A Phase 1 Study of ABT-767 in BRCA1- or BRCA2-Mutation Carriers with Advanced Solid Tumors and in Subjects with High Grade Serous Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

Published: 04-11-2010
Last updated: 04-05-2024

The primary objective of this study is to assess the safety, tolerability, and pharmacokinetics of ABT-767 and the effect of food on ABT-767 bioavailability in subjects with BRCA1 or BRCA2 germ line mutation and associated solid tumors (e.g. breast...

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

Summary

ID

NL-OMON44086

Source
ToetsingOnline

Brief title
M10-976

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: Farmaceutische Industrie

Intervention

Keyword: BRCA-1/2 mutation, Oncology, PARP inhibitor, Phase 1

Outcome measures

Primary outcome

Efficacy: Summaries and analyses will be performed with subjects classified by dose level.

Exploratory efficacy analyses will be performed on the data collected from the expanded safety cohort portion of the study.

Pharmacokinetic: Blood samples for pharmacokinetics of ABT-767 will be collected at designated timepoints throughout the study.

Pharmacodynamic: PBMCs will be assayed for PAR levels to evaluate PARP inhibition and exploratory analysis will be performed to correlate with PK and clinical outcomes

Safety: Adverse events, laboratory profiles, physical exams, ECGs, and vital signs will be assessed throughout the study.

Secondary outcome

Not applicable.

Study description

Background summary

Animal studies have shown that ABT-767 increases the sensitivity of tumor cells so that chemotherapeutic agents are more effective in killing cancer cells and causes tumors to shrink, particularly in tumors with the BRCA1 or BRCA2 mutation. ABT-767 is a PARP inhibitor (blocker). PARP is a naturally occurring protein made by your body that may help cancer cells overcome injury or damage caused by radiation and certain types of anti-cancer drugs, making these treatments less effective. ABT-767 inhibits (blocks) the activity of PARP which may prevent the cancer cell from repairing itself.

Study objective

The primary objective of this study is to assess the safety, tolerability, and pharmacokinetics of ABT-767 and the effect of food on ABT-767 bioavailability in subjects with BRCA1 or BRCA2 germ line mutation and associated solid tumors (e.g. breast, ovarian, prostate, or pancreatic) and in subjects with high grade serous ovarian, primary peritoneal and fallopian tube cancer.

Study design

Phase 1, open-label, dose escalating study

Intervention

ABT-767 is administrated orally. In the dose escalation phase all the subjects receive their first dose ABT-767 at day -3 of cycle 1. From day 1 of cycle 1 the subjects will get a daily dose of ABT-767. Dependent on the pharmacokinetic samples the patient will receive ABT-767 as a once daily dose or a twice-daily dose.The daily dose given to a patient depends on de cohort the patient is in and can therefore differ between patients.
In the extended safety cohort 30 patients will receive the RPTD daily.

Study burden and risks

This is the first clinical study of ABT-767 in humans and no information about adverse events in humans is available. Based on preclinical data possible risk include: fewer circulating blood cells, decreased number of sperm cells, decreased bone density, changes of the thymus gland, and damage to the lining of the intestinal tract. It is not known to what extent these may occur in humans. Side effects may range from mild to life-threatening.

During screening, C1D-4, C1D1 and C1D8 and ECG will be made. At screening and

in the beginning of every odd cylce, with the exception of cycle 1, a radiographic tumor assessment will be performed.

The duration of this phase 1 study is not a fixed time point and therefor it is difficult to esstimate how often the patients will visit the hospital.

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

* Subject must be * 18 years of age.
* Subjects must have histological or cytological confirmation of locally advanced or metastatic
solid tumor, and
- a documented BRCA1 or BRCA2 mutation, OR

- high grade serous ovarian, fallopian tube, or primary peritoneal cancer.
* Subject has an Eastern Cooperative Oncology Group (ECOG) Performance status of 0 to 2.
* Subjects must have adequate hematologic, renal, and hepatic function as follows:
- Bone Marrow: Absolute neutrophil count (ANC * 1,500/mm3 (1.5 × 109/L); Platelets * 100,000/mm3 (100 × 109/L); Hemoglobin * 9.0 g/dL (1.4 mmol/L) (hemoglobin unsupported by transfusion.
- Subject has adequate renal function as demonstrated by serum creatinine value of * 1.5 × the upper limit of normal (ULN) and either an estimated creatinine clearance value of * 50 mL/min as determined by the Cockcroft-Gault formula or a creatinine clearance value of * 50 mL/min/1.73 m2 based on a 24-hour urine collections.
- Subject has adequate liver function as demonstrated by serum bilirubin * 1.5 × ULN and AST and ALT * 2.5 x ULN. For subjects with liver metastasis, AST and ALT < 5 × the ULN.
- PTT must be * 1.5 x ULN and INR < 1.5. Subjects on anticoagulant (such as Coumadin) are allowed on study and will have PTT and INR as determined by the Investigator.
* Women of childbearing potential must agree to use adequate contraception prior to study entry,
for the duration of the study participation, and for 90 days following completion of therapy. Women of childbearing potential must have a negative serum pregnancy test within 21 days prior to initiation of treatment and a negative urine pregnancy test on the first day of study drug
administration. Post-menopausal women must be amenorrheic for at least 12 months to be considered of non-childbearing potential.
Expanded Safety Cohort #1: Subjects with BRCA1 or BRCA2 Mutated
Advanced Solid Tumor
* Histologically or cytologically confirmed 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. Subjects must also have a documented deleterious BRCA1 or BRCA2
mutation.
* Subject must have at least 1 site accessible for acquisition of tumor or cell tissue via percutaneous needle, punch, or excisional biopsy to be eligible for enrollment (e.g., cutaneous or subcutaneous, palpable lymph nodes or lesions safely accessible for biopsy).
* Measurable disease, defined as at least 1 unidimensionally measurable lesion on a CT scan as defined by RECIST version 1.1.
Expanded Safety Cohort #2: Advanced ovarian cancer, with known germ line mutation of BRCA1 or BRCA2 or no mutation in BRCA1 or BRCA2. .
* Histologically or cytologically confirmed 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. Subjects must also have a known status that is either positive or negative for a documented deleterious BRCA1 or BRCA2 mutation
* Subjects with ovarian cancer and non-measurable disease with an elevation of serum CA-125 level by Gynecologic Cancer Intergroup (GCIG) criteria (baseline sample that is at least twice the upper limit of normal and within 2 weeks prior to starting treatment) may also be included.

Exclusion criteria

* Expanded cohort only: Subject has previously received a PARP inhibitor.
* Subject has received anti-cancer therapy including chemotherapy, immunotherapy, radiotherapy, biologic or any investigational therapy within a period of 28 days or 5 half lives (whichever is shorter) prior to Study Day 1.
* Subject has known CNS metastases.
* Subject has unresolved toxicities from prior anti-cancer therapy, defined as any Common Terminology Criteria for Adverse Events (CTCAE v 4.0) grade 2 or higher clinically significant toxicity (excluding alopecia).
* Subject has had major surgery within 28 days prior to Study Day 1.
* Clinically significant uncontrolled condition(s) or any medical condition which in the opinion of the study investigator places the subject at an unacceptably high risk for toxicities.
* Psychiatric illness/social situation that would limit compliance with study requirements.
* Lactating or pregnant female.

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):	17-03-2011
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Niet van toepassing
Generic name:	Niet van toepassing

Ethics review

Approved WMO Date:	04-11-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-02-2011
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-07-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-07-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-10-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	26-11-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-06-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-06-2013
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-07-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-08-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-07-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-07-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	29-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2010-020795-37-NL
CCMO	NL33609.078.10