A Study in Japan and Ex-Japan to Characterize the Pharmacokinetic and Pharmacodynamic Response to Orteronel (TAK-700) in Chemotherapy-Naïve Patients With Castration-Resistant Prostate Cancer

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Primary objective:* To determine whether orteronel 300 mg twice daily (BID) plus prednisone 5 mg BID more effectively reduces serum testosterone levels, compared to placebo plus prednisone 5 mg BID, when administered to patients in JapanSecondary...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms male benign
Study type	Interventional

Summary

ID

NL-OMON37312

Source
ToetsingOnline

Brief title
C21013

Condition

- Reproductive neoplasms male benign
- Prostatic disorders (excl infections and inflammations)

Synonym
castrationresistant prostate cancer (mCRPC), chemotherapy-naïve, metastatic, progressive, prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Millenium Pharmaceuticals
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Castration-Resistant Prostate Cancer, Chemotherapy-Naïve, Orteronel

Outcome measures

Primary outcome

Primary endpoint:

* Percentage of patients in Japan with serum testosterone levels reduced to * 2

ng/dL after 4 weeks of treatment with orteronel 300 mg BID plus prednisone 5 mg

BID, when compared to placebo plus prednisone 5 mg BID

Secondary outcome

Secondairy endpoints:

* Percentage of ex-Japan patients with serum testosterone levels reduced to * 2

ng/dL after 4 weeks of treatment with orteronel 400 mg BID plus prednisone 5 mg

BID, when compared to placebo plus prednisone 5 mg BID

* Serum testosterone levels after 4 weeks of treatment with study drug

(orteronel plus prednisone or placebo plus prednisone) and after 12 weeks of

active treatment with orteronel plus prednisone in all treatment groups

Study description

Background summary

As a selective, nonsteroidal inhibitor of 17,20-lyase, a key intermediary in the testosterone synthesis pathway, orteronel is currently in clinical development as a treatment for men with CRPC, where persistent extragonadal synthesis of androgens in the adrenal cortex or possibly in tumor cells results in sustained tumor stimulation and progression.
This is a randomized, double-blind, placebo-controlled, multiregion study in Japan and ex Japan to characterize the PK and pharmacodynamic responses to orteronel, when administered concomitantly with prednisone, in adult men with CRPC. The primary objective of this study is to determine whether orteronel 300 mg BID plus prednisone 5 mg BID more effectively reduces serum testosterone levels, compared to placebo plus prednisone 5 mg BID, when administered to patients in Japan. Pharmacokinetic and pharmacodynamic data will be collected from patients in Japan and ex-Japan to establish an orteronel dose for patients in Japan that has similar exposure to the global dose for orteronel.
Please refer to section 1.4 of the protocol.

Study objective

Primary objective:
* To determine whether orteronel 300 mg twice daily (BID) plus prednisone 5 mg BID more effectively reduces serum testosterone levels, compared to placebo plus prednisone 5 mg BID, when administered to patients in Japan
Secondary objectives:
* To evaluate the reduction in serum testosterone levels in ex-Japan patients administered orteronel 400 mg BID plus prednisone 5 mg BID, when compared to placebo plus prednisone 5 mg BID
* To determine whether orteronel plus prednisone improves 50% prostate-specific antigen (PSA) response
* To evaluate the effect of orteronel plus prednisone on endocrine markers of pharmacodynamic response
* To characterize the pharmacokinetics of orteronel plus prednisone
* To continue to assess the safety of orteronel plus prednisone in patients with castration resistant prostate cancer (CRPC)
Exploratory objective:
* To explore the pharmacokinetic (PK) -pharmacodynamic response to orteronel plus prednisone in patients in Japan and ex-Japan

Study design

This is a double-blind, placebo-controlled, multiregion study in Japan and ex-Japan to characterize the PK and pharmacodynamic responses to orteronel when administered concomitantly with prednisone.
Following the Screening period, patients will be randomized to receive study drug (orteronel or placebo) BID in a double-blind fashion.
Serial blood and urine samples for PK analysis of the study drug and metabolite(s) will be collected at the time points specified.

At Cycle 2, Day 1, patients randomized to placebo will receive active treatment with orteronel at the initially assigned dose level. Patients already randomized to active treatment with orteronel will continue to receive their current dose level.
After completing Cycle 5, Day 1 assessments, patients may enter the follow-up portion of the study. Patients may remain on treatment at the discretion of the investigator and treated according to the standard of care, returning to the site for follow-up visits at the time points specified.

Intervention

Patients in Japan will be randomized to receive orteronel 200 mg BID, orteronel 300 mg BID, or placebo (placebo in Cycle 1 only). Ex Japan patients will be randomized to receive orteronel 200 mg BID, orteronel 400 mg BID, or placebo (placebo in Cycle 1 only). Study drug will be administered concomitantly with prednisone (or commercially available equivalent) 5 mg BID continuously throughout the study.

Study burden and risks

For a complete overview of the procedures please refer to the *schedule of events* in the protocol.
The patients will have to take the study medication and prednisone twice per day on set timepoint.
There is an extended farmacokinetic and farmacodynamic research related to this study.
Patients will be asked to complete a medication diary during the active treatment period (first 4 cycles). Herein they note the timepoint of a meal before intake of the study medication and the timepoint of intake of Orteronel and prednisone. No questionnaires will be completed.

Patients receiving Orteronel noted the following side effects:
Feeling tired, headache, high aminotransferases, decline of LVEF, itching and rash, worsening performance, worsening but controlled hypertension, episodic nausea, vomiting, diarrhea, and dehydration (see IB for more detailed about safety). Until now the identified risks related to oreteronel treatment:
nausea, vomiting, feeling tired, hypertension, rash, and androgen deprivation.

Some laboratory tests on the study drug (TAK-700) showed that one breakdown product of the study drug (TAK-700) may have activity that could cause an undesired change in the genes or chromosomes. This potential change could increase the risk of developing a secondary cancer in addition to the prostate cancer. If a genetic or chromosomal change happens in the sperm and the patient does father a baby, the change could be passed on to the child and could have an adverse effect on the developing fetus. Studies to see if this potential genetic or chromosomal change occurs in animals have not been

conducted and the effect in humans from activity of the breakdown product is not known.

Contacts

Public
Millenium Pharmaceuticals

Landsdowne Street 40
Cambridge, Masachussets MA 02139
US
Scientific
Millenium Pharmaceuticals

Landsdowne Street 40
Cambridge, Masachussets MA 02139
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Male patients 18 years or older.
2. Voluntary written consent must be given before performance of any study-related procedure not part of standard medical care, with the understanding that consent may be withdrawn by the patient at any time without prejudice to future medical care.
3. Histologically or cytologically confirmed diagnosis of prostate adenocarcinoma.
4. Prior surgical castration or concurrent use of an agent for medical castration (eg, GnRH analogue).
5. PSA * 2 ng/mL at screening.

6. Progressive disease based on PSA and/or radiographic criteria.

Exclusion criteria

1. Prior therapy with orteronel, ketoconazole, aminoglutethimide, or abiraterone.
2. Known hypersensitivity to compounds related to orteronel, orteronel excipients, prednisone (or commercially available equivalent), or GnRH analogue.
3. All antiandrogen therapy (including bicalutamide) is excluded within 4 weeks before the first dose of study drug. Any other therapies for prostate cancer, other than GnRH analogue therapy, such as progesterone, medroxyprogesterone, progestins (megesterol), or 5-alpha reductase inhibitors (eg, finasteride or dutasteride), must be discontinued 2 weeks before the first dose of study drug.
4. Continuous daily use of oral prednisone (or commercially available equivalent), oral dexamethasone, or other systemic corticosteroids for more than 2 weeks within the 3 months before screening (inhaled, nasal, and local steroids [eg, joint injection] are allowed).
5. Prior chemotherapy for prostate cancer, with the exception of neoadjuvant/adjuvant therapy as part of initial primary treatment for local disease that was completed 2 or more years before screening.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-01-2013
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Orteronel
Generic name:	Orteronel
Product type:	Medicine
Brand name:	Prednisone
Generic name:	Prednisone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-08-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-11-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-03-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-04-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-03-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-10-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-05-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-05-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-06-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2012-001539-30-NL
ClinicalTrials.gov	NCT01666314
CCMO	NL40913.060.12