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A preliminary study of the safety, immunogenicity and clinical efficacy of TroVax® given in conjunction with interleukin 2 (IL-2) in the treatment of stage IV renal cell cancer

Submission date
16/10/2008

Recruitment status
No longer recruiting

Registration date
10/11/2008

Overall study status
Completed

Last Edited
01/02/2019

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00083941

Secondary identifying numbers
TV2Renal

Study information

Scientific Title
Phase II trial of Modified Vaccinia Ankara (MVA) virus expressing 5T4 and high dose Interleukin-2 (IL-2) in patients with metastatic renal cell carcinoma.

Study objectives
To determine the safety of TroVax® administered to renal cancer patients alongside interleukin 2 (IL-2).

Ethics approval required
Old ethics approval format

Ethics approval(s)
This study was approved by the Columbia University Institutional Review Board on 08/18/2004 (ref: A0805).

Study design
Interventional phase II open-label single-arm trial

Primary study design
Interventional

Secondary study design
Other

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Renal cancer

Interventions
Patients complying with the entry criteria will be invited to enter the study. After giving fully informed consent, patients will be subjected to a medical history and physical examination to document general fitness to proceed with the trial. Previous exposure to small pox vaccine will be noted. The diagnosis should be confirmed histologically from the patient's records. If possible, a retained sample will be obtained to stain for 5T4. If a fresh sample is taken, it may be cryopreserved and also examined for 5T4. At that time, metastases will be documented using relevant CT scans (chest, abdomen, pelvic). An MRI scan of the brain will be obtained. A cardiac stress test and pulmonary function tests will be obtained in appropriate patients.

Blood will also be drawn for haematology and clinical chemistry, full blood count with differential white cell and platelet counts, urea and electrolytes, liver function tests (total bilirubin, AST, ALT, GGT, alkaline phosphatase), serum proteins, calcium, phosphate, glucose and creatinine), pituitary hormone screen (ACTH, TSH, LH, FSH), antinuclear and anti-skeletal muscle antibodies and immunological testing (antibodies to 5T4 and vector, cellular responses to 5T4; 100 ml). In potentially fertile women, a pregnancy test will be obtained. A urine sample will be obtained for urinalysis for protein and blood. This screen should not occur more than two weeks before the immunisation schedule begins.

At week 0, the patients will be immunised with a single intramuscular injection of 1 ml of TroVax® 10x. This dose will be given without IL-2. Then, every three to four weeks for four injections, TroVax® will be given in the morning. These doses may be given in conjunction with IL-2. Immediately before each injection, blood will be drawn for immunological testing (100 ml). Before the injection, blood will also be drawn for clinical pathology (full blood count and clinical chemistry). A urine sample will be obtained for urinalysis for protein and blood.

IL-2 will be given intravenously (IV) in a dose of 600,000 IU/kg every eight hours for up to 15 injections in each cycle. The first dose will be given in the afternoon of the same day as the second TroVax® injection. These cycles of TroVax® and IL-2 will be repeated every 3-4 weeks depending upon patient tolerance and clinical response. Cycles of IL-2 will always commence in the afternoon after TroVax® has been given in the morning. If IL-2 is not tolerated, it may be suspended but treatment with TroVax® will be continued so long as it is well tolerated. TroVax® may be given for up to three months (i.e. injection 5) to patients with progressive disease so long as no other anticancer treatment (i.e. chemotherapy, interferon alpha or radiotherapy) is considered indicated for them.

CT scans (chest abdomen, pelvis) will be obtained to restage the disease at weeks 9-10 and 15-16 (i.e. after two and four doses of IL-2 and/or 3 and 5 doses of TroVax®).

A blood sample for immunological testing (100 ml) will be obtained three and eight weeks after the fifth TroVax® injection (4 and 5 months).

Following the CT scan at 15-16 weeks patients will be followed at three monthly intervals, commencing at six months. Patients whose disease is progressing at this point may not be treated further with TroVax® but may be kept on study and observed at three monthly intervals. Patients whose disease has stabilised or responded will be offered three further injections of TroVax® at months 6, 9 and 12. Patients whose disease progresses or who experience serious or severe adverse events related to TroVax® will stop treatment with TroVax® but may be kept on study and reviewed at three monthly intervals. If the patient requires further treatment with established anticancer agents, these will be recorded in the CRF.

At each visit, from week 12 to month 12, regardless of disease status, blood will be obtained (prior to the injection of TroVax®, if indicated) for clinical pathology, pituitary hormone screen, autoantibodies and immunological testing (100 ml). A urine sample will be obtained for urinalysis for protein and blood. The disease will be restaged using CT scans (chest abdomen, pelvis).

When TroVax® is being administered, patients will return 3 weeks after each TroVax® injection for immunological testing (100 ml).

After month 12, patients will return at three monthly intervals for a further 12 months. At each visit, the disease will be restaged using CT scans (chest abdomen, pelvis) in accordance with

current institutional guidelines. Blood (100 ml) will be obtained for immunological testing, autoantibodies and pituitary function tests. A urine sample will be obtained for urinalysis for protein and blood. Patients, who at the end of this period, have stable or responding disease may be followed at three monthly intervals until disease progression occurs.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
TroVax®

Primary outcome measure
Safety:
1. To assess the safety and tolerability of TroVax® injections when given as a therapeutic vaccine to patients with metastatic renal cell cancer. Safety was assessed for a maximum of 24 months or however long the patients remained on study.
2. To assess the immune responses induced by treatment with TroVax®. Immunology was assessed throughout the protocol for a maximum of 24 months or until the patient came off the study.

Secondary outcome measures
Efficacy:
The following were assessed using computerised tomography (CT) scans at baseline, Week 10, 16 and then every 3 months up to 24 months or as long as the patient remained on study:
1. Tumour response rates
2. Time to disease progression
3. Two year survival

Overall study start date
01/01/2004

Completion date
11/07/2008

Eligibility

Key inclusion criteria
1. Both males and females, aged 18 years or more
2. Metastatic renal clear cell adenocarcinoma, histologically proven by biopsy of the primary tumour and/or a metastasis. If a fresh specimen is obtained for diagnostic purposes, it may be frozen and stained for 5T4. Prior nephrectomy is not required.
3. Requiring treatment with IL-2 and able to tolerate a high dose schedule per institutional standards
4. Performance status (Eastern Cooperative Oncology Group [ECOG]) 0 or 1
5. Expected survival longer than three months
6. No clinically active autoimmune disease
7. Total white cell count d 3 x 10^9/l

8. Platelet count d 90,000/mm^3
9. Serum creatinine 1.6 mg/dl or less
10. Total bilirubin 1.6 mg/dl or less
11. Serum aspartate aminotransferase (AST)/alanine aminotransferase (ALT) T three times the upper limit of normal or 5 times upper limit of normal if liver metastases are present
12. Able to give written informed consent and to comply with the protocol
13. Women must be either post menopausal, rendered surgically sterile or practising a reliable form of contraception (hormonal, intrauterine device or barrier). Men must practise an effective form of birth control, such as barrier protection.
14. Normal cardiac stress test if the patients are older than 50 years of age or have symptoms of cardiac disease
15. Normal pulmonary function tests if the patient is a smoker or is known to have primary lung disease

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
25

Key exclusion criteria
1. Pregnancy, lactation or lack of effective contraception in fertile men and women of childbearing potential
2. Intercurrent serious infections within the 28 days prior to entry to the trial
3. Known to be HIV positive because HIV infection can lead to serious adverse events with vaccination and/or high-dose IL-2
4. Life threatening illness unrelated to cancer
5. Cerebral metastases
6. History of allergic response to previous vaccinia vaccinations
7. Participation in any other clinical trial within the previous 30 days
8. Previous malignancies within the last two years other than successfully treated squamous carcinoma of the skin or in situ carcinoma of the cervix treated with cone biopsy
9. Previous history of major psychiatric disorder requiring hospitalisation or any current psychiatric disorder that would impede the patient's ability to provide informed consent or to comply with the protocol
10. Corticosteroids unless used as an antiemetic
11. Family contact with active eczema, exfoliative skin disorder, pregnancy or other cause of immunocompromise

Date of first enrolment
01/01/2004

Date of final enrolment
11/07/2008

Locations

Countries of recruitment
United States of America

Study participating centre
New York-Presbyterian Hospital/Columbia
New York
United States of America
10032

Sponsor information

Organisation
Oxford BioMedica (UK)

Sponsor details
The Medawar Centre
The Oxford Science Park
Oxford
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OX4 4GA

Sponsor type
Industry

Website
http://www.oxfordbiomedica.co.uk

ROR
https://ror.org/03dp0vf82

Funder(s)

Funder type
Industry

Funder Name
Oxford BioMedica (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	07/01/2009	01/02/2019	Yes	No