Emepepimut-S (Stimuvax) for non-small cell lung cancer – maintenance therapy

SUMMARY

Emepepimut-S is intended to be used as maintenance therapy for the treatment of non-small cell lung cancer (NSCLC). If licensed, emepepimut-S will provide an additional treatment option for this patient group. It is designed to induce a specific immune response to MUC-1, a mucin expressed by more than 90% of common solid tumours, which is thought to decrease the activity of certain immune system cells including killer T-cells.

In the UK, lung cancer is the most common cause of cancer-related death in men and women, with 41,428 new cases in England and Wales and approximately 34,859 registered deaths. In England and Wales, lung cancer has a one-year survival rate of 25% and a five-year survival rate of 7%. Around 80% of newly diagnosed NSCLC patients have advanced (stage III or IV) disease that is incurable at outset.

For stage III NSCLC, treatment aims to relieve symptoms, improve disease control, improve quality of life, and increase survival. The standard therapy for stage III disease is chemoradiation and radiotherapy. Emepepimut-s is currently in phase III clinical trials comparing its effect on survival against treatment with placebo. The trial is expected to complete in September 2014.
TARGET GROUP


TECHNOLOGY

DESCRIPTION

Emepepimut-S (Stimuvax; EMD 351444;) is a 25-mer peptide fragment of MUC-1 encapsulated in a liposomal delivery system. It is designed to induce a specific immune response to MUC-1, a mucin expressed by more than 90% of common solid tumours, which is thought to decrease the activity of certain immune system cells, including killer T-cells. Emepepimut-S is intended to be used post chemo-radiotherapy following a single intravenous (IV) infusion of cyclophosphamide. Emepepimut-S is administered via subcutaneous injection at 806µg once weekly for 8 weeks, followed by maintenance injections at 6 week intervals, commencing week 13.

Emepepimut-S is in phase II clinical trials for breast cancer, colorectal cancer, multiple myeloma, prostate cancer and rectal cancer.

INNOVATION and/or ADVANTAGES

If licensed, emepepimut-S will provide an additional treatment option for this patient group.

DEVELOPER

Merck Serono Limited.

PATIENT GROUP

BACKGROUND

There are two main types of lung cancer, small cell lung cancer and NSCLC. NSCLC accounts for approximately 85% of all lung cancers\(^1\) and is further divided into three common subtypes, namely squamous cell carcinoma, adenocarcinoma and large cell carcinoma\(^2\). Stage IIIb lung cancer describes cancer that has spread from the lungs to lymph nodes in the chest and another major structure such as the oesophagus, heart, or trachea. Or, there may be two or more tumours in the same lung, or a pleural effusion\(^3\). Stage 4 lung cancer represents metastatic lung cancer, where the cancer has spread to distant parts of the body such as the liver, bones or brain\(^3\).

NHS or GOVERNMENT PRIORITY AREA

This topic is relevant to Improving Outcomes: A Strategy for Cancer (2011).
CLINICAL NEED and BURDEN OF DISEASE

In the UK, lung cancer is the most common cause of cancer-related death in men and women. In 2009, there were 41,428 new cases of lung cancer in England and Wales (approximately 48 cases per 100,000 population in the UK and around 34,859 registered deaths (around 39 deaths per 100,000 population in the UK). In England and Wales, lung cancer has a one-year survival rate of 25% and a five-year survival rate of 7%. Around 5.5% of lung cancers are currently considered as cured following treatment. About 90% of lung cancer mortality among men and 80% among women is attributable to smoking.

NSCLC accounts for approximately 85% of all lung cancers and is divided into three common subtypes: squamous cell carcinoma, adenocarcinoma and large cell carcinoma. In England and Wales, approximately 80% of newly diagnosed NSCLC patients have advanced (stage III or IV) disease that is incurable at outset, with a five-year survival rate of less than 1%. An estimated 30% of patients with NSCLC receive first line chemotherapy.

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE Guidance

- NICE technology appraisal in development. Cetuximab for the treatment of advanced non-small cell lung cancer. Date of issue to be confirmed.
- NICE technology appraisal in development. Epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation testing in adults with locally advanced or metastatic non-small cell lung cancer. Date of issue to be confirmed.
- NICE technology appraisal in development. Afatinib for the treatment of locally advanced or metastatic non-small cell lung cancer after previous platinum containing chemotherapy and gefitinib or erlotinib. Suspended July 2011.
• NICE technology appraisal. Pemetrexed for the treatment of non-small cell lung cancer. 2007\textsuperscript{23}
• NICE clinical guideline. Lung cancer: the diagnosis and treatment of lung cancer. 2011\textsuperscript{7}.

**Other Guidance**

• European Society for Medical Oncology (ESMO). Metastatic non-small cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. 2010\textsuperscript{8}.
• ESMO. Early stage and locally advanced (non-metastatic) non-small cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. 2010\textsuperscript{24}.
• SIGN. Management of patients with lung cancer. 2005\textsuperscript{26}.
• Cancer Services Collaborative Improvement Partnership. Lung cancer service improvement guide. 2004\textsuperscript{27}.

**EXISTING COMPARATORS and TREATMENTS**

For stage III NSCLC, treatment aims to relieve symptoms, improve disease control, improve quality of life and increase survival. Treatment includes radiotherapy, chemotherapy, and combinations of chemoradiotherapy. Chemotherapy options for unresectable stage III NSCLC include\textsuperscript{18,21,26,28,29}

- A combination of a single third-generation drug (docetaxel, gemcitabine, paclitaxel, vinorelbine) plus a platinum drug (carboplatin or cisplatin).
- Single agent chemotherapy with a third-generation drug for patients who cannot tolerate a platinum-based combination.
- Gefitinib may be offered for EGFR-TK mutation positive disease.
- Pemetrexed may be offered for adenocarcinoma or large-cell carcinoma.
- Bevacizumab is licensed in combination with platinum-based chemotherapy (not recommended by NICE).

**EFFICACY and SAFETY**

<table>
<thead>
<tr>
<th>Trial</th>
<th>START, NCT00409188, EMR 63325-001; adults; emepepimut-S vs placebo; phase III.</th>
<th>NCT00157196, B25-LG-305, EMR 63325-006; adults; emepepimut-S; phase II.</th>
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<tr>
<td>Sponsor</td>
<td>EMD Serono.</td>
<td>Merck KGaA.</td>
</tr>
<tr>
<td>Status</td>
<td>Ongoing.</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry\textsuperscript{30}.</td>
<td>Abstract\textsuperscript{31,32}, trial registry\textsuperscript{33}.</td>
</tr>
<tr>
<td>Location</td>
<td>EU (inc UK), USA, Canada and other countries.</td>
<td>Canada.</td>
</tr>
<tr>
<td>Design</td>
<td>Randomised, placebo-controlled.</td>
<td>Non-randomised, open-label.</td>
</tr>
<tr>
<td>Participants</td>
<td>n=1,514 (planned); adults; NSCLC; unresectable; stage III; stable disease or objective response following concomitant or sequential chemoradiotherapy</td>
<td>n=420 (planned); adults; NSCLC; unresectable; stage III; stable disease or clinical response following prior chemoradiotherapy.</td>
</tr>
</tbody>
</table>
Schedule

Randomised to cyclophosphamide, 300mg/m² or placebo IV, 3 days prior to emepepimut-S 806µg, or placebo SC, weekly for 8 weeks, followed by emepepimut-S, 806µg or placebo SC, every 6 weeks until disease progression

All participants receive cyclophosphamide, 300mg/m² IV, 3 days prior to emepepimut-S, 930µg SC, weekly for 8 weeks.

Follow-up

48 month follow-up.

24 month follow-up.

Primary outcome/s

Survival.

Safety.

Secondary outcome/s

Time to symptom progression; time to progression; EQ-5D; Lung Cancer Symptom Scale (LCSS); safety.

Survival; EQ-5D; LCSS.

Key results

- 2 year survival, 64%.

Adverse effects (AEs)

- AEs ≥10%: fatigue, dyspnoea, insomnia, anorexia, headache, diarrhoea, paresthesia, abdominal pain, influenza-like illness; urinary tract infection, peripheral neuropathy.

Expected reporting date

Q2 2013.

Q3 2014.

ESTIMATED COST and IMPACT

COST

The cost of emepepimut-S is not yet known.

IMPACT - SPECULATIVE

Impact on Patients and Carers
☑ Reduced mortality/increased length of survival
☐ Other
☑ Reduced symptoms or disability
☐ No impact identified

Impact on Services
☑ Increased use of existing services: ongoing frequent SC injections
☐ Re-organisation of existing services
☐ Other
☐ Decreased use of existing services
☐ Need for new services
☐ None identified

Impact on Costs
☑ Increased drug treatment costs
☐ Other increase in costs
☐ Other: new costs – additional treatment
☐ Reduced drug treatment costs
☐ Other reduction in costs
☐ None identified

Other Issues
☐ Clinical uncertainty or other research question identified
☑ None identified
REFERENCES


