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An international, randomised, double-blind, placebo-controlled, parallel group study to investigate whether a minimum of three doses of TroVax®, added to first-line standard of care therapy, prolongs the survival of patients with locally advanced or metastatic clear cell renal adenocarcinoma

Submission date
30/03/2006

Registration date
18/04/2006

Last Edited
11/04/2019

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Cancer

[X] 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

ClinicalTrials.gov (NCT)

NCT00397345

Protocol serial number
TV3/001/06

Study information

Scientific Title
An international, randomised, double-blind, placebo-controlled, parallel group study to investigate whether a minimum of three doses of TroVax®, added to first-line standard of care therapy, prolongs the survival of patients with locally advanced or metastatic clear cell renal adenocarcinoma

Acronym
TRIST

Study objectives
To investigate whether a minimum of three doses of TroVax, when added to the standard of care for locally advanced or metastatic clear cell renal adenocarcinoma prolong surival

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
International, randomised, double-blind, placebo-controlled, parallel group study

Primary study design
Interventional

Study type(s)
Quality of life

Health condition(s) or problem(s) studied
Locally advanced or metastatic clear cell renal adenocarcinoma

Interventions
Dosing with TroVax via intramuscular injections into the upper arm muscle versus placebo

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Trovax

Primary outcome(s)

Primary efficacy endpoints:
1. The survival event rate ratio in the TroVax arm versus the placebo in the modified intent to treat population based on the log of the hazard ratio derived from the Cox proportional hazards regression model. A Bayesian monitoring approach will be used for evaluating the event ratio.

The key objective of this study is to determine whether TroVax® is able to prolong survival in patients receiving first line standard of care if given sufficient time to induce an immune response. Prior studies indicate that three injections of TroVax® reliably induced an immune response to the 5T4 tumour antigen in almost all patients. In phase II studies, no patients discontinued treatment because of failure to tolerate TroVax®. In the event that any patient in this study does discontinue study medication before the third injection of TroVax® or placebo it will be assumed that they received the maximum tolerated number of injections and those patients will be included in the analysis of the primary objective.
All randomised patients who receive three injections of TroVax®/placebo or who cannot tolerate three injections will be included in this modified intent to treat analysis.
A confirmatory analysis will also be carried out using the intent to treat (ITT) population (and is included as a secondary endpoint).
Analysis is triggered by a predetermined number of deaths occurring after the third injection of TroVax® or placebo in the study population or when specified by an independent Data Safety Monitory Board based on analyses of interim data. (Deaths occurring before the third injection of TroVax® or placebo will not be included in the number triggering the primary efficacy analysis unless attributed by the investigator to TroVax® or placebo.)

Primary safety endpoints:
1. The number of adverse events (serious and non-serious) in the intent to treat population in the TroVax® versus the placebo arm
2. The laboratory variables (complete blood count and chemistry panel) in the intent to treat population in the TroVax® versus the placebo arm

Key secondary outcome(s))

1. The proportion of patients in the TroVax versus placebo arms in the modified intent to treat population with progression-free survival at 26 weeks based on a comparison of baseline and week 26 (+/- 1 week) radiological data and using response evaluation criteria in solid tumors (RECIST) criteria. Data will be adjudicated (blinded peer review).
2. The survival event rate ratio in the intent to treat population in the TroVax® versus the placebo arm, based on the log of the hazard ratio derived from the Cox proportional hazards regression model
3. Tumour response rates according to the investigators reported interpretation of the radiological reports based on RECIST criteria observed in the modified intent to treat population
4. The quality of life score for TroVax versus placebo as measured by quality of life questionnaire core 30 items (QLQ30) and EuroQoL questionnaires in the intent to treat and per protocol populations

Immunology endpoint:
1. Anti-5T4 antibody levels (additional measures of immune response including specific measures of cellular response will be investigated at some centres. Each will be the subject of a separate related protocol and informed consent for specific study sites and will be conditional upon regulatory and Institutional Review Board (IRB) or Ethics Committee approval before implementation).

Completion date
01/09/2009

Eligibility

Key inclusion criteria
1. Signed informed consent. The patient must be competent to give written informed consent and comply with the protocol requirements.
2. Locally advanced or metastatic, histologically proven clear cell renal carcinoma
3. Primary tumour surgically removed (some residual advanced primary tumour may remain)
4. At least four weeks post surgery or radiotherapy
5. First-line. No prior therapy for renal cancer except surgery or radiotherapy
6. Measurable disease
7. Aged 18 years or more
8. Patient expected to survive a minimum of 12 weeks (i.e. in the opinion of the investigator there is a >90% probability that the patient will survive >12 weeks if treated with the selected standard of care)
9. Free of clinically apparent autoimmune disease (including no prior confirmed diagnosis or treatment for autoimmune disease including systemic lupus erythematosis, Graves disease, Hashimotos thyroiditis, multiple sclerosis, insulin-dependant diabetes mellitus or systemic (non-joint) manifestations of rheumatoid disease)
10. Total white cell count ≥3 x 10^9 /l and lymphocyte count ≥1 x 10^9 /l
11. Serum creatinine ≤1.5 times the upper limit of normal
12. Bilirubin ≤2 times the upper limit of normal and a serum glutamic pyruvic transaminase (SGPT) of ≤4 times the upper limit of normal
13. Women must be either post menopausal, or rendered surgically sterile or, if of child bearing potential, must have been practising a reliable form of contraception (oral contraception and barrier method) for at least three months prior to the first dose of TroVax® and must continue while they are being treated with TroVax®. Men must practise a reliable form of contraception (barrier or vasectomy) while they are being treated with TroVax®.
14. No acute changes on 12-lead electrocardiogram (ECG)
15. Ejection fraction documented as not less than 45% or no clinical suspicion that cardiac ejection fraction is less than 45%. (If clinical suspicion exists the ejection fraction should be measured according to local site procedures).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria

1. Cerebral metastases. (Known from previous investigations or clinically detectable)
2. Previous exposure to TroVax®
3. Serious infections within the 28 days prior to entry to the trial
4. Known to test positive for human immunodeficiency virus (HIV) or hepatitis B or C
5. Life threatening illness unrelated to cancer
6. History of allergic response to previous vaccine vaccinations
7. Known allergy to egg proteins
8. Known hypersensitivity to neomycin
9. Participation in any other clinical trial of a licensed or unlicensed drug within the previous 30 days or during the course of this trial
10. Previous malignancies within the last 10 years other than successfully treated squamous carcinoma of the skin or in situ carcinoma of the cervix treated with cone biopsy
11. Previous history of major psychiatric disorder requiring hospitalization or any current psychiatric disorder that would impede the patients ability to provide informed consent or to comply with the protocol
12. Oral corticosteroid use unless prescribed as replacement therapy in the case of adrenal insufficiency
13. Ongoing use of agents listed in locally approved prescribing information as causing immunosuppression
14. Prior history of organ transplantation
15. Pregnancy or lactation

Date of first enrolment
01/09/2006

Date of final enrolment
01/09/2009

Locations

Countries of recruitment
United Kingdom

Belgium

France

Germany

Israel

Netherlands

Poland

Romania

Russian Federation

Spain

Switzerland

Ukraine

United States of America

Study participating centre
Genitourinary Oncology Clinic
Houston
United States of America
77030

Sponsor information

Organisation
Oxford BioMedica

ROR
https://ror.org/03dp0vf82

Funder(s)

Funder type
Industry

Funder Name
Oxford BioMedica UK Ltd.

Results and Publications

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	15/11/2010	26/02/2019	Yes	No
Plain English results				No	Yes