Tertomotide for locally advanced or metastatic pancreatic cancer

SUMMARY

Tertomotide is intended to be used for the treatment of locally advanced or metastatic pancreatic cancer. If licenced, tertomotide will provide an additional treatment option for this patient group who currently have few effective therapeutic options.

Pancreatic cancer is the ninth most common cancer in the UK and the fifth most common cause of death from cancer, with more than 95% of those affected dying of their disease. The 1-year survival rate is low, at around 12%, and less than 3% survive to 5 years. Pancreatic cancer is rare before the age of 45 – the majority of cases occur between 60-80 years of age. In 2011, there were 7,434 registered deaths due to pancreatic cancer in England and Wales.

Curative surgery is an option for only around 4% of the overall patient population. The aim of treatment is usually palliative, to improve quality of life and relieve symptoms. Chemotherapy options include gemcitabine alone or in combination with capecitabine, FOLFIRINOX, capecitabine or 5-fluorouracil. Second line therapy may be considered for a small proportion of patients. Palliative surgery and endoscopic placement of biliary drainage stents, and palliative radiotherapy may be provided to control disease symptoms. Tertomotide is currently in one ongoing phase III clinical trial comparing its effect in combination with gemcitabine and capecitabine against treatment with gemcitabine and capecitabine alone. This trial is expected to complete in Q3 2013.
TARGET GROUP

- Pancreatic cancer: locally advanced or metastatic – concurrent or sequential treatment with chemotherapy.

TECHNOLOGY

DESCRIPTION

Tertomotide (GV1001; hTERT-(611-626); telomerase peptide vaccine) is a peptide vaccine that targets telomerase, a ribonucleoprotein complex responsible for providing cancer cells with a potentially unlimited capacity to divide. Based on telomerase peptides, the vaccine stimulates T-cells to recognise and destroy cancer cells via recognition of the telomerase target whilst leaving healthy cells unharmed. Tertomotide is administered intradermally at 0.56mg on days 1, 3 and 5 of week 1, then once weekly for weeks 2, 3, 4 and 6, then once monthly, concurrently or sequentially in combination with chemotherapy. GM-CSF will be used as an adjuvant at 75µg, given 10-15 minutes prior to each administration of tertomotide.

Tertomotide is in phase III clinical trials for non-small cell lung cancer and in phase II for hepatocellular carcinoma.

INNOVATION and/or ADVANTAGES

If licensed, tertomotide will provide an additional treatment option for this patient group who currently have few effective therapeutic options.

DEVELOPER

KAEL-GemVax Company Limited.

AVAILABILITY, LAUNCH OR MARKETING

Tertomotide is a designated orphan drug in the EU and USA and is in phase III clinical trials.

PATIENT GROUP

BACKGROUND

Pancreatic cancer is the ninth most common cancer in the UK and the fifth most common cause of death from cancer\(^a\). It may arise in the head, body or tail of the pancreas and symptoms, which include jaundice, nausea, diarrhoea, weight loss, loss of appetite and severe pain, vary depending on the tumour site\(^a,3\). The most common subtype is ductal adenocarcinoma, which accounts for over 90% of cases\(^b\). Other subtypes include acinar cell carcinoma, cystic tumours, neuroendocrine tumours, lymphoma\(^4\), pancreatoblastoma and squamous cell carcinoma\(^a\).

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\(^a\) Expert personal communication
NHS or GOVERNMENT PRIORITY AREA

This topic is relevant to: Improving Outcomes: A Strategy for Cancer (2011).

CLINICAL NEED and BURDEN OF DISEASE

Pancreatic cancer has one of the worst prognoses of all solid tumours, with >95% of those affected dying of their disease. The high mortality rate is, at least in part, due to the vast majority of patients presenting at an advanced stage. Patients with unresectable, locally advanced disease have a median survival of 6-11 months, and patients with metastatic disease have a median survival of 2-6 months. The 1-year survival rate is low, at around 12%, and less than 3% survive to 5 years. Pancreatic cancer affects both sexes equally, with a lifetime risk of 1 in 77 for men and 1 in 79 for women. It is rare before the age of 45 years; 80% of cases occur between 60-80 years of age.

In 2008, there were 7,179 new diagnoses of pancreatic cancer in England and Wales, and 7,434 deaths were registered in 2011 (ICD10 C25). In 2011-12, there were 24,871 hospital admissions due to pancreatic cancer in England, resulting in 31,351 finished consultant episodes and 95,819 bed days.

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE Guidance

Other Guidance
- European Society for Medical Oncology & European Society of Digestive Oncology. Pancreatic adenocarcinoma: ESMO-ESDO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2012.

EXISTING COMPARATORS and TREATMENTS

Curative surgery is currently a treatment option for only around 4% of the overall patient population. As the majority of cases are diagnosed at advanced stages, the aim of...
treatment is usually palliative; to improve quality of life and relieve symptoms and to have a modest improvement in survival. Current options include\textsuperscript{3,5,b}:

- Chemotherapy – single agent gemcitabine, gemcitabine in combination with capecitabine, FOLFIRINOX (fluorouracil, oxaliplatin and irinotecan); or (rarely) monotherapy with capecitabine or 5-fluorouracil.
- Second line therapy may be considered for a small proportion of patients, if fit enough for subsequent treatment – fluoropyrimidines (fluorouracil or capecitabine) or oxaliplatin in combination with gemcitabine.
- Concurrent chemo-radiotherapy – for locally advanced disease only.
- Palliative surgery and endoscopic placement of biliary drainage stents to control symptoms such as those due to jaundice and gastric outlet obstruction.
- Palliative radiotherapy for control of symptoms associated with localised disease, such as pain.

### EFFICACY and SAFETY

| Trial | NCT00425360, CDR0000528021, CRUK-TELOVAC-V4, EUDRACT-2006-000461-10, EU020693, ISRCTN43482138; tertomotide in combination with gemcitabine and capecitabine vs gemcitabine and capecitabine; phase III. | NCT00358566, PX115.1.1-302, EUCRACT-2005-005014-21; tertomotide in sequential combination with gemcitabine vs gemcitabine; phase III. |
|---|---|
| Sponsor | Royal Liverpool University Hospital. | Pharmexa A/S. |
| Status | Ongoing. | Terminated. |
| Source of information | Trial registry\textsuperscript{14,15}. | Abstract\textsuperscript{16}, trial registry\textsuperscript{17}, manufacturer\textsuperscript{18}. |
| Location | UK. | EU, USA and Australia. |
| Design | Randomised, active-controlled. | Randomised, active-controlled. |
| Participants | n=1,110 (planned); aged 18 years and older; pancreatic cancer; locally advanced or metastatic. | n=365; aged 18-75 years; pancreatic cancer; unresectable, locally advanced or metastatic. |
| Schedule | Randomised to: Arm 1: Gemcitabine, 1,000mg/m\textsuperscript{2} IV, on days 1, 8 and 15, with capecitabine, 830mg/m\textsuperscript{2} oral, twice daily on days 1-21 of a 28 day cycle. Arm 2: Gemcitabine, 1,000mg/m\textsuperscript{2} IV, on days 1, 8, and 15, with capecitabine, 830mg/m\textsuperscript{2} oral, twice daily on days 1-21 of a 28 day cycle for 2 cycles, followed by sargramostim\textsuperscript{c}, 75µg intradermal and tertomotide, 0.56mg intradermal, on days 1, 3 and 5 in week 9, then once weekly in weeks 10-12 and 14, then once monthly. Arm 3: Gemcitabine, 1,000mg/m\textsuperscript{2} IV, on days 1, 8 and 15, with capecitabine, 830mg/m\textsuperscript{2} oral, twice daily on days 1-21 of a 28 day cycle, with sargramostim, 75µg intradermal and tertomotide, 0.56mg intradermal, on days 1, 3 and 5, then once weekly for weeks 2-4 and 6, then once monthly. | Randomised to tertomotide, 0.56mg intradermal with sargramostim on days 1, 3, 5, 8, 15, 22 and 36, then every 4 weeks, or gemcitabine, 1,000mg/m\textsuperscript{2}, IV, once weekly for 7 weeks, then on days 8, 15 and 22 of a 28 day cycle. On progression, tertomotide patients continue on tertomotide with concomitant gemcitabine. |

\textsuperscript{b} Expert personal communication

\textsuperscript{c} A recombinant granulyte macrophage colony-stimulating factor (GM-CSF).
Follow-up | Active treatment period until disease progression or toxicity; follow-up until death. | 2 year follow-up.
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Primary outcome | Survival at 1 year. | Overall survival (OS).
Secondary outcome/s | Time to progression; EORTC QLQ C30; clinical benefit response rate; objective response; toxicity; survival and response assessed by delayed-type hypersensitivity; CA19-9. | Progression free survival (PFS); immune analysis; quality of life; ECOG performance status; weight changes; pharmacoeconomics.
Key results | - | For tertomotide and gemcitabine respectively: OS (months), 5.9, 7.3 (HR = 0.8, 95% CI 0.6-1.0); median PFS (months), 1.9, 3.7 (HR = 0.5, 95% CI 0.4-0.7).
Adverse effects (AEs) | - | Grade 3-4 AEs for tertomotide and gemcitabine respectively (%): gastrointestinal, 8, 6; infection, 5, 5; vascular disorders 3, 2; neutropenia 3, 6.
Expected reporting date | Q3 2013. | -

**ESTIMATED COST and IMPACT**

**COST**

The cost of tertomotide is not yet known. The costs of selected treatments for locally advanced or metastatic pancreatic cancer are summarised below:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Cost for 3 months¹³⁻¹⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine</td>
<td>1,000mg/m², once weekly infusion for 7 of an 8 week cycle, followed by 3 weekly infusions in a 4 week cycle.</td>
<td>£3,240</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>1,000mg/m² twice daily for 21 days of a 28 day cycle.</td>
<td>£916.71</td>
</tr>
<tr>
<td>5-fluorouracil</td>
<td>12mg/kg for 3 days, then 6mg/kg on alternate days for 3 further doses, repeated every 4 weeks.</td>
<td>£172.80</td>
</tr>
</tbody>
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**IMPACT - SPECULATIVE**

**Impact on Patients and Carers**

☑ Reduced mortality/increased length of survival  ☐ Reduced symptoms or disability
☐ Other:  ☐ No impact identified

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¹ EORTC QLQ: European Organization for Research and Treatment of Cancer quality of life questionnaire.
³ ECOG: Eastern Cooperative Oncology Group.
⁴ HR: hazard ratio
⁵ Based on an average bodyweight of 77.9kg and an average surface area of 1.88m². Assumes wastage.
Impact on Services

- Increased use of existing services: need for additional intradermal injections
- Decreased use of existing services
- Re-organisation of existing services
- Need for new services
- Other: None identified

Impact on Costs

- Increased drug treatment costs
- Reduced drug treatment costs
- Other increase in costs: Other reduction in costs:
- Other: uncertain unit cost compared to existing treatments
- None identified

Other Issues

- Clinical uncertainty or other research question identified: None identified

REFERENCES


