Clinical trial results:
Phase II Evaluating Efficacy of Temsirolimus in 2 Line Therapy for Patients With Advanced Bladder Cancer (VESTOR)

Summary

EudraCT number	2009-011049-15
Trial protocol	FR
Global end of trial date	15 December 2016

Results information

Result version number	v1 (current)
This version publication date	05 February 2022
First version publication date	05 February 2022

Trial information

Trial identification

Sponsor protocol code	IB 2009–08

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01827943
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Institut Bergonié
Sponsor organisation address	229 cours de l'Argonne, Bordeaux, France, 33076
Public contact	Regulatory Affairs Management Desk, Institut Bergonié, drci@bordeaux.unicancer.fr
Scientific contact	Regulatory Affairs Management Desk, Institut Bergonié, drci@bordeaux.unicancer.fr

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	23 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 December 2014
Global end of trial reached?	Yes
Global end of trial date	15 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate efficacy of Temsirolimus in terms of 2-month non-progression rate (RECIST V1.1)

Protection of trial subjects:

A supervisory committee is constitued to evaluate the benefit/risk ratio along the study period.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 November 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 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)	24
From 65 to 84 years	29
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

•Men or women of at least 18 years of age
•Histologically proven Bladder cancer
•Locally advanced or metastatic disease (stage IV)

Period 1

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

Arms

Arm title	Temsirolimus

Arm description:

Temsirolimus was administered intravenously at a dose of 25 mg in a weekly 30 min infusion and was associated to anti-H1 treatment. One cycle corresponded to 4 weeks of treatment.

Arm type	Experimental
Investigational medicinal product name	Torisel
Investigational medicinal product code	Temsirolimus
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Torisel® will be administered at a fixed dose of 25mg, once a week.
A cycle will consist of 4 injections: D1, D8, D15, D22.
Pre-medication with 25 to 50 mg of diphenhydramine IV (or a comparable anti-H1 antihistamine) should be initiated approximately 30 minutes prior to the Temsirolimus infusion.

Number of subjects in period 1	Temsirolimus
Started	54
Completed	45
Not completed	9
Never treated because of rapid progression	1
Protocol deviation	8

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	54	54	
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			
median	65		
full range (min-max)	41 to 87	-	
Gender categorical Units: Subjects			
Female	12	12	
Male	42	42	

End points

End points reporting groups

Reporting group title	Temsirolimus

Reporting group description:

Temsirolimus was administered intravenously at a dose of 25 mg in a weekly 30 min infusion and was associated to anti-H1 treatment. One cycle corresponded to 4 weeks of treatment.

Primary: Non-progression rate at 2 months

End point title	Non-progression rate at 2 months[1]

End point description:

Non-progression rate is defined as the rate of participants in complete or partial response or stable disease according to RECIST V1.1.

Complete response is defined as the disappearance of all target lesions, partial response is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters and stable disease occurs when neither sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for progression, taking as reference the smallest sum diameters while on study.

End point type	Primary

End point timeframe:

2 months

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: No statistical test has been performed, only the confidence interval calculation

End point values	Temsirolimus			
Subject group type	Reporting group			
Number of subjects analysed	45[2]			
Units: percentage of patients				
number (confidence interval 95%)	48.9 (33.7 to 64.2)			

Notes:

[2] - 45 eligible patients with at least one treatment administration and tumor assessment at 2 months

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

OS was was defined as the time from the treatment initiation to death due to any cause. Participants without documented death were censored at the date of the last follow-up or last patient contact. The OS was calculated using the product-limit (Kaplan-Meier) method for censored data.

End point type	Secondary

End point timeframe:

Through Database Cutoff Date of 23-Jan-2015 (up to approximately 5 years and 7 months - median follow-up time of 14 months)

End point values	Temsirolimus			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: months				
median (confidence interval 95%)	7.2 (5.2 to 9.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

End point title	Progression-free survival

End point description:

Progression-free survival (PFS) was defined as the time from the initiation of treatment to the first documented progression (as per RECIST v1.1) or death (due to any cause), whichever occurs first. Per RECIST 1.1, PD was defined as ≥20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of ≥5 mm. Patients alive and progression free were censored at the date of last follow-up or last patient contact. The PFS per RECIST 1.1 was calculated using the product-limit (Kaplan-Meier) method for censored data.

End point type	Secondary

End point timeframe:

Through Database Cutoff Date of 23-Jan-2015 (up to approximately 5 years and 7 months - median follow-up time of 14 months)

End point values	Temsirolimus			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: months				
median (confidence interval 95%)	2.8 (1.8 to 3.7)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse event are reported from the signature of the informed consent form to 30 days after the last treatment administration.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3.0

Reporting groups

Reporting group title	Temsirolimus

Reporting group description: -

Serious adverse events	Temsirolimus		
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 53 (66.04%)		
number of deaths (all causes)	40		
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Fatigue (asthenia, lethargy, malaise)			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fever			
subjects affected / exposed	6 / 53 (11.32%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	0 / 0		
Constitutional Symptoms - Other (Specify, __)			
subjects affected / exposed	13 / 53 (24.53%)		
occurrences causally related to treatment / all	3 / 15		
deaths causally related to treatment / all	0 / 6		
Respiratory, thoracic and mediastinal disorders			
Adult Respiratory Distress Syndrome (ARDS)			

subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pulmonary/Upper Respiratory - Other (Specify, __)				
subjects affected / exposed	3 / 53 (5.66%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 1			
Psychiatric disorders				
Confusion				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mood alteration				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Platelet				
subjects affected / exposed	3 / 53 (5.66%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Fracture				
subjects affected / exposed	1 / 53 (1.89%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Hemorrhage, CNS	Additional description: Cerebral hemmorhage			
subjects affected / exposed	2 / 53 (3.77%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	2 / 2			
Blood and lymphatic system disorders				
Hemoglobin				

subjects affected / exposed	3 / 53 (5.66%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Ocular/visual - other, specify			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Ileus, GI (functional obstruction of bowel, i.e., neuroconstipation)			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mucositis/stomatitis (clinical exam)			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Obstruction, GI			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Vomiting			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Liver dysfunction/failure (clinical)			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pain - Other (Specify, __)			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	0 / 0		

Renal and urinary disorders			
Renal failure			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Renal/Genitourinary - Other (Specify, __)			
subjects affected / exposed	2 / 53 (3.77%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary retention (including neurogenic bladder)			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Musculoskeletal/Soft Tissue - Other (Specify, __)			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pain			
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection - Other (Specify, __)	Additional description: 1 grade 5 septic shock		
subjects affected / exposed	9 / 53 (16.98%)		
occurrences causally related to treatment / all	4 / 10		
deaths causally related to treatment / all	1 / 1		
Infection with unknown ANC	Additional description: Vaginal infection		
subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Glucose, serum-high (hyperglycemia)	Additional description: DISRUPTION OF HIS DIABETES		

subjects affected / exposed	1 / 53 (1.89%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

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

Non-serious adverse events	Temsirolimus		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	53 / 53 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
General disorders and administration site conditions			
Constitutional Symptoms - Other (Specify, __)			
subjects affected / exposed	20 / 53 (37.74%)		
occurrences (all)	21		
Fatigue (asthenia, lethargy, malaise)			
subjects affected / exposed	39 / 53 (73.58%)		
occurrences (all)	43		
Fever (in the absence of neutropenia, where neutropenia is defined as ANC <1.0 x 10e9/L)			
subjects affected / exposed	26 / 53 (49.06%)		
occurrences (all)	21		
Edema:limb			
subjects affected / exposed	14 / 53 (26.42%)		
occurrences (all)	14		
Pain			
subjects affected / exposed	29 / 53 (54.72%)		
occurrences (all)	61		
Pain - Other (Specify, __)			
subjects affected / exposed	5 / 53 (9.43%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			

Hemorrhage, pulmonary/upper respiratory subjects affected / exposed occurrences (all)	6 / 53 (11.32%) 6		
Cough subjects affected / exposed occurrences (all)	6 / 53 (11.32%) 6		
Dyspnea (shortness of breath) subjects affected / exposed occurrences (all)	6 / 53 (11.32%) 7		
Pulmonary/Upper Respiratory - Other (Specify, __) subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 4		
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	5 / 53 (9.43%) 5		
Mood alteration subjects affected / exposed occurrences (all)	13 / 53 (24.53%) 15		
Investigations			
Leukocytes (total WBC) subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 4		
Platelets subjects affected / exposed occurrences (all)	16 / 53 (30.19%) 24		
Weight loss subjects affected / exposed occurrences (all)	11 / 53 (20.75%) 12		
Cholesterol, serum-high (hypercholesteremia) subjects affected / exposed occurrences (all)	7 / 53 (13.21%) 7		
Injury, poisoning and procedural complications			

Rash/desquamation			
subjects affected / exposed	8 / 53 (15.09%)		
occurrences (all)	10		
Nervous system disorders			
Taste alteration (dysgeusia)			
subjects affected / exposed	10 / 53 (18.87%)		
occurrences (all)	10		
Dizziness			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Neuropathy: sensory			
subjects affected / exposed	6 / 53 (11.32%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
Hemoglobin			
subjects affected / exposed	26 / 53 (49.06%)		
occurrences (all)	40		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	13 / 53 (24.53%)		
occurrences (all)	13		
Diarrhea			
subjects affected / exposed	15 / 53 (28.30%)		
occurrences (all)	20		
Dry mouth/salivary gland (xerostomia)			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Gastritis (including bile reflux gastritis)			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Gastrointestinal - Other (Specify, __)			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Hemorrhoids			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	5		

Mucositis/stomatitis (clinical exam) subjects affected / exposed occurrences (all)	19 / 53 (35.85%) 23		
Mucositis/stomatitis (functional/symptomatic) subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 4		
Nausea subjects affected / exposed occurrences (all)	23 / 53 (43.40%) 24		
Obstruction, GI subjects affected / exposed occurrences (all)	6 / 53 (11.32%) 7		
Vomiting subjects affected / exposed occurrences (all)	15 / 53 (28.30%) 19		
Skin and subcutaneous tissue disorders Dermatology/Skin - Other (Specify, __) subjects affected / exposed occurrences (all)	13 / 53 (24.53%) 20		
Dry skin subjects affected / exposed occurrences (all)	14 / 53 (26.42%) 14		
Pruritus/itching subjects affected / exposed occurrences (all)	8 / 53 (15.09%) 11		
Renal and urinary disorders Hemorrhage, GU subjects affected / exposed occurrences (all)	3 / 53 (5.66%) 5		
Renal failure subjects affected / exposed occurrences (all)	9 / 53 (16.98%) 10		
Renal/Genitourinary - Other (Specify, __) subjects affected / exposed occurrences (all)	4 / 53 (7.55%) 4		

Musculoskeletal and connective tissue disorders			
Metabolic/Laboratory - Other (Specify, __)			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Musculoskeletal/Soft Tissue - Other (Specify, __)			
subjects affected / exposed	6 / 53 (11.32%)		
occurrences (all)	6		
Infections and infestations			
Infection - Other (Specify, __)			
subjects affected / exposed	31 / 53 (58.49%)		
occurrences (all)	45		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	23 / 53 (43.40%)		
occurrences (all)	26		
Dehydration			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Albumin, serum-low (hypoalbuminemia)			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Calcium, serum-low (hypocalcemia)			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	4		
Glucose, serum-high (hyperglycemia)			
subjects affected / exposed	6 / 53 (11.32%)		
occurrences (all)	6		
Potassium, serum-high (hyperkalemia)			
subjects affected / exposed	3 / 53 (5.66%)		
occurrences (all)	3		
Potassium, serum-low (hypokalemia)			
subjects affected / exposed	4 / 53 (7.55%)		
occurrences (all)	6		
Triglyceride, serum-high (hypertriglyceridemia)			

subjects affected / exposed occurrences (all)	13 / 53 (24.53%) 16		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 January 2011	Protocol V3 dated 16-jun-2010
25 July 2012	Protocol V4 dated 20-oct-2011
30 April 2014	Protocol V5 dated 09-apr-2013
28 January 2015	Protocol V6 dated 08-oct-2014

Notes:

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/29454321