National Horizon Scanning Centre

Panitumumab (Vectibix) for first-line metastatic colorectal cancer

June 2008

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The National Horizon Scanning Centre Research Programme is part of the National Institute for Health Research
Panitumumab (Vectibix) for first-line metastatic colorectal cancer

Target group
- Metastatic colorectal cancer expressing non-mutated (wild-type) KRAS gene – first line.

Technology description
Panitumumab (Vectibix) is a fully human recombinant IgG2 kappa monoclonal antibody (mAb) that binds to the epidermal growth factor receptor (EGFR), blocking critical signalling pathways and inhibiting the growth of tumours expressing EGFR. The company suggest that panitumumab may initially be used in addition to current chemotherapies, and could be used in patients unable to tolerate treatment with cetuximab. Panitumumab is administered intravenously at 6mg/kg every two weeks.

Panitumumab is licensed as third line monotherapy for metastatic colorectal cancer. It is in phase III clinical trials for head and neck cancer.

Innovation and/or advantages
Panitumumab is a fully human mAb and therefore may have a lower incidence of anaphylaxis and infusion reactions compared to mouse derived mAbs.

Developer
Amgen Ltd.

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).

Relevant guidance

NICE clinical guidelines
- Improving outcomes in colorectal cancers. 2004¹.
- Diagnosis and management of colorectal and anal cancer. Expected date of issue to be confirmed².

NICE technology appraisals
- Irinotecan for the adjuvant treatment of colon cancer. Expected date of issue to be confirmed³.
- Cetuximab for the first line treatment of metastatic colorectal cancer. Expected date of issue to be confirmed⁴.
- Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer. 2007⁵.
- Capecitabine and oxaliplatin for adjuvant treatment of stage III colon cancer (adjuvant). 2006⁶.
- Irinotecan, oxaliplatin and raltitrexed (review) for colorectal cancer. 2005⁷.
- Capecitabine and tegafur with uracil for metastatic colorectal cancer. 2003⁸.

Other guidance
• Association of Coloproctology of GB and Ireland. Guidelines for the management of colorectal cancer, 3rd edition. 2007\textsuperscript{10}.

Clinical need and burden of disease
Colorectal cancer is the third most common cancer in the UK with 36,109 new cases in England and Wales in 2004 and 16,092 deaths registered in 2004\textsuperscript{11,12}. Estimates of those presenting with metastatic colorectal cancer range from 20-55\%\textsuperscript{13}. In a study published by Amado et al\textsuperscript{14}, KRAS mutations were identified in 43\% of 463 patients with metastatic colorectal cancer, expressing EGFR in \geq 1\% of tumour cells. The 5-year survival rate for metastatic colorectal disease is 12\%.

Existing comparators and treatments
First line treatment for metastatic colorectal cancer includes chemotherapy regimens with fluorouracil (5-FU) plus folic acid (FA); 5-FU/FA and irinotecan; 5-FU/FA and oxaliplatin; capecitabine or tegafur in combination with uracil; and capecitabine monotherapy (for those patients who cannot tolerate combination therapy). Bevacizumab in combination with 5-FU plus FA, with or without irinotecan, is also licensed for first line metastatic colorectal cancer but is not recommended by NICE for this indication.

Efficacy and safety
There are numerous phase II or III studies in the 2nd line setting either ongoing or published.

<table>
<thead>
<tr>
<th>Trial code, name, phase</th>
<th>PRIME\textsuperscript{15}; FOLFOX + panitumumab vs. FOLFOX alone; phase III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Amgen</td>
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<tr>
<td>Status</td>
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<tr>
<td>Location</td>
<td>Europe (inc. UK); Australia; Canada; South Africa; South America</td>
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<tr>
<td>Design</td>
<td>Randomised; open label</td>
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<tr>
<td>Participants in trial</td>
<td>n=1183 enrolled; untreated metastatic colorectal cancer; ECOG performance status of 0, 1, or 2.</td>
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<tr>
<td>Arm 1</td>
<td>FOLFOX: oxaliplatin 85 mg/m\textsuperscript{2} over 2 hours on day 1, leucovorin 200 mg/m\textsuperscript{2} over 2 hours on days 1 and 2, 5-FU 400 mg/m\textsuperscript{2} IV bolus over 2-4 minutes, followed by 600 mg/m\textsuperscript{2} IV infusion over 22 hours on days 1 and 2. Panitumumab 6 mg/kg over 1 hour on day 1 every two weeks.</td>
</tr>
<tr>
<td>Arm 2</td>
<td>FOLFOX regimen as in arm 1 every two weeks.</td>
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<tr>
<td>Primary outcome</td>
<td>Progression free survival (PFS)</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td>Overall survival (OS); objective response rate; duration of response (DOR); Time to progression (TTP); safety and tolerability.</td>
</tr>
<tr>
<td>Expected reporting date</td>
<td>Estimated completion date: 2010.</td>
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<thead>
<tr>
<th>Trial code, name, phase</th>
<th>20060314\textsuperscript{16}; Panitumumab plus FOLFIRI; phase II</th>
<th>20025409\textsuperscript{17}. Panitumumab with irinotecan/leucovorin/5-FU; two part study; phase II</th>
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<td>Status</td>
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<tr>
<td>Location</td>
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<tr>
<td>Design</td>
<td>Open label; single group assignment</td>
<td>Randomised; open label</td>
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</tbody>
</table>
Participants in trial  
n=150; adults; untreated metastatic colorectal cancer. ECOG performance status of 0, 1, or 2. 6 mg/kg panitumumab (IV) on day 1 of each 14 day treatment cycle just prior to administration of FOLFIRI (irinotecan, 5-FU, leucovorin). Treatment until progression or unacceptable toxicity.

n=19 (part 1) and n=24 (part 2). Untreated metastatic adenocarcinoma of the colon or rectum; ECOG performance status of 0/1.

Part 1: Panitumumab 2.5 mg/kg weekly with irinotecan, 5-FU (bolus), and leucovorin.
Part 2: As with part 1, except bolus 5-FU replaced with infusional 5-FU (FOLFIRI).

Follow-up  
56 days

Part 1: 48 weeks or until disease progression or other reason for treatment discontinuation.
Part 2: until progression of disease or other reason for removal from study.

Primary outcome  
Overall response rate

Tolerability (measured by grade 3/4 diarrhoea)

Secondary outcomes  
PFS, disease control rate, DOR, Time to response, TTP, duration of stable disease, time to treatment failure, safety.

Part 1 and Part 2: tumour response, TTP, PFS, OS, safety.

Key results  
-

Objective response rates were 46% in part 1 and 42% in part 2. Disease control rates were 74% in part 1 and 79% in part 2. Median PFS (95% CI) was 17 months for part 1 and 22.5 months for part 2.

Expected reporting date  
Estimated completion date: September 2009

Adverse effects  
-

Grade 3/4 diarrhoea occurred in 11 patients (58%) in part 1 and 6 patients (25%) in part 2. Skin related toxicity.

Estimated cost and cost impact

The cost of panitumumab has yet to be determined. Laboratory tests to determine KRAS status are additional costs to consider.

Potential or intended impact – speculative

Patients

- Reduced morbidity
- Reduced mortality or increased survival
- Improved quality of life for patients and/or carers
- Other:
- None identified

- Quicker, earlier or more accurate diagnosis or identification of disease
- Other:
- None identified

Services

- Increased use: Additional IV infusion
- Service reorganisation required
- Staff or training required
- Other:
- None identified

- Decreased use
- Other:
- None identified
Costs

☐ Increased unit cost compared to alternative
☐ New costs: used in combination with current therapies
☐ Increased costs: more patients coming for treatment
☐ Increased costs: capital investment needed
☐ Savings:
☐ Other:

References

2 National Institute for Health and Clinical Excellence. Diagnosis and management of colorectal and anal cancer. Clinical guideline. Expected date of issue to be confirmed.
3 National Institute for Health and Clinical Excellence. Irinotecan for the adjuvant treatment of colon cancer. Technology appraisal. Expected date of issue to be confirmed.

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