline characteristics

Reporting groups

Reporting group title	Accrual

Reporting group description: -

Reporting group values	Accrual	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	70		
standard deviation	± 10	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	11	11	

Subject analysis sets

Subject analysis set title	NeoNivo
Subject analysis set type	Full analysis

Subject analysis set description:
Full analysis

Reporting group values	NeoNivo		
Number of subjects	16		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			

From 65-84 years 85 years and over			

Age continuous Units: years arithmetic mean standard deviation	 70 ± 10		
Gender categorical Units: Subjects			
Female Male	5 11		

End points

End points reporting groups

Reporting group title	All patients
Reporting group description: all patients	
Subject analysis set title	NeoNivo
Subject analysis set type	Full analysis
Subject analysis set description: Full analysis	

Primary: Serious adverse events

End point title	Serious adverse events[1]
End point description:	
End point type	Primary
End point timeframe: baseline - 100 days after nivolumab	

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: 6 SAEs were detected, no statistical analysis was performed on adverse events, only descriptive statistics were used.

End point values	NeoNivo			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: SAE				
number (not applicable)	6			

Attachments (see zip file)	20240204_AEs.docx

Statistical analyses

No statistical analyses for this end point

Secondary: [18F]BMS-986192 and [18F]-FDG SUVpeak in tumor lesions before and on-treatment

End point title	[18F]BMS-986192 and [18F]-FDG SUVpeak in tumor lesions before and on-treatment
End point description:	
End point type	Secondary
End point timeframe: baseline - follow-up scan	

End point values	NeoNivo			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: SUVpeak				
median (inter-quartile range (Q1-Q3))	5.2 (3.5 to 8.5)			

Attachments (see zip file)	Imaging outcome/20240204_imaging.docx

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Imaging I/Work-up till 100 days after nivolumab

Adverse event reporting additional description:

Adverse events are defined as any undesirable experience occurring to a subject during the study, whether or not considered related to radioactive tracers or nivolumab treatment. All adverse events were evaluated by an investigator who is a qualified physician, according to the NCI CTCAE, version 5.0

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	5

Reporting groups

Reporting group title	All patients

Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 16 (37.50%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Cardiac disorders			
Cardiac asthma			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Stroke			
subjects affected / exposed	1 / 16 (6.25%)		
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 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Malnutrition	Additional description: Hospitalisation due to malnutrition		

subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumoniae	Additional description: Zie details in end point table		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)		
Cardiac disorders			
Edema limbs	Additional description: 1 grade 2		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Atrial flutter	Additional description: 1 grade 1		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Sinus bradycardia	Additional description: 1 grade 1		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Supraventricular tachycardia	Additional description: 1 grade 1		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Blood laboratory abnormality	Additional description: 14 grade 1, 3 grade 2		
subjects affected / exposed	16 / 16 (100.00%)		
occurrences (all)	16		
General disorders and administration site conditions			
Insomnia	Additional description: 3 grade 1		
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Fatigue	Additional description: 1 grade 1		

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain	Additional description: 1 grade 1		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhea	Additional description: 6 grade 1		
subjects affected / exposed	6 / 16 (37.50%)		
occurrences (all)	6		
Constipation	Additional description: 4 grade 1		
subjects affected / exposed	4 / 16 (25.00%)		
occurrences (all)	4		
Vomiting	Additional description: 1 grade 1, 2 grade 2		
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Eczema	Additional description: 2 grade 2		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Dermatitis	Additional description: 1 grade 1		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Renal and urinary disorders			
Urine retention	Additional description: 1 grade 2		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

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