



## Clinical trial results:

### Veliparib (ABT888) Monotherapy for Patients with BRCA germline mutation and Platinum-Resistant or Partially Platinum-Sensitive Relapse of Epithelial Ovarian Cancer

#### Summary

EudraCT number	2011-002099-18
Trial protocol	DK
Global end of trial date	29 January 2016

#### Results information

Result version number	v1 (current)
This version publication date	03 December 2021
First version publication date	03 December 2021

#### Trial information

##### Trial identification

Sponsor protocol code	Veli-BRCA
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01472783
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Vejle Hospital
Sponsor organisation address	Beriderbakken 4, Vejle, Denmark, 7100
Public contact	Clinical Trial Unit, Vejle Hospital, kfe.onko@rsyd.dk
Scientific contact	Clinical Trial Unit, Vejle Hospital, kfe.onko@rsyd.dk

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	01 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 January 2016
Global end of trial reached?	Yes
Global end of trial date	29 January 2016
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Phase I:

To determine:

- Maximum-tolerated dose (MTD)
- Dose-limiting toxicities (DLT)
- Recommended phase II dose

Phase II:

To investigate the response rate in platinum-resistant and partially platinum sensitive ovarian cancer patients with known BRCA mutations treated with veliparib monotherapy.

Protection of trial subjects:

Patients were offered antiemetics to treat potential veliparib-induced nausea and vomiting.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2011
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	Denmark: 49
Worldwide total number of subjects	49
EEA total number of subjects	49

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)	39

From 65 to 84 years	10
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The phase I part of the study accrued patients from November 2011 to August 2012 and continued in phase II from September 2012 to March 2015 with enrollment of a total of 48 patients, 16 patients in phase I and 32 patients in phase II.

### Pre-assignment

Screening details:

The phase II was intended to include 33 patients according to protocol, but 1 patient was withdrawn after inclusion because pathology and chart review revealed that her primary diagnosis was not OC but endometrial cancer, and she was withdrawn because of this protocol violation. Most of the included patients were heavily pretreated.

### Period 1

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

### Arms

Arm title	Phase II arm
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Arm description:

The phase II included patients from September 2012 to March 2015 with enrollment of a 32 patients in phase II. The phase II was intended to include 33 patients according to protocol, but 1 patient was withdrawn after inclusion because pathology and chart review revealed that her primary diagnosis was not OC but endometrial cancer, and she was withdrawn because of this protocol violation.

Arm type	Experimental
Investigational medicinal product name	Veliparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Patients received oral veliparib twice daily on days 1 to 28 (4-weekly treatment cycle). The starting dose in the phase I dose escalating study was 300 mg twice a day (BID)

<b>Number of subjects in period 1</b>	Phase II arm
Started	49
Completed	49

## Baseline characteristics

## End points

### End points reporting groups

Reporting group title	Phase II arm
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Reporting group description:

The phase II included patients from September 2012 to March 2015 with enrollment of a 32 patients in phase II. The phase II was intended to include 33 patients according to protocol, but 1 patient was withdrawn after inclusion because pathology and chart review revealed that her primary diagnosis was not OC but endometrial cancer, and she was withdrawn because of this protocol violation.

Subject analysis set title	Response rate
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Subject analysis set type	Per protocol
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Subject analysis set description:

Overall response: Combined CA125 biomarker and RECIST response.

Tumor assessment was performed at baseline and after every third cycle by computed tomography scans of chest, abdomen, and pelvis according to RECIST version 1.1 and by CA-125 GCIG-modified criteria every third cycle. Response and progression were determined by using the definitions incorporating RECIST 1.1 and CA-125 as agreed by the GCIG. Patients were not evaluable (NE) by RECIST if they had no measurable target lesions according to RECIST version 1.1 (then patients could be included only if they had CA-125 measurable disease), and patients were NE by CA-125 RECIST criteria if their baseline CA-125 value was less than 70 kU/L and could vice versa be enrolled in the protocol only if they had RECIST-measurable disease.

Subject analysis set title	PFS
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Subject analysis set type	Per protocol
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Subject analysis set description:

Progression-free survival was measured from date of first dose of study treatment to progression or death, whichever came first.

Subject analysis set title	OS
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Subject analysis set type	Per protocol
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Subject analysis set description:

Overall survival was calculated from date of first dose of study treatment to date of death of any cause.

### Primary: Response rate

End point title	Response rate <sup>[1]</sup>
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End point description:

Overall response: Combined CA125 biomarker and RECIST response.

End point type	Primary
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End point timeframe:

Tumor assessment was performed at baseline and after every third cycle by computed tomography scans of chest, abdomen, and pelvis according to RECIST version 1.1 and by CA-125 GCIG-modified criteria every third cycle.

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: The primary endpoint is descriptive and there is no comparisons and therefore no p-values. Simon's 2-stage minimax design was used for assessment of the phase II part of the trial. The target level for response was set at 40% and 20% as the lower level of clinical interest. With a significance level of 5% and a power of 80%, the trial was planned to include 18 patients in the first step (stage I). If more than 10 patients among the 33 patients responded, the trial was defined as sufficiently powered.

End point values	Phase II arm	Response rate		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	32 <sup>[2]</sup>	32		
Units: Response rate				
Complete response (CR)	2	2		
Partial response (PR)	19	19		
Stable Disease (SD)	2	2		
Progressive disease (PD)	8	8		
Non evaluable (NE)	1	1		

Notes:

[2] - Response rate only included for phase II part of the study (N=32)

## Statistical analyses

No statistical analyses for this end point

### Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)
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End point description:

End point type	Secondary
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End point timeframe:

Progression-free survival was measured from date of first dose of study treatment to progression or death, whichever came first.

End point values	Phase II arm	PFS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	32 <sup>[3]</sup>	32		
Units: PFS (months)				
median (confidence interval 100%)	5.6 (5.2 to 7.3)	5.6 (5.2 to 7.3)		

Notes:

[3] - PFS calculated for the phase II part of the trial.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Overall survival (OS)

End point title	Overall survival (OS)
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End point description:

End point type	Secondary
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End point timeframe:

Overall survival was calculated from date of first dose of study treatment to date of death of any cause

<b>End point values</b>	Response rate	PFS	OS	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	32	32	32	
Units: OS (months)				
median (confidence interval 100%)	1 (1 to 1)	5.6 (5.2 to 7.3)	13.7 (10.2 to 17.3)	

## Statistical analyses

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No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From trial initiation on Nov 1, 2011 to Feb 1, 2016.

Date of Death was followed beyond 2016 until death of all included subjects.

Assessment type	Systematic
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### Dictionary used

Dictionary name	CTCAE
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Dictionary version	4.0
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### Reporting groups

Reporting group title	Toxicity
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Reporting group description: -

Serious adverse events	Toxicity		
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 49 (55.10%)		
number of deaths (all causes)	49		
number of deaths resulting from adverse events	0		
Vascular disorders			
Tromboembolic event - pulmonary embolism	Additional description: Subjects affected/exposed 1/49 occurens causally related to treatment / all 0/1 death causally related to treatment/all0(0)		
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pain	Additional description: Subjects affected/exposed 7/88 occurens causally related to treatment / all 0/9 death causally related to treatment/all 0/0		
subjects affected / exposed	7 / 49 (14.29%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Fatigue	Additional description: Subjects affected/exposed 2/49 occurens causally related to treatment / all 1/49 death causally related to treatment/all 0/0		
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	3 / 49 (6.12%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Reduced general condition			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fracture	Additional description: Subjects affected/exposed 2/49 occurs causally related to treatment / all 0/2 death causally related to treatment/all 0/0		
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Tremor	Additional description: Subjects affected/exposed 1/49 occurs causally related to treatment / all 0/1 death causally related to treatment/all 0/0		
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anemia	Additional description: Subjects affected/exposed 3/49 occurs causally related to treatment / all 0/3 death causally related to treatment/all 0/0		
subjects affected / exposed	3 / 49 (6.12%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Abdominal pain	Additional description: Abdominal Pain - Subjects affected/exposed: 4/49  - occurrences causally related to treatment / all: 0/4 - deaths causally related to treatment / all: 0/0		
subjects affected / exposed	4 / 49 (8.16%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Nausea	Additional description: - Subjects affected/exposed: 6/49  - occurrences causally related to treatment / all: 4/7 - deaths causally related to treatment / all: 0/0		
subjects affected / exposed	6 / 49 (12.24%)		
occurrences causally related to treatment / all	4 / 7		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	5 / 49 (10.20%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	7 / 49 (14.29%)		
occurrences causally related to treatment / all	4 / 7		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	1 / 49 (2.04%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Metastatic Spinal cord compression	Additional description: Subjects affected/exposed 2/49 occurens causally related to treatment / all 0/2 death causally related to treatment/all 0/0		
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Fever			
subjects affected / exposed	4 / 49 (8.16%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration	Additional description: Subjects affected/exposed 2/49 occurens causally related to treatment / all 1/2 death causally related to treatment/all 0/0		
subjects affected / exposed	2 / 49 (4.08%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Toxicity		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 49 (20.41%)		
Investigations			
Grade 3-4 toxicity	Additional description: Grade 3-4 toxicities subjects affected / exposed 10/49 occurrences 12		
subjects affected / exposed	10 / 49 (20.41%)		
occurrences (all)	12		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28763368>