Girentuximab (Rencarex) for renal cell carcinoma

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The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
Girentuximab (Rencarex) for renal cell carcinoma

Target group
- Renal cell carcinoma (RCC): clear cell histology, non-metastatic – adjuvant therapy.

Technology description
Girentuximab (Rencarex, cG250) is a chimeric immunoglobulin G monoclonal antibody that triggers antibody-dependent cell-mediated cytotoxicity. Girentuximab activates natural killer cells by binding to carbonic anhydrase IX (CAIX), a tumour cell surface antigen that is expressed in 90% of all clear cell RCCs (ccRCC). Girentuximab is intended to be an adjuvant therapy for the treatment of patients with non-metastatic RCC. It is administered intravenously (IV) with a loading dose of 50mg, followed by 20mg once weekly for 23 weeks.

Girentuximab has been studied in phase II clinical trials for the treatment of metastatic RCC alone and in combination with the cytokines interleukin-2 (IL-2) or interferon-alpha-2a (IFN alpha-2a).

Innovation and/or advantages
If licensed, girentuximab would offer the first adjuvant treatment option for patients at high risk of relapse of recurrent disease.

Developer
Wilex.

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

NHS or Government priority area
This topic is relevant to the NHS Cancer Plan (2000) and Cancer Reform Strategy (2007).

Relevant guidance
- NICE guidance on cancer services. Improving outcomes in urological cancers – the manual. 2002\(^1\).
- Peer Review Team – National Cancer Action Team. Revised urology cancer measures. 2008\(^4\).

Clinical need and burden of disease
RCC is the most common form of kidney cancer and accounts for around 3% of all adult cancers in the UK\(^5\). In England and Wales, an estimated 90% of adult kidney cancers are RCCs\(^6\) and approximately 70-80% of all RCCs have a clear cell component\(^7\). An estimated 70% of patients with RCC present with localised or locally advanced disease which is potentially curable by surgery\(^8\). However, for those patients with locally aggressive tumours, recurrence rates are high at 35-65%\(^15\).
RCC is nearly twice as common in men as in women, and most commonly affects adults aged 50-80 years\textsuperscript{5,9}. In Europe, approximately 25% of cases of kidney cancer are attributable to obesity and 25% of cases in men are attributable to smoking\textsuperscript{2}.

In England there were 16,306 admissions for kidney cancer (ICD C64-66, C68), resulting in 82,610 bed days and 19,241 finished consultant episodes in 2009-10\textsuperscript{10}. The estimated five-year survival rate for RCC is 44%\textsuperscript{5}. In 2009, there were 3,317 deaths registered from kidney cancer (ICD C64-66, C68) in England and Wales\textsuperscript{11}.

**Existing comparators and treatments**

The main objective of adjuvant therapy in RCC is to increase the likelihood of a cure. In the 70% of patients who present with localised or locally advanced RCC, the disease is potentially curable with surgery alone (nephrectomy)\textsuperscript{8}. However, tumour recurrence rates are high with recurrent advanced and/or metastatic RCC being largely resistant to chemotherapy, radiotherapy and hormonal therapy. There are currently no approved agents for the adjuvant treatment of RCC patients following nephrectomy.

**Efficacy and safety**

<table>
<thead>
<tr>
<th>Trial</th>
<th>ARISER, NCT00087022, CDR0000372830, WILEX-WX-2003-07-HR; girentuximab vs placebo; phase III.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Wilex.</td>
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<tr>
<td>Status</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry.</td>
</tr>
<tr>
<td>Location</td>
<td>USA, Canada, Brazil and Argentina.</td>
</tr>
<tr>
<td>Design</td>
<td>Randomised, placebo-controlled.</td>
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<tr>
<td>Participants and schedule</td>
<td>n=864; adults; non-metastatic primary ccRCC; prior nephrectomy within previous 12 weeks; high-risk criteria (tumour stage $\geq$3a, or node positive disease, or grade $\geq$3 Fuhrman or any other nuclear grading system with at least 3 grades). Randomised to girentuximab or placebo IV once weekly for 24 weeks. Girentuximab group receive 50mg IV loading dose, followed by 20mg IV once weekly for weeks 2-24.</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Active treatment period 24 weeks; 5 yr follow-up.</td>
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<tr>
<td>Primary outcomes</td>
<td>Disease free survival; overall survival.</td>
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<tr>
<td>Secondary outcomes</td>
<td>Quality of life; safety.</td>
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<tr>
<td>Expected reporting date</td>
<td>Sept 2013.</td>
</tr>
</tbody>
</table>

**Estimated cost and cost impact**

The cost of girentuximab is not yet known.

**Claimed or potential impact – speculative**

Patients

- ✔ Reduced mortality or increased length of survival
- □ Reduction in associated morbidity or improved quality of life for patients and/or carers
- □ Quicker, earlier or more accurate diagnosis or identification of disease
- □ Other: None identified
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Services
- Increased use: once weekly IV administration.
- Decreased use
- Other: None identified

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

Other issues
- Clinical uncertainty or other research question identified:
  The effectiveness of girentuximab alone (without surgery) and the ideal period of adjuvant therapy have not yet been established.
- None identified

References

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