Clinical trial results:
A phase II study of ABT-263 as single agent in women with platinum resistant/refractory recurrent ovarian cancer

Summary

EudraCT number	2015-000193-35
Trial protocol	FR
Global end of trial date	08 March 2019

Results information

Result version number	v1 (current)
This version publication date	27 March 2021
First version publication date	27 March 2021

Trial information

Trial identification

Sponsor protocol code	MONAVI-1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02591095
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Centre François Baclesse
Sponsor organisation address	3 Avenue du Général Harris, CAEN, France,
Public contact	LECONTE, Centre François Baclesse, 33 0231455002, a.leconte@baclesse.unicancer.fr
Scientific contact	JOLY, Centre François Baclesse, 33 0231455002, f.joly@baclesse.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	15 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 January 2019
Global end of trial reached?	Yes
Global end of trial date	08 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine activity of ABT-263 for patients with a platinum resistant/refractory recurrent ovarian cancer

Protection of trial subjects:

Independent data monitoring committee

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 January 2016
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: 47
Worldwide total number of subjects	47
EEA total number of subjects	47

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)	26
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

52 patients in screening

Period 1

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

Arms

Arm title	Navitoclax

Arm description:

Patients will be treated with oral Navitoclax (ABT-263) 150 mg daily for the Lead-in Period (7 to 14 days maximum, depends on platelets level). A subject may only proceed from the Lead-in Period to the defined dose level of 250 mg daily for Cycle 1 Day 1 and beyond if platelet count is ≥ 50,000/mm3 and platelets are stable or rising and thereafter.
Cycle duration is defined as 21 days.

Arm type	Experimental
Investigational medicinal product name	Navitoclax
Investigational medicinal product code	ABT263
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

250 mg daily

Number of subjects in period 1[1]	Navitoclax
Started	46
Completed	46

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 1 patient has been included in the study but not received the treatment according to investigator's decision

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	46	46	
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)	26	26	
From 65-84 years	20	20	
85 years and over	0	0	
Age continuous Units: years			
median	63		
full range (min-max)	38 to 80	-	
Gender categorical Units: Subjects			
Female	46	46	
Male	0	0	

Subject analysis sets

Subject analysis set title	Efficacy
Subject analysis set type	Full analysis

Subject analysis set description:

Efficacy set is defined as patients who received at least one treatment dose and for which at least two tumor assessment are available (baseline and after treamtent).

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

Patients who received at least one dose of treatment.

Reporting group values	Efficacy	Safety	
Number of subjects	44	46	
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)	24	26	
From 65-84 years	20	20	
85 years and over	0	0	
Age continuous			
Units: years			
median			
full range (min-max)			
Gender categorical			
Units: Subjects			
Female	44	46	
Male	0	0	

End points

End points reporting groups

Reporting group title	Navitoclax

Reporting group description:

Patients will be treated with oral Navitoclax (ABT-263) 150 mg daily for the Lead-in Period (7 to 14 days maximum, depends on platelets level). A subject may only proceed from the Lead-in Period to the defined dose level of 250 mg daily for Cycle 1 Day 1 and beyond if platelet count is ≥ 50,000/mm3 and platelets are stable or rising and thereafter.
Cycle duration is defined as 21 days.

Subject analysis set title	Efficacy
Subject analysis set type	Full analysis

Subject analysis set description:

Efficacy set is defined as patients who received at least one treatment dose and for which at least two tumor assessment are available (baseline and after treamtent).

Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

Patients who received at least one dose of treatment.

Primary: Progression-Free Survival

End point title	Progression-Free Survival

End point description:

Primary endpoint is the Progression-Free Survival median time. Using a Case & Morgan EDA two-stage design with a 10% one-sided alpha risk and a power of 85%, and the following assumptions :
H0 : median PFS <= 2.5 months is equivalent with a 3-month PFS rate <= 0.435
H1 : median PFS >= 4.5 months is equivalent with a 3-month PFS rate >= 0.630
19 assessable patients were needed to be included in the first step. Except if the interim analysis would conclude the study had to be stopped for futility, 22 additional patients had to be enrolled for a total of 41 assessable patients. Interim analysis has not been performed since the total number of evaluable patients has been reached faster than planned (9 months instead of 24 months), during the data monitoring (inclusions were not suspended during this time, as planned in the protocol). Efficacy was evaluated at final analysis only.
At the final analysis, the Case & Morgan test statistic Z2=-4.86 > C2=1.188

End point type	Primary

End point timeframe:

Date extraction done on march 8th 2019

End point values	Navitoclax	Efficacy		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	44	44		
Units: months				
median (confidence interval 95%)	1.64 (1.59 to 2.30)	1.64 (1.59 to 2.30)		

Attachments (see zip file)	Progression-Free Survival/PFS.PNG

Statistical analyses

Statistical analysis title	Further results
Statistical analysis description: 3-month Progression-Free Survival Rate, with 95% confidence interval.	
Comparison groups	Navitoclax v Efficacy
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	3-month PFS rate
Point estimate	22.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.18
upper limit	39.2

Secondary: Clinical response

End point title	Clinical response
End point description:	
End point type	Secondary
End point timeframe: over the period of study	

End point values	Efficacy			
Subject group type	Subject analysis set			
Number of subjects analysed	44			
Units: patients	16			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Database extracted on march 5th 2019.

Adverse event reporting additional description:

All serious adverse events have been reported.
Only adverse events observed in at least 5% of patients have been reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Overall

Reporting group description:

Data about death has been actualised in december 2020.

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 46 (30.43%)		
number of deaths (all causes)	44		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Lymphoedema			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Dyspnoea			
subjects affected / exposed	2 / 46 (4.35%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Nervous system disorders			

Cerebral oedema				
subjects affected / exposed	1 / 46 (2.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Oedema				
subjects affected / exposed	1 / 46 (2.17%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	1 / 46 (2.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Gastrointestinal disorders				
Vomiting				
subjects affected / exposed	1 / 46 (2.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	1 / 46 (2.17%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	1 / 46 (2.17%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	2 / 46 (4.35%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
Large intestinal obstruction				
subjects affected / exposed	1 / 46 (2.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Hepatobiliary disorders			
Hepatic lesion			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	46 / 46 (100.00%)		
Investigations			
Weight loss			
subjects affected / exposed	7 / 46 (15.22%)		
occurrences (all)	12		
Creatinine increased			
subjects affected / exposed	11 / 46 (23.91%)		
occurrences (all)	27		
Bilirubin increased			
subjects affected / exposed	7 / 46 (15.22%)		
occurrences (all)	11		
Alanine aminotransferase increased			
subjects affected / exposed	19 / 46 (41.30%)		
occurrences (all)	46		
Aspartate aminotransferase increased			

subjects affected / exposed	23 / 46 (50.00%)		
occurrences (all)	62		
Alkaline phosphatase increased			
subjects affected / exposed	25 / 46 (54.35%)		
occurrences (all)	66		
Gamma GT increased			
subjects affected / exposed	21 / 46 (45.65%)		
occurrences (all)	51		
Uric acid increased			
subjects affected / exposed	4 / 46 (8.70%)		
occurrences (all)	9		
Blood lactate dehydrogenase increased			
subjects affected / exposed	5 / 46 (10.87%)		
occurrences (all)	11		
Vascular disorders			
Hypertension			
subjects affected / exposed	12 / 46 (26.09%)		
occurrences (all)	27		
Haemorrhage			
subjects affected / exposed	6 / 46 (13.04%)		
occurrences (all)	8		
Lymphoedema			
subjects affected / exposed	4 / 46 (8.70%)		
occurrences (all)	7		
Nervous system disorders			
Sensory neuropathy			
subjects affected / exposed	11 / 46 (23.91%)		
occurrences (all)	28		
Headache			
subjects affected / exposed	5 / 46 (10.87%)		
occurrences (all)	16		
Dysgeusia			
subjects affected / exposed	4 / 46 (8.70%)		
occurrences (all)	11		
Paraesthesia			

subjects affected / exposed	3 / 46 (6.52%)		
occurrences (all)	4		
Dizziness			
subjects affected / exposed	3 / 46 (6.52%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	22 / 46 (47.83%)		
occurrences (all)	60		
Neutropenia			
subjects affected / exposed	14 / 46 (30.43%)		
occurrences (all)	35		
Lymphopenia			
subjects affected / exposed	37 / 46 (80.43%)		
occurrences (all)	127		
Anaemia			
subjects affected / exposed	36 / 46 (78.26%)		
occurrences (all)	100		
Thrombocytopenia			
subjects affected / exposed	45 / 46 (97.83%)		
occurrences (all)	143		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	36 / 46 (78.26%)		
occurrences (all)	94		
Pain			
subjects affected / exposed	19 / 46 (41.30%)		
occurrences (all)	67		
Oedema			
subjects affected / exposed	10 / 46 (21.74%)		
occurrences (all)	21		
Oedema peripheral			
subjects affected / exposed	3 / 46 (6.52%)		
occurrences (all)	10		
Eye disorders			

Dry eye			
subjects affected / exposed	4 / 46 (8.70%)		
occurrences (all)	7		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	24 / 46 (52.17%)		
occurrences (all)	65		
Vomiting			
subjects affected / exposed	17 / 46 (36.96%)		
occurrences (all)	38		
Constipation			
subjects affected / exposed	8 / 46 (17.39%)		
occurrences (all)	23		
Diarrhoea			
subjects affected / exposed	21 / 46 (45.65%)		
occurrences (all)	37		
Abdominal pain			
subjects affected / exposed	16 / 46 (34.78%)		
occurrences (all)	32		
Gastrointestinal disorder			
subjects affected / exposed	4 / 46 (8.70%)		
occurrences (all)	4		
Ascites			
subjects affected / exposed	7 / 46 (15.22%)		
occurrences (all)	12		
Dry mouth			
subjects affected / exposed	3 / 46 (6.52%)		
occurrences (all)	11		
Abdominal distension			
subjects affected / exposed	6 / 46 (13.04%)		
occurrences (all)	10		
Dyspepsia			
subjects affected / exposed	6 / 46 (13.04%)		
occurrences (all)	10		
Hemorrhoids			

subjects affected / exposed	3 / 46 (6.52%)		
occurrences (all)	8		
Reflux gastritis			
subjects affected / exposed	11 / 46 (23.91%)		
occurrences (all)	33		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 46 (15.22%)		
occurrences (all)	16		
Dyspnoea			
subjects affected / exposed	11 / 46 (23.91%)		
occurrences (all)	22		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	10 / 46 (21.74%)		
occurrences (all)	27		
Anxiety			
subjects affected / exposed	6 / 46 (13.04%)		
occurrences (all)	11		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 46 (15.22%)		
occurrences (all)	16		
Muscle contracture			
subjects affected / exposed	4 / 46 (8.70%)		
occurrences (all)	11		
Infections and infestations			
Infection without neutropenia			
subjects affected / exposed	3 / 46 (6.52%)		
occurrences (all)	4		
Gingivitis			
subjects affected / exposed	3 / 46 (6.52%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	19 / 46 (41.30%)		
occurrences (all)	46		
Hyperglycaemia			
subjects affected / exposed	4 / 46 (8.70%)		
occurrences (all)	6		
Hyperuricaemia			
subjects affected / exposed	11 / 46 (23.91%)		
occurrences (all)	18		
Hypoalbuminaemia			
subjects affected / exposed	11 / 46 (23.91%)		
occurrences (all)	21		
Hypocalcaemia			
subjects affected / exposed	5 / 46 (10.87%)		
occurrences (all)	6		
Hypokalaemia			
subjects affected / exposed	12 / 46 (26.09%)		
occurrences (all)	18		
Hypomagnesaemia			
subjects affected / exposed	9 / 46 (19.57%)		
occurrences (all)	15		
Hyponatraemia			
subjects affected / exposed	5 / 46 (10.87%)		
occurrences (all)	5		

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