National Horizon Scanning Centre

TroVax (MVA-5T4) for locally advanced or metastatic renal cell carcinoma – with first line therapy

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The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
TroVax (MVA-5T4) for locally advanced or metastatic renal cell carcinoma – with first line therapy

Target group
- Clear cell renal adenocarcinoma: locally advanced or metastatic - in combination with first-line therapy.

Technology description
TroVax (MVA-5T4) is a therapeutic cancer vaccine designed to stimulate a patient’s immune system to recognise and destroy cancer cells. The vaccine targets the tumour antigen 5T4 (Oxford BioMedica Antigen 1; OBA1), which is broadly expressed in a wide range of solid tumours, but not on normal adult tissues. The product consists of an engineered poxvirus (modified vaccine Ankara MVA) that produces the 5T4 protein, and induces an anti-5T4 immune response in patients. The immune response is expected to eliminate tumour cells expressing 5T4.

In the phase III trial TroVax is administered by intramuscular injection at a dose of $1 \times 10^9$ TCID50/ml in 1ml, at intervals of up to 8 weeks apart, for a maximum of 13 doses.

Innovation and/or advantages
TroVax has a unique mechanism of action, and may increase survival and decrease tumour burden and progression with minimal toxicity - confirmation from clinical trials is required.

Developer
Sanofi-Aventis; Oxford BioMedica.

Availability, launch or marketing dates, and licensing plans:
In phase III clinical trials.

NHS or Government priority area:
This topic is relevant the NHS Cancer Plan (2000).

Relevant guidance
- NICE multiple technology appraisal in development. Bevacizumab, sorafenib, sunitinib and temsirolimus for renal cell carcinoma. Expected January 2009\(^1\).
- NICE interventional procedures guidance. Cryotherapy for renal cancers. 2007\(^2\).
- NICE interventional procedures guidance. Percutaneous radiofrequency ablation of renal cancer. 2004\(^3\).
- NICE guidance on cancer services. Improving outcomes in urological cancers – the manual. 2002\(^4\).

- European Association of Urology. Guidelines on Renal Cell Carcinoma. 2007\(^6\).
- Cancer Care Ontario - Program in Evidence-Based Care. Clinical practice guideline. Interleukin-2 in the treatment of patients with unresectable or metastatic renal cell cancer. 2006\(^7\).

\(^a\) TCID50: 50% Tissue Culture Infective Dose
Clinical need and burden of disease

Kidney cancers account for around 2% of all cancers in the UK. In 2004, there were 6,180 new kidney cancers diagnosed in England and Wales, of which an estimated 85-90% (5,253-5,562 cancers) were renal cell carcinomas 8,1. Clear cell renal adenocarcinoma is the most common type of RCC. RCC is nearly twice as common in men than women, and most commonly affects adults aged 50-70 years. In 2005, there were 3,134 deaths from kidney cancer in England and Wales 9. Patients presenting with metastatic RCC have a median survival of only 6-12 months and a two-year survival rate of 10-20%10.

Approximately a quarter of patients present with advanced disease, including locally invasive or metastatic renal cell carcinoma representing around 1,300-1,390 new patients per year (1,248 patients per year)11. In addition, an estimated 50% of patients who have curative resection for earlier stages will develop recurrent and/or metastatic disease (up to around 2,000 patients)1. Without treatment, median survival is only 6-12 months, and the two-year survival rate is 10-20%12.

Existing comparators and treatments

Advanced RCC is largely resistant to both hormonal and chemo-therapy. The standard treatment is immunotherapy with interferon alpha (IFN-alpha), and less commonly interleukin-2 (IL-2). Not all patients are suitable for immunotherapy. These therapies achieve overall response rates of 4-31%13, and are often associated with severe morbidity (physical and mental side effects). There are currently no standard treatments for patients with metastatic disease who do not respond to immunotherapy.

Other licensed therapeutic options:
- Sunitinib (Sutent): first and second line therapy for advanced and/or metastatic RCC.
- Sorafenib (Nexavar): first line therapy for RCC patients who are unsuitable for cytokine therapy or second line therapy following cytokine failure.
- Temsirolimus (Torisel): an IV mTOR inhibitor, indicated as first line therapy in patients with >3 poor prognostic indicators.
- Bevacizumab (Avastin): first line therapy in combination with IFN.

Efficacy and safety

There are four small, non-randomised or with historical control trials in renal cancer either ongoing or available in abstract or press release. In two of these trials, 24 of 35 evaluable patients showed disease control: two patients had complete responses, three had partial responses, and 19 had stable disease for periods exceeding three months, including three patients that were stable for 17 months14,15.

<table>
<thead>
<tr>
<th>Trial name or code</th>
<th>TroVax Renal Immunotherapy Survival Trial (TRIST); phase III16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Oxford BioMedica</td>
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<tr>
<td>Status</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Location</td>
<td>USA, EU, Israel, Eastern Europe, Russia, Spain</td>
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<tr>
<td>Design</td>
<td>Randomised; double-blind; placebo control.</td>
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<tr>
<td>Participants in trial</td>
<td>n=700; locally advanced or metastatic clear cell renal adenocarcinoma; ≥18 years of age; primary tumour surgically removed (residual tumour may remain). Randomised to either minimum of 3 doses (maximum 13 doses) of TroVax or placebo between 3-8 weeks apart, and first-line standard of care treatment (INF-α, IL-2, or sunitinib).</td>
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<tr>
<td>Follow-up</td>
<td>For survival</td>
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</tbody>
</table>
## Primary outcome
Survival

## Secondary outcomes
Progressive disease at 6 months; tumour response by RECIST\(^b\); quality of life.

## Adverse effects
Adverse reports so far: flu-like symptoms.

### Estimated cost and cost impact
The cost of TroVax is currently unknown.

### Potential or intended impact – speculative

#### Patients
- Reduced morbidity
- Quicker, earlier or more accurate diagnosis or identification of disease
- Reduced mortality or increased survival
- Other:
- Improved quality of life for patients and/or carers
- Non identified

#### Services
- Increased use: attendance for immunisation
- Decreased use
- Service reorganisation required
- Other:
- Staff or training required
- Non identified

#### Costs
- Increased unit cost compared to alternative
- New costs: additional therapy
- Increased costs: more patients coming for treatment
- Increased costs: capital investment needed
- Savings:
- Other:

### References


\(^b\) RECIST: response evaluation criteria in solid tumours.
