An Extension Study to Evaluate the Safety of Veliparib as Single Agent Therapy or in Combination with Chemotherapy in Subjects with Solid Tumors

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON40491

Source
ToetsingOnline

Brief title
M14-144

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Cancer, Solid tumors

Research involving
Human

Sponsors and support

Primary sponsor: AbbVie b.v.
Source(s) of monetary or material Support: AbbVie b.v.

Intervention

Keyword: Open-label extension, Solid tumors, Veliparib

Outcome measures

Primary outcome

Efficacy:

The efficacy endpoints are objective response rate (ORR),

time-to-disease-progression (TTP),

progression-free-survival (PFS), and overall survival (OS). Radiographic

results will be evaluated

through the application of response evaluation criteria in solid tumors

(RECIST) 1.1.

Safety:

Adverse events, laboratory profiles, physical examinations, vital signs will be

evaluated throughout the

study. The Medical Dictionary for Regulatory Activities (MedDRA) will be used

with adverse event

reports. NCI CTCAE 4.0 criteria will be applied to adverse event reports and

laboratory variable values.

All subjects treated with veliparib will be included in the summaries.

Secondary outcome

NA

Study description

Background summary

This study is designed to evaluate the effect of veliparib in subjects with solid tumors to
test the safety and tolerability of veliparib as monotherapy or in combination with
carboplatin/paclitaxel or modified FOLFIRI. This study will allow subjects who enrolled
in the M10-020 QTc study to continue with treatment. Previous early stage studies have
been designed to test the safety and tolerability of veliparib as monotherapy or in
combination with chemotherapy.

Study objective

This study is designed as an extension to other veliparib clinical studies. The primary objective of this
study is to evaluate the safety and tolerability of veliparib monotherapy, veliparib in combination with
carboplatin/paclitaxel, or veliparib in combination with modified
5-Flourouracil, irinotecan, and Folinic
acid (FOLFIRI).
The secondary objectives are:
* To evaluate the effect of veliparib monotherapy, veliparib in combination with carboplatin/paclitaxel or veliparib in combination with modified FOLFIRI on progression free
survival in subjects with solid tumors.
* To assess the objective response rate, overall survival and time to progression in subjects with
solid tumors.

Study design

This will be a three arm, open-label study. Subjects with solid tumors who have completed Study M12-020 may be enrolled in this study. Enrollment into a particular treatment arm is at the discretion of the investigator. The treatment to which the subject is enrolled should be appropriate based on the tumor type. A CT scan of the full chest, abdomen, and pelvis (or MRI) to determine the extent of tumor burden will be performed for all tumor assessments at Screening (within 28 days of C1D1), per standard of care (interval of 6 - 9 weeks) from C1D1, and at the Final Visit (if not performed within the last 4 weeks). The CT scans will be performed until evidence of

tumor progression occurs. Study visits
will be conducted as described in the protocol for each dosing arm.
The total duration of the study is difficult to determine as the study will continue until all subjects enrolled have reached an endpoint of progressive disease or are discontinued due to toxicity or withdraw consent. Once the subject discontinues there will be a final visit and a 30 day follow-up.
Subjects will be followed for survival for 2 years unless they withdraw consent for follow-up.

Intervention

This study will consist of 3 treatment arms:
- Arm A Veliparib Monotherapy
Subjects enrolled into the veliparib monotherapy arm may be started at 300 mg twice daily (BID). Each cycle will be 28 days.

- Arm B Veliparib Intermittent Dosing in Combination with Carboplatin and Paclitaxel
Subjects enrolled in the intermittent veliparib dosing arm will be dosed with veliparib 120 mg BID on Days 1 - 7 in combination with carboplatin AUC 6 and paclitaxel 175 or 200 mg/m2, per the investigator's discretion and as appropriate for the tumor type, every 21 days on Day 1 of each cycle.

- Arm C Veliparib Intermittent Dosing in Combination with Modified FOLFIRI
Subjects may be dosed with veliparib 200 mg BID on Days 1 - 5 and Days 15 - 19 in combination with modified FOLFIRI.

Study burden and risks

The burden for the subjects consists of extra visits to the site and mainly extra blood draws.

The main toxicities associated with veliparib to date are mechanism based and are not clearly distinguished from those expected of the base regimens with which veliparib is combined. Hematological toxicities, such as thrombocytopenia and neutropenia, and gastrointestinal (GI) disturbances such as nausea and vomiting, are the main toxicities observed to date.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

A subject will be eligible for study participation if he/she meets the following criteria:
1. Subject must be >= 18 years of age.
2. Subject has histologically or cytologically confirmed solid malignancy that is metastatic or unresectable and for which standard curative measures or other therapy that may provide clinical benefit do not exist or are no longer effective.
4. Subject is appropriate for treatment with veliparib monotherapy (should have tumor with defects in DNA repair mechanisms (i.e., BRCA mutated breast cancer or high grade ovarian cancer with or without BRCA mutation), or veliparib in combination with carboplatin/paclitaxel or in combination with FOLFIRI (all subjects with advanced solid tumors are eligible for combination treatment).
5. Subjects with known brain metastases must have clinically controlled neurologic symptoms.
6. Subject has an Eastern Cooperative Oncology Group (ECOG) performance score of 0 - 1.
7. Subject must have adequate bone marrow, renal and hepatic function per local laboratory reference range as follows:
* Bone marrow: Absolute Neutrophil count (ANC) >= 1,500/µL; Platelets >= 100,000/mm3; (independent of platelet transfusions within 3 months prior to starting study drug); Hemoglobin >= 9.0 g/dL;
* Renal function: serum creatinine <= 2.0 mg/dL or calculated creatinine clearance >= 50

mL/min;
* Hepatic function and enzymes: AST and ALT <= 2.5 × the upper limit of normal (ULN) of institution's normal range; Bilirubin <= 1.5 × ULN. Subjects with liver metastases may have an AST and ALT of <= 5.0 × ULN.
* Subject must voluntarily sign and date an informed consent, approved by an Independent Ethics
Committee (IEC)/Institutional Review Board (IRB), prior to the initiation of and screening for study-specific procedures.

Exclusion criteria

A subject will not be eligible for study participation if he/she meets any of the following criteria:
1. If the subject has clinically significant and uncontrolled major medical condition(s) including but not limited to:
* Uncontrolled seizure disorder, including focal or generalized seizure within the last 12 months;
* Uncontrolled nausea/vomiting/diarrhea;
* Active uncontrolled infection;
* Symptomatic congestive heart failure;
* Unstable angina pectoris or cardiac arrhythmia;
* Psychiatric illness/social situation that would limit compliance with study requirements;
* Any medical condition, which in the opinion of the study investigator, places the subject at an unacceptably high risk for toxicities.
2. Subjects who have previously experienced a hypersensitivity reaction to either carboplatin or cremophor/paclitaxel should be excluded from enrollment in Arm B.
4. Subject has received any of the following anti-cancer therapies 21 days prior to the first dose of study drug:
* Chemotherapy, immunotherapy, radiotherapy
* Any investigational therapy, including targeted small molecule agents, with the following exceptions:
* Hormonal anticancer therapy must be stopped 7 days before starting C1D1,
* Hormones for hypothyroidism, estrogen replacement therapy (ERT), or agonists required to suppress serum testosterone or estrogen levels (e.g., LHRH, GnRH, etc.) for subjects with prostate, breast and ovarian cancer if on a stable dose for 21 days prior to the first dose of study drug.
* Subject may have received a veliparib regimen any time prior to C1D1.
5. Subject has received a biologic agent for anti-neoplastic intent within 30 days prior to the first dose of study drug.
6. Subject who requires parenteral nutrition, tube feeding or has evidence of partial bowel obstruction or perforation within 28 days prior to study drug administration.
7. The subject has had another active malignancy within the past 3 years except for any cancer in situ that the Principal Investigator considers to be cured.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-06-2014
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Carboplatin
Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Irinotecan Hydrochloride
Generic name:	Irinotecan hydrochloride
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Leucovorin
Generic name:	Folinic Acid
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Paclitaxel
Generic name:	Paclitaxel
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	Veliparib
Generic name:	Veliparib

Ethics review

Approved WMO Date:	12-12-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-03-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-04-2014
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-05-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-05-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-06-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-10-2014
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-12-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-08-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-08-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-09-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-003137-16-NL
ClinicalTrials.gov	NCT02033551
CCMO	NL46475.042.13