Nivolumab (Opdivo) for gastric and gastroesophageal junction adenocarcinoma – third and fourth line

NIHR HSRIC ID: 12940

Lay summary

Nivolumab is a new drug to treat advanced stomach cancer. It is delivered straight into the blood via a drip. Nivolumab may help the body’s immune system to fight the disease. Stomach cancer is an unusual type of cancer, and gastric and gastroesophageal junction adenocarcinoma are the most common types of stomach cancer. Nivolumab may offer a new treatment option for people whose cancer has returned following previous treatments.

This briefing is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information.

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TARGET GROUP

- Gastric and gastroesophageal junction adenocarcinoma: unresectable advanced or recurrent – third or fourth 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 trials¹, nivolumab was administered via intravenous (IV) infusion at 3mg/kg every 2 weeks until disease progression.

Nivolumab is licensed in the EU for advanced melanoma (with or without ipilimumab), locally advanced or metastatic non-small cell lung cancer, and advanced renal cell carcinoma. Recognised adverse effects (≥10%) include: pneumonitis, infusion reaction, decreased appetite, diarrhoea, nausea, rash, pruritus, fatigue, hypocalcaemia, lymphopaenia, leucopaenia, thrombocytopenia, anaemia, hypercalcaemia, hyperkalaemia, hypokalaemia, hypomagnesaemia, hyponatraemia, and increased serum levels of AST, ALT, alkaline phosphatase, lipase, amylase, and creatinine².

Nivolumab is also in phase III clinical trials for glioblastoma, hepatocellular carcinoma, multiple myeloma, oesophageal cancer, small cell lung cancer, urogenital cancer and squamous cell carcinoma of the head and neck, and in phase II trials for acute myeloid leukaemia, breast cancer, chronic lymphocytic leukaemia, diffuse large B cell lymphoma, follicular lymphoma, myelodysplastic syndromes, ovarian cancer, and uveal melanoma.

INNOVATION and/or ADVANTAGES

If licensed, nivolumab will offer an additional treatment option for patients with unresectable advanced or recurrent gastric cancer.

DEVELOPER

Bristol-Myers Squibb.

AVAILABILITY, LAUNCH OR MARKETING

In phase III clinical trials.

PATIENT GROUP

BACKGROUND

There are several different types of stomach cancer, the most common being gastric or gastroesophageal junction adenocarcinoma, which starts in the glandular cells of the
stomach lining and accounts for 95% of stomach cancers in the UK. Initial symptoms are often vague and are similar to the symptoms of other stomach conditions. Early symptoms include heartburn or indigestion, burping, loss of appetite and feeling full after eating only a small amount. Symptoms of advanced stomach cancer may include a lack of appetite and subsequent weight loss, fluid in the abdomen and blood in the stool. Risk factors include age, gender, family history, infection with *Helicobacter pylori*, a diet low in fruit and vegetables and high in processed meats or smoked foods, smoking, being overweight, and long-term acid reflux or stomach conditions that cause changes to the stomach lining.

### CLINICAL NEED and BURDEN OF DISEASE

Stomach cancer is the 16th most common cancer in the UK, accounting for around 2% of all new cases. It is more common in men than women, with approximately 4,600 cases diagnosed in men, and 2,500 cases in women in 2013. Around half of all new cases of stomach cancer are diagnosed in people aged over 75 years. Due to the nature of symptoms, stomach cancer is often diagnosed at an advanced stage, with around 14% diagnosed at stage 3 (locally advanced), and 80% diagnosed at stage 4 (metastatic). Survival is poor, with around 75% of cases presenting with disease too established for curative treatment, and the majority will develop progressive disease following first line treatment. Approximately 15% of people with stomach cancer in England and Wales survive their disease for 10 years or more, and around 19% survive for 5 years or more. In 2014-15, there were 19,534 hospital admissions due to stomach cancer (ICD-10 C16) in England, accounting for 28,849 finished consultant episodes and 68,097 bed days. In England and Wales, 3,949 deaths were registered due to stomach cancer in 2014. The population likely to be eligible to receive third or fourth line treatment for gastric cancer could not be estimated from available published sources.

### PATIENT PATHWAY

### RELEVANT GUIDANCE

#### NICE Guidance


#### NHS England Policies and Guidance

CURRENT TREATMENT OPTIONS

The aim of treatment in advanced gastric or gastroesophageal junction adenocarcinoma is to prevent progression, extend survival and relieve symptoms with minimal adverse effects. There is no standard treatment for previously treated advanced disease and the role of therapy beyond second line in advanced gastric cancer has not yet been established\textsuperscript{10,16}. Treatment options include chemotherapy, palliative radiotherapy and palliative surgery\textsuperscript{9}. Current pharmacological options for advanced gastric cancer include\textsuperscript{9,13,17}:

- **Chemotherapy** – ECF (epirubicin, cisplatin and fluorouracil), EOF (epirubicin, oxaliplatin and fluorouracil), ECX (epirubicin, cisplatin and capecitabine), EOX (epirubicin, oxaliplatin and capecitabine), docetaxel and irinotecan, FOLFIRI (leucovorin, fluorouracil and irinotecan), mitomycin C and capecitabine.
- **Biological therapy** – trastuzumab (for HER2-positive disease).

EFFICACY and SAFETY

<table>
<thead>
<tr>
<th>Trial</th>
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<td>NCT02267343, ONO-4538-12; nivolumab vs placebo; phase III.</td>
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<th>Sponsor</th>
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<td>Ono Pharmaceutical Co. Ltd.</td>
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<th>Status</th>
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<tr>
<td>Ongoing.</td>
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<tr>
<th>Source of information</th>
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<tbody>
<tr>
<td>Trial registry\textsuperscript{1}.</td>
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<tr>
<th>Location</th>
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<tbody>
<tr>
<td>Japan, Korea and Taiwan.</td>
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<table>
<thead>
<tr>
<th>Design</th>
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<td>Randomised, placebo-controlled.</td>
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<th>Participants</th>
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<td>n=480 (planned); aged ≥20 yrs; gastric and gastroesophageal junction adenocarcinoma; unresectable advanced or recurrent; refractory to or intolerant to standard therapy.</td>
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<th>Schedule</th>
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<td>Randomised to nivolumab, 3mg/kg IV every 2 weeks; or placebo, IV every 2 weeks.</td>
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<th>Follow-up</th>
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<td>Active treatment until disease progression.</td>
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<th>Primary outcome/s</th>
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<td>Overall survival.</td>
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<th>Secondary outcome/s</th>
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<td>Progression-free survival; objective response date; duration of response; safety.</td>
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<th>Expected reporting date</th>
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<td>Not reported.</td>
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ESTIMATED COST and IMPACT

COST

The company state that a 4ml vial (10mg/ml) of nivolumab costs £439. A dose of 3mg/kg for an adult weighing 70kg would therefore cost £2,634 per patient per dose. A 10ml vial will cost £1,097.
### IMPACT - SPECULATIVE

#### Impact on Patients and Carers

- Reduced mortality/increased length of survival
- Reduced symptoms or disability
- Other
- 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
- None identified

#### Other Issues

- Clinical uncertainty or other research question identified
- None identified

### REFERENCES