PREVAIL: A Multinational Phase 3, Randomized, Double-Blind, Placebo-Controlled Efficacy and Safety Study of Oral MDV3100 in Chemotherapy-Naïve Patients with Progressive Metastatic Prostate Cancer Who Have Failed Androgen Deprivation Therapy

Published: 22-10-2010
Last updated: 04-05-2024

The purpose of this study is to evaluate the efficacy and safety of MDV3100, a novel potent androgen-receptor antagonist without known agonist activity, in asymptomatic or mildly symptomatic patients with progressive metastatic prostate cancer who...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON39962

Source
ToetsingOnline

Brief title
PREVAIL

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
Prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Medivation Inc
Source(s) of monetary or material Support: The Sponsor

Intervention

Keyword: Chemo-Naïve Metastatic Prostate Cancer

Outcome measures

Primary outcome

Co-Primary Objectives

• To determine the benefit of MDV3100 as compared to placebo as assessed by

overall survival;

• To determine the benefit of MDV3100 as compared to placebo as assessed by

radiographic progression-free survival (rPFS).

Secondary outcome

Key Secondary Objectives

• To determine the benefit of MDV3100 as compared to placebo as assessed by

time to first skeletal-related event;

• To determine the benefit of MDV3100 as compared to placebo as assessed by

time to initiation of cytotoxic chemotherapy.

Study description

Background summary

Worldwide, prostate cancer ranks third in cancer incidence and sixth in cancer mortality in men. Prostate cancer growth is dependent on androgens, and

depleting or blocking androgen action has been a mainstay of treatment for over 6 decades. Despite the early sensitivity of tumors to hormonal strategies, tumors that progress despite androgen deprivation generally represent a transition to the lethal variant of the illness. Once patients progress on docetaxel, there is currently no approved second line therapy and most patients ultimately succumb to this disease.

Because overexpression of the androgen receptor is a common feature of progressive prostate cancer, second generation anti-androgen therapies that are more potent and that are pure antagonists may be effective in such patients.

Study objective

The purpose of this study is to evaluate the efficacy and safety of MDV3100, a novel potent androgen-receptor antagonist without known agonist activity, in asymptomatic or mildly symptomatic patients with progressive metastatic prostate cancer who have disease progression despite androgen deprivation therapy.

Study design

The PREVAIL study is a multinational Phase 3, randomized, double-blind, placebo-controlled efficacy and safety study of oral MDV3100 (160 mg/day) in asymptomatic or mildly symptomatic patients with progressive metastatic prostate cancer who have disease progression despite androgen deprivation therapy. Patients must not have been previously treated with cytotoxic chemotherapy. Approximately 1,680 patients will be centrally randomized 1:1. Randomization will be stratified by investigative site.

Intervention

Study drug therapy (MDV3100 or placebo) is given as four oral capsules taken as one dose per day. Study drug therapy should be continued as long as the patient is tolerating the study drug and continues androgen deprivation therapy (i.e., surgical castration or ongoing gonadotropin GnRH-analogue therapy) until confirmed radiographic disease progression or a skeletal related event AND one of the two following events: 1) initiation of cytotoxic chemotherapy; or 2) initiation of an investigational agent for treatment of prostate cancer If another non-cytotoxic systemic anti-neoplastic agent is initiated, study drug therapy may be continued per the Investigator*s clinical judgment as long as the patient is tolerating the study drug and continues androgen deprivation therapy. Radiation therapy, vaccine therapy, and initiation of bisphosphonates or other approved bone targeting agents, and standard of care steroid and pain management are allowed and should not result in discontinuation of study drug therapy. Study drug should be discontinued prior to initiation of a cytotoxic

chemotherapy or another investigational agent.

Study burden and risks

A discussion was presented in section E9 of this document.

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

The inclusion criteria apply to patients receiving enzalutamide or placebo during double-blind treatment.
Eligible patients must meet all inclusion criteria.;1. Received randomized double-blind treatment in PREVAIL;

2. Open-label day 1 visit is within 6 months after this amendment is approved and becomes effective at the study site;
3. Is willing to maintain androgen deprivation therapy with a gonadotropin-releasing hormone (GnRH) agonist/antagonist or has had a bilateral orchiectomy;
4. Is able to swallow enzalutamide capsules whole and to comply with study requirements throughout the study.

Exclusion criteria

The exclusion criteria apply only to patients starting new treatment with enzalutamide after receiving placebo as randomized treatment. Each patient must NOT meet any of the following criteria:
1. Is taking commercially available enzalutamide (Xtandi);
2. Has any clinically significant cardiovascular, dermatologic, endocrine, gastrointestinal, hematologic, hepatic, infectious, metabolic, neurologic, psychological, pulmonary, or renal disorder or any other condition, including excessive alcohol or drug abuse, or secondary malignancy, that may interfere with study participation in the opinion of the investigator or medical monitor;
3. Has current or previously treated brain metastasis or active leptomeningeal disease;
4. Has a history of seizure or a condition that may increase the risk of seizure;
5. Has total bilirubin >= 1.5-times the upper limit of normal (ULN) (except patients with a diagnosis of Gilbert*s disease); alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >= 2.5-times ULN at screening. For patients with documented liver metastases, ALT and AST exclusion is > 5-times ULN;
6. Has creatinine > 2 mg/dL (177 µmol/L) at screening.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-06-2011
Enrollment:	80
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Xtandi
Generic name:	Enzalutamide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	22-10-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-03-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-04-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-05-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-04-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	01-05-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-07-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-08-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-09-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-04-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-01-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-03-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-07-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-09-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	05-12-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-12-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-08-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-01-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-08-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-11-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-03-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-08-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2010-020821-41-NL
ClinicalTrials.gov	NCT01212991
CCMO	NL33544.091.10