Clinical trial results:
Phase II clinicPhase II clinical trial on the combination of avelumab and axitinib for the treatment of patients with recurrent glioblastomaal trial on the combination of avelumab and axitinib for the treatment of patients with recurrent glioblastoma

Summary

EudraCT number	2017-000200-23
Trial protocol	BE
Global end of trial date	16 September 2020

Results information

Result version number	v1 (current)
This version publication date	12 May 2021
First version publication date	12 May 2021
Summary attachment (see zip file)	Gliavax article (JITCGliavax_12pag.pdf)

Trial information

Trial identification

Sponsor protocol code	2017-BN-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03291314
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	16 September 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To estimate the anti-tumor effect of combination therapy with Avelumab and Axitinib in patients with recurrent/progressive glioblastoma following prior therapy with surgery, radiation therapy and Temozolomide (on both strata seperatly)

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: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 54
Worldwide total number of subjects	54
EEA total number of subjects	54

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)	47

From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were screened for eligibility by history, physical examination, blood and urinary analysis (including blood chemistry, hematological, endocrinological tests
and dipstick proteinuria), electrocardiography, MRI of the brain and 18F-FET-PET/CT of the brain

Pre-assignment

Screening details:

Willing and able to give written informed consent
Histologically confirmed diagnosis of World Health Organization Grade IV malignant glioma
Documentation of recurrent

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Axitinib and Avelumab

Arm type	Experimental
Investigational medicinal product name	Axitinib
Investigational medicinal product code	
Other name	Inlyta
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Axitinib 5mg twice a day

Investigational medicinal product name	Avelumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous drip use

Dosage and administration details:

Avelumab 10mg/kg until confirmed progression of disease, unacceptable toxicity, the patient's refusal to continue study treatment, or death of the patient.

Arm title	Cohort 2

Arm description:

Axitinib

Arm type	Experimental
Investigational medicinal product name	Axitinib
Investigational medicinal product code	
Other name	Inlyta
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Axitinib 5mg twice a day

Number of subjects in period 1	Cohort 1	Cohort 2
Started	27	27
Completed	27	27

Baseline characteristics

Reporting groups

Reporting group title	Treatment (overall period)

Reporting group description: -

Reporting group values	Treatment (overall period)	Total	
Number of subjects	54	54	
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)	47	47	
From 65-84 years	7	7	
85 years and over	0	0	
Age continuous Units: years			
median	55		
full range (min-max)	20 to 76	-	
Gender categorical Units: Subjects			
Female	20	20	
Male	34	34	

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description: Axitinib and Avelumab	
Reporting group title	Cohort 2
Reporting group description: Axitinib	

Primary: Progression free survival (6-month PFS%)

End point title	Progression free survival (6-month PFS%)
End point description: The percentage of patients who are alive and free-from confirmed tumor progression at 6-month (24 weeks) following the date of randomisation (6-month PFS%)	
End point type	Primary
End point timeframe: Progression-free survival at 6 months (6-m-PFS%), per immunotherapy response assessment for neuro-oncology criteria	

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	27		
Units: the number of patients	27	27		

Statistical analyses

Statistical analysis title	one-stage Fleming design
Statistical analysis description: Sample size Cohort-1 is determined according to one-stage Fleming design. Avelumab plus axitinib worthy of further investigations if a 6-m-PFS% of >50% is observed (p(0)=0.30 and p(1)= 0.50). With alpha error of 0.10, and a beta error of 0.20, a sample size of 26 patients is required.The outcome of patients recruited to Cohort-2 is considered to be of an exploratory nature and no predefined statistical hypothesis was used to calculate the sample size for this cohort.	
Comparison groups	Cohort 1 v Cohort 2
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05 [2]
Method	see remark above

Notes:

[1] - determination of efficacy in a Phase two trial design

[2] - not relevant for this study, as both cohorts were not compared to each other

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: -

Serious adverse events	Study population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 54 (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	Study population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 54 (100.00%)		
Cardiac disorders			
Hypertension	Additional description: 22 patients had a grade 1-2; 4 patients had a grade 3		
subjects affected / exposed	26 / 54 (48.15%)		
occurrences (all)	26		
Nervous system disorders			
Dysphonia	Additional description: 36 patients had a grade 1-2		
subjects affected / exposed	36 / 54 (66.67%)		
occurrences (all)	36		
Blood and lymphatic system disorders			
Lymphopenia	Additional description: 25 patients had a grade 1-2, 2 patients had a grade 3		
subjects affected / exposed	27 / 54 (50.00%)		
occurrences (all)	27		

Thrombocytopenia	Additional description: 24 patients had a grade 1-2; 1 patients had a grade 3		
subjects affected / exposed	25 / 54 (46.30%)		
occurrences (all)	25		
Erythrocytosis	Additional description: 18 patients had a grade 1-2		
subjects affected / exposed	18 / 54 (33.33%)		
occurrences (all)	18		
Alanine aminotransferase increase	Additional description: 13 patients had a grade 1-2 ; 1 patient had a grade 3		
subjects affected / exposed	14 / 54 (25.93%)		
occurrences (all)	14		
Neutrophilia	Additional description: 9 patients had a grade 1-2		
subjects affected / exposed	9 / 54 (16.67%)		
occurrences (all)	9		
Aspartate aminotransferase increase	Additional description: 8 patients had a grade 1-2 ; 1 patient had a grade 3		
subjects affected / exposed	9 / 54 (16.67%)		
occurrences (all)	9		
Gamma-glutamyltransferase increase	Additional description: 4 patients had a grade 1-2 ; 5 patients had a grade 3		
subjects affected / exposed	9 / 54 (16.67%)		
occurrences (all)	9		
General disorders and administration site conditions			
Fatigue	Additional description: 21 patients had a grade 1-2; 4 patients had a grade 3		
subjects affected / exposed	25 / 54 (46.30%)		
occurrences (all)	25		
Gastrointestinal disorders			
Diarrhea	Additional description: 24 patients had a grade 1-2, 2 patients had a grade 3		
subjects affected / exposed	26 / 54 (48.15%)		
occurrences (all)	26		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism	Additional description: 3 patients had a grade 4		
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
Endocrine disorders			
Thyroid-stimulating hormone increase	Additional description: 15 patients had a grade 1-2; 1 patients had a grade 3		
subjects affected / exposed	16 / 54 (29.63%)		
occurrences (all)	16		
Infections and infestations			

Mucositis/aphtosis	Additional description: 13 patients had a grade 1-2		
subjects affected / exposed	13 / 54 (24.07%)		
occurrences (all)	13		

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