Nivolumab (Opdivo) for stage IV or recurrent non-small cell lung cancer – first line

LAY SUMMARY

Non-small cell lung cancer is the most common type of lung cancer. It is often diagnosed late and is difficult to treat once it has spread to other parts of the body.

Nivolumab is a new drug for the treatment of non-small cell lung cancer. It is given as a drip into a vein once every two weeks. Some studies have suggested nivolumab may be used as a first line treatment and helpful for people who have non-small cell lung cancer that has spread to other parts of the body. Studies are currently ongoing to see how well nivolumab works and how safe it is to use.

If nivolumab is licensed for use in the UK, it could be a new treatment option for patients with advanced non-small cell lung cancer, which may improve survival and cause fewer side effects than current treatments (usually chemotherapy).

NIHR HSRIC ID: 11574
**TARGET GROUP**

Non-small cell lung cancer (NSCLC): stage IV or recurrent – first line.

**TECHNOLOGY**

**DESCRIPTION**

Nivolumab (Opdivo; anti-PD-1 monoclonal antibody - Medarex/Ono; BMS936558; MDX1106; ONO4538) is a fully human IgG4 monoclonal antibody targeting the programmed cell death-1 receptor (PD-1). PD-1 is expressed on the surface of activated lymphocytes and acts as part of an immune checkpoint pathway. PD-1 blockade by nivolumab may activate T-cell responses and promote an anti-tumour immune response. In phase III clinical trials, nivolumab is administered via intravenous (IV) infusion alone, or in combination with ipilimumab, or in combination with platinum-doublet chemotherapy.

Nivolumab (Opdivo) is licensed in the EU as monotherapy for the treatment of advanced, unresectable or metastatic melanoma in adults (first and second line therapy). Nivolumab is also licensed for the treatment of locally advanced or metastatic squamous non-small cell lung cancer (second line therapy). Very common (>10%) reported adverse events include diarrhoea, nausea, rash, pruritus, fatigue, lymphopenia, thrombocytopenia, anaemia and increases in serum levels of AST, ALT, total bilirubin, alkaline phosphatase and creatinine. Common reported adverse events include upper respiratory tract infection, infusion related reaction, hypothyroidism, hyperthyroidism, hyperglycaemia, hyponatraemia, decreased appetite, peripheral neuropathy, headache, dizziness, hypertension, pneumonitis, dyspnoea, cough, colitis, stomatitis, vomiting, abdominal pain, constipation, vitiligo, dry skin, erythema, alopecia, musculoskeletal pain, arthralgia, pyrexia, oedema, increased lipase, increased amylase, and neutropenia.

Nivolumab is currently in clinical trials in the EU for:
- Glioblastoma; phase III.
- Head and neck cancer; phase III.
- Renal cancer; phase III.
- Follicular lymphoma; phase II.
- Hodgkin lymphoma; phase II.
- Bladder cancer; phase II.

**INNOVATION and/or ADVANTAGES**

If licensed, nivolumab will provide an additional first line, non-cytotoxic chemotherapy treatment option for patients with NSCLC.

**DEVELOPER**

Bristol-Myers Squibb.

**AVAILABILITY, LAUNCH OR MARKETING**

In phase III clinical trials.
NSCLC is the most common type of lung cancer, accounting for approximately 85-90% of all lung cancers\(^3\). The most common NSCLC subtypes are squamous cell carcinoma (45%), adenocarcinoma (45%), and large cell carcinoma (10%)\(^4\). The subtype of NSCLC relates to the site of origin, reflecting the variation in respiratory tract epithelium from the bronchi to alveoli, with adenocarcinoma (the most common form) usually originating in peripheral lung tissue\(^5\). The symptoms of NSCLC include haemoptysis, malaise, significant weight loss, dyspnoea and voice loss\(^5\). Smoking is the main cause of lung cancer and it is responsible for more than 80% of cases\(^3\).

In the UK, lung cancer is the most common cause of cancer-related death in men and women, accounting for 22% of all cancer deaths\(^6\). In 2010, there were 37,290 new cases of lung cancer in England and Wales (representing around 47 cases per 100,000 population\(^7\)), equating to approximately 33,500 cases of NSCLC (around 15,000 squamous cell carcinoma). In England, one-year survival rates are estimated to be 30% for men and 35% for women, with five-year survival rates falling to 8% and 11% respectively\(^8\). Around 5.5% of lung cancers are considered cured with currently available treatments\(^9\). Approximately 48% of new cases will have stage IV disease that is incurable at diagnosis\(^10\), with a five-year survival rate of less than 1%\(^11\).

In 2014-15, there were 89,247 hospital admissions in England due to lung cancer (ICD-10 C34), accounting for 109,339 finished consultant episodes and 278,868 bed days\(^12\). In 2014, there were 30,851 deaths from lung cancer registered in England and Wales\(^13\).

NICE Guidance

- NICE technology appraisal in development. Erlotinib and gefitinib for treating non-small cell lung cancer that has progressed following prior chemotherapy (review of TA162 and TA175) (ID620). Expected date of issue to be confirmed.

Other Guidance

• European Society for Medical Oncology. Metastatic non-small cell lung cancer (NSCLC): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. 2014

CURRENT TREATMENT OPTIONS

For NSCLC, stage IV disease is considered incurable with current technologies, therefore the aim of therapy is to relieve symptoms, control disease progression, improve quality of life and increase survival. Treatment options include surgery, chemotherapy, biological therapy and radiation therapy, alone or in combination.

First line treatment options include:
• Chemotherapy – pemetrexed, gemcitabine, docetaxel, paclitaxel or vinorelbine alone or in combination with carboplatin or cisplatin.
• Erlotinib or gefitinib (for EGFR-TK mutation positive patients).
• Debulking bronchoscopic procedures.
• Photodynamic therapy.
• Brachytherapy.

**EFFICACY and SAFETY**

<table>
<thead>
<tr>
<th>Trial</th>
<th>CheckMate 227, CA209-227 2014-003630-23, NCT02477826, nivolumab alone or in combination with ipilimumab or platinum-doublet chemotherapy; phase III.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Bristol Myers Squibb.</td>
</tr>
<tr>
<td>Status</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry¹.</td>
</tr>
<tr>
<td>Location</td>
<td>EU (incl UK), USA, Canada and other countries.</td>
</tr>
<tr>
<td>Design</td>
<td>Randomised, active-controlled.</td>
</tr>
<tr>
<td>Participants</td>
<td>n=1,980 (planned); ≥18 years; histologically confirmed stage IV or recurrent NSCLC with no prior systemic anticancer therapy; Eastern Cooperative Oncology Group (ECOG) performance status (PS) ≤1; measurable disease according to RECIST 1.1 criteria.</td>
</tr>
<tr>
<td>Schedule</td>
<td>Randomised to IV nivolumab; IV nivolumab plus ipilimumab; nivolumab plus platinum doublet chemotherapy; or platinum doublet chemotherapy including gemcitabine with cisplatin or gemcitabine with carboplatin for squamous histology or pemetrexed with cisplatin or pemetrexed with carboplatin for non-squamous histology. The dose and treatment schedules have not been reported.</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Active treatment until disease progression or toxicity. Follow-up period up to 48 months.</td>
</tr>
<tr>
<td>Primary outcomes</td>
<td>Overall survival; progression-free survival.</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td>Objective response rate; disease related symptom improvement measured by the Lung Cancer Symptom Score.</td>
</tr>
<tr>
<td>Expected reporting date</td>
<td>December 2020.</td>
</tr>
</tbody>
</table>

**ESTIMATED COST and IMPACT**

**COST**

The cost of nivolumab is not yet known. The cost of other selected treatments for NSCLC are summarised below²:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Per dose²²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Docetaxel</td>
<td>75mg/m² IV, every 21 days</td>
<td>£900</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>75mg/m² IV, every 21 days</td>
<td>£75</td>
</tr>
<tr>
<td>Erlotinib (Tarceva)</td>
<td>150mg oral, once daily</td>
<td>£1,632 (30 day cost)</td>
</tr>
</tbody>
</table>

¹ Based on an average surface area of 1.88m² and an average weight of 77.9kg. Assumes wastage.
IMPACT - SPECULATIVE

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

Impact on Health and Social Care Services
☐ Increased use of existing services
☐ Decreased use of existing services
☐ Re-organisation of existing services
☐ Need for new services
☐ Other:
☑ None identified

Impact on Costs and Other Resource Use
☐ Increased drug treatment costs
☐ Reduced drug treatment costs
☐ Other increase in costs
☐ Other reduction in costs:
☑ Other: uncertain unit cost compared to existing chemotherapy regimes
☐ None identified

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

REFERENCES


