A Drug-Drug Interaction, Safety and Efficacy Study With JNJ-56021927 (ARN-509) and Abiraterone Acetate in Subjects With Metastatic Castration-Resistant Prostate Cancer

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The purpose of this study is to find out how well JNJ-56021927 works when it is given along with abiraterone acetate and prednisone to treat prostate cancer. The safety of JNJ-56021927 when used with abiraterone acetate will also be studied. How...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Prostatic disorders (excl infections and inflammations)
Study type	Interventional

Summary

ID

NL-OMON44408

Source
ToetsingOnline

Brief title
DDI Study With JNJ-56021927 and Abiraterone Acetate in Prostate Cancer

Condition

- Prostatic disorders (excl infections and inflammations)

Synonym
prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Johnson & Johnson Pharmaceutical
Source(s) of monetary or material Support: Janssen Research and Development

Intervention

Keyword: Abiraterone, JNJ-56021927, Prostate Cancer

Outcome measures

Primary outcome

The primary objective is to evaluate the effect of JNJ-56021927 on steady state abiraterone pharmacokinetics in subjects with Metastatic Castration-Resistant Prostate Cancer (mCRPC) during combination treatment of JNJ-56021927 with abiraterone acetate plus prednisone.

Secondary outcome

The secondary objectives of this study are:

* To characterize the safety profile of JNJ-56021927 in combination with AAP

* To evaluate clinical efficacy of JNJ-56021927 in combination with AAP

* To characterize the pharmacokinetic (PK) profile of JNJ-56021927 when dosed in combination with AAP

Study description

Background summary

At present, there is no cure for advanced prostate cancer. The goal is to develop a treatment that will allow men with prostate cancer to live longer lives and to slow down the potential for prostate cancer spreading in your body.

Study objective

The purpose of this study is to find out how well JNJ-56021927 works when it is given along with abiraterone acetate and prednisone to treat prostate cancer. The safety of JNJ-56021927 when used with abiraterone acetate will also be studied. How long JNJ-56021927 and abiraterone acetate stay in and act on the body is also looked at and it is examined if JNJ-56021927 is influencing the concentrations of abiraterone acetate in your blood.
The safety of the combination is also investigated and potentially it will provide dosing recommendations for abiraterone acetate in future studies when combined with JNJ-56021927.

Study design

This is a multicenter, phase 1b, open-label study to investigate the interaction between JNJ-56021927 and abirateroneacetate.
All patients in this study will receive the same treatment.
Behandeling wordt voortgezet zolang de prostaatkanker niet verslechterd en zolang de onderzoeksgeneesmiddelen goed worden verdragen.

Intervention

The study will consist of a 28-day screening phase, a treatment phase and a follow-up phase.

During the screening phase the eligibility is determined.

At the start of the treatment phase all subjects will take AA and prednisone for 7 days (Cycle 1, Day 1 to Cycle 1, Day 7). Then from Cycle 1, Day 8 onwards they will proceed with the combined daily intake of AAP + JNJ-56021927. Treatment cycles will be 28 days.
A 24-hour PK profile for abiraterone will be obtained on Day 7 (Cycle 1, day 7) and on day 36 (Cycle 2, day 8). A 24-hour PK profile for JNJ-56021927 will be obtained on day 36 (Cycle 2, day 8).

All subjects will continue on study until disease progression, withdrawal of consent, lost to follow-up, or the occurrence of unacceptable toxicity. Upon discontinuation from study drug, subjects will return for an EoT visit no longer than 30 days after their last dose.

Study burden and risks

This is described in the patient information as follows:

Side effects from study drug (JNJ-56021927, abiraterone acetate or prednisone)
• You may have side effects from taking the study treatment (JNJ-56021927, abiraterone acetate and prednisone). Doctors don*t yet know all of the side effects that could happen. You will be watched carefully during this study for

any side effects.
• Sometimes during a study the Sponsor may learn new facts about the study medications/treatments. It is possible that this information might make you change your mind about being in the study. If new information is discovered, your study doctor will tell you about it right away.
• Side effects may be mild or serious. It is not possible to tell which side effect will affect you or how mild or severe the side effect might become. We can only tell you what other people have experienced. Please talk with your study doctor about these side effects.
• Tell your study doctor about any side effect, problem or unusual experience that you have while taking part in this study. This may decrease the chance that the side effect continues or becomes worse.
• Sometimes there are other medications that your study doctor can give you to make the side effect better or make you more comfortable. If a severe side effect does develop, you and your study doctor may decide it is in your best interest to stop taking part in the study.
• If you chose, you always have the right to withdraw from the study. In addition, you will be provided with the telephone numbers of people who can answer any questions about the study, your rights as a study participant and for you to report any side effects.

Side effects and Risks associated with JNJ-56021927:
At this time, around 130 patients have been treated with JNJ-56021927. Risks and side effects that may be possibly related to JNJ-56021927 include:
Likely (>10%): Fatigue, Diarrhea, Nausea, Skin rash, Abdominal pain, Changes in thyroid function
Less Likely (1- 10%): Constipation, Taste alterations, Itching, Decreased appetite, Dizziness, Hot flashes, Insomnia, Increase in blood cholesterol
Rare but serious (<1%): Tremors or seizures (only observed in animals studies)

JNJ-56021927 provides high daily doses of Vitamin E. You should not take additional vitamin E while taking this study drug. The long term effects and safety of taking high daily doses of vitamin E are not clear, but some studies have shown a higher death rate in people taking high daily doses of vitamin E. Side effects reported with vtamin E include feeling tired, headache, diarrhea, stomach cramps, nausea, weakness and blurred vision.
JNJ-56021927 is formulated in bovine-derived gelatin capsules and therefore carries a theoretical risk of transmission of bovine-associated infectious agents, including organisms associated with bovine spongiform encephalopathy which is a fatal neurological disease.

Side Effects and Risks associated with abiraterone acetate:
At present, known side effects related to abiraterone acetate include:
Frequent (>= 20%) [May occur in 20 or more patients in 100]
• edema peripheral (swelling of the legs as a result of the body keeping too much fluid)
• hypokalaemia (low blood potassium, a mineral that helps regulate heart

rate/function, fluid balance in the body and is needed for adequate body function)

Very Common (>= 10% to 19%) [May occur between 10 and 19 patients in 100]
• hypertension (high blood pressure)
• urinary tract infection

Common (> 5% to 9%) [May occur between 5 to 9 patients in 100]
• alanine aminotransferase increased (an enzyme in the blood that measures the function of the liver)
• aspartate aminotransferase increased (an enzyme in the blood that measures the function of the liver)
• dyspepsia (uncomfortable feeling in upper belly, indigestion)
• hematuria (presence of blood in the urine)
• fractures (a break in the bone)

Less Common (< 5% [May occur in fewer than 5 patients in 100]
• hypertriglyceridaemia (high levels of fats (triglycerides) in the blood)
• cardiac failure (heart failure, the heart is unable to supply enough blood flow to meet the body's needs.)
• angina pectoris (chest pain)
• arrhythmia (changes in the rhythm of the heart)
• atrial fibrillation (a fast and irregular heartbeat)
• tachycardia (rapid heartbeats)
Uncommon (< 1%) [May occur between 1 and 9 patients in 1000]
• adrenal insufficiency (decreased function of adrenal glands that normally help maintain blood pressure, balance minerals and fluid in your body)

Rare (<0.1%) [May occur between 1 and 10 patients in 10000]
• allergic alveolitis (swelling and irritation of the lung) has been reported in one patient. The patient recovered after discontinuation of abiraterone acetate.

There is a small chance of severe allergic reaction to the drug which may be life-threatening.
Abiraterone acetate may cause harm to the liver. Fewer than 10% of patients taking abiraterone acetate have had abnormal blood levels of liver enzymes. Interruption or discontinuation of the treatment with abiraterone acetate was sufficient to normalize the liver enzymes in majority of these cases. Your liver function will be monitored closely by blood tests every two weeks for the first 3 months of the study and monthly thereafter. If elevations in your liver function enzymes are observed, the dose of your study medication will be adjusted or discontinued.
Abiraterone acetate should be used with caution in patients with a history of heart disease. Before treatment with abiraterone acetate, high blood pressure must be controlled and low potassium must be corrected. Potassium is needed for proper function of your heart, and other essential body systems.

It is important that you contact your study doctor right away if you cannot come to your regularly scheduled visit or get your blood tests. This is because some patients have no symptoms when their blood potassium is low. Contact your study doctor immediately if:
• You feel weak; have constipation, muscle pain, or cramps. These symptoms may be caused by low blood potassium.
• Your appetite decreases, or if you develop diarrhea. Potassium may become low if you are not eating well, or is lost through diarrhea.

Side Effects, and Risks Associated with Prednisone
Prednisone is given with abiraterone acetate to reduce or stop some of the side effects of abiraterone acetate, such as high blood pressure, low blood potassium, and swelling of the legs.
You should tell the study doctor if you have ever had a reaction to prednisone. You may ask your doctor for printed information about prednisone and the potential side effects (this is called a package insert).
• Prednisone is a type of drug called a corticosteroid. Corticosteroids can weaken your body*s ability to fight off infection, and can make infections hard to diagnose or treat. If you develop fever, or suspect you have an infection, you should alert your study doctor right away.
• Other side effects caused by corticosteroids are:
• Fluid retention
• Stomach bleeding
• Indigestion
• Seizures
• Swelling of the brain
• Emotional changes
• Mood swings or severe depression
• Eye problems such as cataracts or glaucoma
• Insomnia (sleeplessness, wakefulness)
• Elevated blood sugar (for diabetics, this can make your glucose level more difficult to control)
• Increased blood calcium (extra calcium is stored in your bones or passed out of your body in urine and stool).
Possible risks associated with long term use of corticosteroids:

Cushing*s syndrome: Taking corticosteroids over a long period of time can cause a condition called Cushing*s syndrome. Symptoms of Cushing*s syndrome include:
• Weight gain
• Muscle weakness
• A moon-faced appearance
• Thin, fragile skin
• Brittle bones
• Purplish stripe marks on the skin

Adrenal insufficiency may occur due to long term use of steroid medicines taken orally. It can be life threatening at times of major illness and extreme

physical stress. Symptoms of adrenal insufficiency include:
• Weakness and fatigue
• Low blood pressure
• Nausea
• Vomiting
• Diarrhea
• Irritability and/or restlessness

Prednisone should never be stopped suddenly. If you need to stop your doctor will advise on how to slowly cut down the dose and stop the drug. If you were to stop taking prednisone suddenly you could have:
• Weakness and tiredness
• Very low blood pressure
• Very low blood sugar
• Abnormal blood minerals

While these reactions are usually not severe, they are potentially fatal if not treated.
Side effects from tests:
• Blood draw: Taking blood may cause bruising at the place where the needle goes into the skin. Fainting, and in rare cases infection, may occur.
• ECG Risk: There is generally no risk with having an ECG. The sticky patches may pull your skin or cause redness or itching.
• CT and bone scan Risk: CT scans and bone scan do create low levels of radiation, which has a small potential to cause cancer and other defects. However, the risk associated with any one scan is small.

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

1. Men >= 18 years of age or older (inclusive).;2. Eastern Cooperative Oncology Group (ECOG) performance status <=2;3. Histologically or cytologically confirmed adenocarcinoma of the prostate.;4. Metastatic disease documented by positive bone scan, or visceral metastasis, or lymph;node disease documented on CT or MRI scans;5. Prostate cancer progression documented by PSA progression according to;PCWG2 or by appearance of new bone lesions on radionuclide bone scan;according to PCWG2 or by radiographic progression according to mRECIST 1.1;6. Surgically or medically castrated, with testosterone levels of < 50 ng/dL (< 1.7 nM). If;the subject is being treated with GnRH analogs (subject who has not undergone bilateral;orchiectomy), this therapy must have been initiated at least 4 weeks prior to Cycle 1 Day 1 and must be continued throughout the study;7. Resolved any acute toxicity to Grade <=1 (except alopecia or Grade <= 2 neuropathy) due;to prior chemotherapy or radiotherapy;8. Bone sparing therapies (eg, bisphosphonates, denosumab) usage is allowed if subjects;are on a stable dose for at least 4 weeks prior to Cycle 1, Day 1;9. Adequate bone marrow and organ function defined as: Hemoglobin >=9.0 g/dL, independent of transfusion and/or growth factor support; ANC count >=1,500 cells/mm3 independent of growth factor support within the prior 3 months; Platelet count >=75,000/µL independent of transfusion and/or growth factor;support within the prior 3 months; Serum albumin >=3.0 g/dL;Serum creatinine <1.5 × upper limit of normal (ULN) or calculated creatinine;clearance >= 50 mL/min/1.73m2; Serum potassium >= 3.5 mmol/L; Total bilirubin < 1.5 × ULN (Subjects with Gilbert*s Syndrome may be enrolled;if the total bilirubin is < 3 mg/dL with predominance of indirect bilirubin); Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) <= 2.5 ×;ULN; Electrocardiogram showing QTc <= 480 msec;10. Any number of prior hormonal interventions [including 1st generation antiandrogens;(flutamide, bicalutamide, nicalutamide), CYP17 inhibitors (eg AA), 2nd generation;androgen antagonists (e.g. enzalutamide), steroids, estrogens, finasteride, dutasteride];for PC are allowed. These therapies, except for GnRH analogs, must have been;discontinued for minimally 4 weeks before first dose of study drug. Enzalutamide must;have been discontinued for minimally 8 weeks before first dose of study drug.;11. Ability to swallow study drug whole as a capsule/tablet;12. A man who is heterosexually active with a woman of childbearing potential

must agree;to use a double barrier method of birth control such as a condom along with another;effective contraceptive method [partner using occlusive cap (diaphragm or;cervical/vault caps) with spermicidal foam/gel/film/cream/suppository, contraceptive pill, contraceptive patch, IUD, tubal ligation or status post hysterectomy)]. All men;must also not donate sperm during the study and for 3 months after receiving the last;dose of study drug;13. Each subject must sign an informed consent document indicating that they understand;the purpose of and procedures required for the study and are willing to participate in the;study

Exclusion criteria

Any potential subject who meets any of the following criteria will be excluded from participating;in the study.;1. Known brain metastases;2. Pathological finding consistent with small cell carcinoma of the prostate;3. Administration of an investigational agent within 4 weeks of Cycle 1 Day 1;4. Chemotherapy, or immunotherapy for the treatment of PC within 4 weeks of Cycle 1 day 1;5. Therapies that must be discontinued or substituted at least 4 weeks prior to Cycle 1 Day 1 include the following: Medications known to lower the seizure threshold (see Section 8.3); Herbal and non-herbal products that may decrease PSA levels (ie, saw palmetto, pomegranates or pomegranate juice); Medications known to induce drug metabolizing enzymes such as dexamethasone, rifampicin, carbamazepine, phenytoin, phenobarbital, St. John*s;wort, etc. (see Section 8.3); Potent inhibitors of CYP3A4 (see Section 9.3);6. Subjects currently treated with spironolactone;7. Subject has known allergies, hypersensitivity, or intolerance to prednisone or the excipients of prednisone, AA or JNJ-56021927 (refer to Investigator's Brochures for AA and JNJ-56021927 and package insert for Prednisone) ;8. Known hypersensitivity to Vitamin E;9. History of seizures or presence of a condition that may pre-dispose to seizure (eg, prior;stroke within 1 year prior to Cycle 1 Day 1, brain arteriovenous malformation,Schwannoma, meningioma, or other benign CNS or meningeal disease, which may require treatment with surgery or radiation therapy);10. Any prior malignancy (other than adequately treated basal cell or squamous cell skin;cancer, superficial bladder cancer, or any other cancer in situ currently in complete;remission) within 3 years prior to Cycle 1 Day 1;11. History or evidence for any of the following: severe or unstable angina or myocardial;infarction within 12 months prior to Cycle 1 Day 1, symptomatic congestive heart failure, arterial or venous thromboembolic events (eg, pulmonary embolism, cerebrovascular accident including transient ischemic attacks), clinically significant;ventricular arrhythmias or New York Heart Association (NYHA) Class III to IV heart disease;12. Presence of uncontrolled hypertension (systolic BP >= 160 mmHg or diastolic BP >= 100;mmHg). Subjects with a history of hypertension are allowed, provided that BP is;controlled to within these limits by anti-hypertensive treatment;13. Presence of gastrointestinal disorder affecting absorption;14. History or evidence for adrenal insufficiency or hyperaldosteronism;15. Active infection (eg, human immunodeficiency virus [HIV] or viral hepatitis) or other;medical condition that would make prednisone (corticosteroid) use contraindicated;16. Any chronic medical condition requiring a higher dose of corticosteroid than 10 mg;prednisone daily within 4 weeks prior to Cycle 1 Day 1 and up to Cycle 2 Day 8;17. Subject has any condition for which, in the opinion of the investigator, participation;would not be in the best interest of the subject (eg, compromise the well-being)

or that;could prevent, limit, or confound the protocol-specified assessments;18. Subject is an employee of the investigator or study site, with direct involvement in the;proposed study or other studies under the direction of that investigator or study site, as;well as family members of the employees or the investigator.

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):	15-10-2014
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N.Ap.
Generic name:	JNJ-56021927
Product type:	Medicine
Brand name:	Predinsone Acis
Generic name:	Prednisone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Zytega
Generic name:	Abiraterone Acetate
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	02-07-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-10-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-03-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-04-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-06-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-06-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-08-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	17-09-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-02-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-02-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-10-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-10-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-02-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-03-2017
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	EUCTR2014-001426-14-NL
CCMO	NL49397.078.14