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Study investigating intravenously administrated Oncocort in patients with metastatic prostate cancer

Submission date	Recruitment status	[_] Prospectively registered
20/12/2019	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
02/01/2020	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
23/08/2021	Cancer	

Plain English summary of protocol

Background and study aims
Prostate cancer can develop when cells in the prostate start to grow in an uncontrolled way. Castration-resistant prostate cancer (CRPC) is prostate cancer that keeps growing even when the amount of testosterone in the body is reduced to very low levels. Corticosteroids (such as dexamethasone) have demonstrated activity in men with CRPC. Corticosteroids, often known as steroids, are an anti-inflammatory medicine prescribed for a wide range of conditions. They're a man-made version of hormones normally produced by the adrenal glands (two small glands that sit on top of the kidneys).
A liposomal formulation of dexamethasone may be more effective in fighting cancer. Liposomes are small lipid particles, the drug is encapsulated in the liposomes. The purpose of a liposomal formulation is to prolong the exposure to dexamethasone and to target the cancer sites, as these sites absorb and break down the particles in a different manner compared to other tissues.

The aim of this study is to investigate the effects of two different dosing strategies with a liposomal formulation of dexamethasone.

Who can participate?
Adult male patients with castration-resistant, metastatic prostate cancer, for whom no other treatment options remain except corticosteroid use.

What does the study involve?
Patients are treated for ten weeks with intravenous administrations of a liposomal formulation of dexamethasone.

What are the possible benefits and risks of participating?
Although there is no currently proven benefit for participating patients, it is thought that liposomal formulation of dexamethasone may reduce corticosteroid side effects and may have an inhibitory effect on tumour growth in patients with mCRPC, possibly delaying disease progression.

Where is the study run from?
Centre for Human Drug Research, The Netherlands

When is the study starting and how long is it expected to run for?
March 2017 to August 2019

Who is funding the study?
Enceladus Pharmaceutical, The Netherlands

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2016-003121-42

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CHDR1635

Study information

Scientific Title
A Phase I-IIa, open-label, single-center, dose-escalating study to evaluate the safety, pharmacokinetics and pharmacodynamics of intravenous pegylated liposomal dexamethasone sodium phosphate as monotherapy in patients with castration-resistant metastatic prostate cancer

Study objectives
The objective of the study is to determine the safety, tolerability, pharmacokinetics and pharmacodynamic effects of liposomal dexamethasone (Oncocort™) in patients with metastatic prostate cancer

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/11/2016, Stichting Beoordeling Ethiek Biomedisch Onderzoek (Ethics and Biomedical Research Review Board) (Dr. Nassaulaan 10, 9401 HK Assen, The Netherlands; tel not provided; email not provided), ref: n/a

Study design
Exploratory monocentre open-label prospective stage I-IIa dose-escalating study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Castration-resistant metastatic prostate cancer

Interventions
Intravenous pegylated liposomal dexamethasone sodium phosphate

Part A (patients 1-5): doses of 10 and 20 mg, dosing of 10 mg on day 1, dosing of 20 mg on days 8, 22, 36, 50 and day 64. Duration of infusion was 2.5 hours, drug administration started at a rate of 0.05 mL/minute over the first 40 minutes. The infusion rate was increased to 0.5 mL/min for the next 20 minutes and was then increased to 5 ml/min onwards

Part B (patients 6-10): 18.5 mg on days 1, 8, 15, 22, 29, 36, 43, 50, 57, 64. The duration of infusion was 2.5 hours, drug administration started at a rate of 0.05 mL/minute over the first 40 minutes. The infusion rate was increased to 0.5 mL/min for the next 20 minutes and was then increased to 5 ml/min onwards

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Intravenous pegylated liposomal dexamethasone sodium phosphate

Primary outcome measure
Safety and tolerability
1. Blood chemistry and haematology and Vital signs:
1.1. Heart rate (bpm),
1.2. Systolic and diastolic blood pressure (mmHg),
1.3. Breath frequency (breaths per minute), and
1.4. Temperature (degrees Celsius) are assessed for clinically significant abnormalities.
Measurements are taken at screening (up to -28 days before the first dose) and at follow-up (10 weeks after study start). For participants in part A it is measured on days 1, 2, 5, 8, 9, 12, 22, 36, 50, 64, and participants in part B on days 1, 2, 4, 8, 9, 12, 15, 22, 29, 36, 43, 50, 57, 64.
1.5. ECGs are made and assessed for clinically significant abnormalities at screening and follow-up and for participants in part A on days 1, 2, 5, 8, 9, 12, 22, 36, 50, 64, and participants in part B on days 1, 2, 4, 8, 9, 12, 15, 22, 29, 36, 43, 50, 57, 64.
2. Routine laboratory assessments are measured, by assessment of blood chemistry (Sodium, chloride, potassium, calcium, inorganic phosphate, total protein, albumin, total cholesterol, triglycerides, glucose, creatinine, uric acid, total bilirubin2, alkaline phosphatase, AST, ALT, gamma-GT and LDH) and haematology:
2.1. Haemoglobin
2.2. Mean Corpuscular volume (MCV)
2.3. Mean corpuscular haemoglobin (MCH)
2.4. Mean corpuscular haemoglobin concentration (MCHC)
2.5. Haematocrit
2.6. Red cell count (RBC)
2.7. Total white cell count (WBC)
2.8. Leukocyte differential count
2.9. Platelet count
2.10. Differential blood count, including: basophils, eosinophils, neutrophils, lymphocytes, and monocytes.
These laboratory outcomes are measured for participants in part A on days 1, 2, 5, 8, 9, 12, 22, 36, 50, 64, and participants in part B on days 1, 2, 4, 8, 9, 12, 15, 22, 29, 36, 43, 50, 57, 64

Secondary outcome measures
Pharmacokinetics and pharmacodynamics of liposomal dexamethasone (Oncocort™) in patients with metastatic prostate cancer from baseline to end of study.

1. Pharmacokinetic endpoints:
PK is measured by blood sampling at baseline, 1h, 2h, 3h, 4h, 6h, 8h, 12h, 24h, 48h and 96 hours after dosing on days 1 and 8. In addition, patients in Part B have a pre-dose sample on days 12, 15, 22, 29, 36, 43, 50, 57, 64. From these samples, the serum concentrations of dexamethasone and dexamethasone phosphate were measured
2. Pharmacodynamic effect endpoints:
Pharmacodynamic effects are measured by:
2.1. Comprehensiveness of bone metastases as assessed in scintigraphy/CT at 10 weeks compared to baseline
2.2. Complement activation at baseline, after 24 hours and pre-dose on day 8

2.3. PSA, cortisol, sex steroids, fasted glucose, lymphocyte count, at screening and follow-up and on days 1, 22, 36, 50

Overall study start date
01/12/2016

Completion date
09/08/2019

Eligibility

Key inclusion criteria
1. Adult patients with mCRPC and one or more metastases in the bone, confirmed by bone scintigraphy, MRI or CT-scan within 6 weeks before first dosage
2. Able to participate, and willing to give written informed consent and to comply with the study restrictions
3. Body mass index (BMI) of 18 kg/m2 or higher (inclusive) and a minimum weight of 50 kg
4. Not yet, or no longer eligible for other, registered therapy other than glucocorticoids
5. Live expectancy in good clinical condition (WHO 0-1) for more than 3 months

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
10

Total final enrolment
9

Key exclusion criteria
1. Concomitant disease or condition that could interfere with, or for which the treatment might interfere with, the conduct of the study, or that would, in the opinion of the investigator, pose an unacceptable risk to the patient
2. Contraindication for glucocorticoids as judged by clinician or investigator
3. Use of systemic glucocorticosteroids within 4 weeks before first dosage, with exception of topical and inhalation steroids
4. Any confirmed and clinically significant allergic reactions (urticaria or anaphylaxis, non-active hay fever is acceptable). Allergy or hypersensitivity against any drug, including any component of the study drug, biologic therapy or IV radiocontrast agent
5. Clinically significant abnormalities, as judged by the investigator, following a detailed medical history, a physical examination including vital signs, 12-lead ECG and laboratory test results

(including hepatic and renal panels, complete blood count, chemistry panel and urinalysis). In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant
6. History or symptoms of any significant disease including (but not limited to) neurological, psychiatric, endocrine, cardiovascular, respiratory, gastrointestinal, hepatic, or renal disorder that may aggravate due to study participation and jeopardize the health status of the patient
7. Any infection within 1 month prior to drug administration
8. Positive Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening
9. History of alcohol or substance abuse
10. Use of CYP3A4-inhibiting drugs or food (grapefruit, grapefruit juice, grapefruit-containing products, Seville oranges, or pomelo-containing products, and quinine containing drinks within 14 days prior to dosage
11. Participation in an investigational drug or device study within 3 months prior to screening
12. Donation of blood over 500 mL within three months prior to screening
13. Vaccination within 6 weeks prior to start of treatment or planned vaccination up to 90 days after the final dose
14. Unwillingness or inability to comply with the study protocol for any other reason
15. Expected fulminant progression of disease

Date of first enrolment
16/03/2017

Date of final enrolment
01/10/2018

Locations

Countries of recruitment
Netherlands

Study participating centre
Centre for Human Drug Research
Zernikedreef 08
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Sponsor information

Organisation
Enceladus Pharmaceuticals (Netherlands)

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Sponsor type
Industry

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ROR
https://ror.org/05h13e956

Funder(s)

Funder type
Industry

Funder Name
Enceladus Pharmaceutical

Results and Publications

Publication and dissemination plan
The researchers plan to publish the results of this study in 2020.

Intention to publish date
01/04/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		20/08/2021	23/08/2021	Yes	No