



Clinical trial results:

PHASE II STUDY OF NEOADJUVANT NIVOLUMAB IN PATIENTS WITH GLIOBLASTOMA MULTIFORME

Summary

EudraCT number	2015-000442-39
Trial protocol	ES
Global end of trial date	01 March 2017

Results information

Result version number	v1 (current)
This version publication date	30 September 2021
First version publication date	30 September 2021

Trial information

Trial identification

Sponsor protocol code	Neo-Nivo
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02550249
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Clínica Universidad de Navarra
Sponsor organisation address	Avda. Pío XII,36, Pamplona, Spain, 31008
Public contact	UCEC, Clínica Universidad de Navarra, 34 948 255 400 2723, ucicec@unav.es
Scientific contact	UCEC, Clínica Universidad de Navarra, 34 948 255 400 2723, ucicec@unav.es

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	02 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 March 2017
Global end of trial reached?	Yes
Global end of trial date	01 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess changes in PD-L1 and CD8 expression induced by neoadjuvant nivolumab in GBM. For that purpose we will compare GBM tissue of patients before and after treatment with neoadjuvant nivolumab.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 August 2015
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	Spain: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	22
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were offered participation in the trial in the neuroncology clinics of University of Navarra.

Pre-assignment

Screening details:

Patients over 18 years with GBM that are candidates to primary or salvage resection surgery. In patients undergoing primary surgery, diagnosis of GBM should be confirmed by previous biopsy or previous partial resection. In patients with recurrent GBM, diagnosis of progression will be confirmed either by previous biopsy or by the RANO criteria.

Period 1

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

Arms

Arm title	Experimental group
------------------	--------------------

Arm description:

Patients from two subgroups were recruited to the study; patients who required salvage surgery to treat relapsed disease (n = 27) as well as patients who required surgery for primary tumor resection (n = 3) were recruited. These patients were administered a 3mg/kg dose of nivolumab. 2 weeks after nivolumab administration they underwent surgery. Patients received postsurgical doses of nivolumab every 2 weeks progression or unacceptable toxicity. For the three patients who underwent primary surgical treatment, nivolumab was stopped to receive standard-of-care chemoradiotherapy (CRT). In two of these cases, nivolumab was reintroduced following completion of chemoradiotherapy. These patients have not relapsed and they remain on nivolumab maintenance therapy without toxicity

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	BMS-936558
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

weeks ($\pm$ 3 days) before the surgery. Patients received postsurgical doses of nivolumab every 2 weeks ($\pm$ 3 days) until radiologic progression or unacceptable toxicity.

Number of subjects in period 1	Experimental group
Started	30
Completed	29
Not completed	1
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment period
-----------------------	------------------

Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	30	30	
Age categorical			
Units: Subjects			
Adults (18-64 years)	22	22	
From 65-84 years	8	8	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	20	20	

End points

End points reporting groups

Reporting group title	Experimental group
Reporting group description:	
Patients from two subgroups were recruited to the study; patients who required salvage surgery to treat relapsed disease (n = 27) as well as patients who required surgery for primary tumor resection (n = 3) were recruited. These patients were administered a 3mg/kg dose of nivolumab. 2 weeks after nivolumab administration they underwent surgery. Patients received postsurgical doses of nivolumab every 2 weeks progression or unacceptable toxicity. For the three patients who underwent primary surgical treatment, nivolumab was stopped to receive standard-of-care chemoradiotherapy (CRT). In two of these cases, nivolumab was reintroduced following completion of chemoradiotherapy. These patients have not relapsed and they remain on nivolumab maintenance therapy without toxicity	

Primary: Overall Survival (OS) and Progression-free survival (PFS)

End point title	Overall Survival (OS) and Progression-free survival (PFS) ^[1]
End point description:	
End point type	Primary
End point timeframe:	
Throughout the 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: Overall survival (O) and progression-free survival (PFS) were determined by the Kaplan-Meier method. There is no comparison between groups since there is only one arm in the trial design.

End point values	Experimental group			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Months				
median (confidence interval 95%)				
OS	7.3 (5.4 to 7.9)			
PFS	4.1 (2.8 to 5.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All non-SAE should be collected during the treatment period and for a minimum of 100 days following the last dose of study treatment. All SAEs must be collected that occur during the screening period and within 100 days of discontinuation dosing.

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

Dictionary used

Dictionary name	BMS
-----------------	-----

Dictionary version	ND
--------------------	----

Reporting groups

Reporting group title	Experimental group
-----------------------	--------------------

Reporting group description: -

Serious adverse events	Experimental group		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 30 (10.00%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor bleeding			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Liver function tests			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Experimental group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 30 (16.67%)		
Blood and lymphatic system disorders			

Anemia subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Hepatobiliary disorders Liver function tests subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Endocrine disorders Autoimmune primary hyperthyroidism subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 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

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30742120>