NIHR | Innovation Observatory

# HEALTH TECHNOLOGY BRIEFING
# AUGUST 2019

# Avelumab for gastric or gastro-oesophageal junction cancer - first line maintenance

| | | | |
|---|---|---|---|
| **NIHRIO ID** | 11945 | **NICE ID** | 9645 |
| **Developer/Company** | Merck Serono Ltd | **UKPS ID** | 649473 |

| | |
|---|---|
| **Licensing and market availability plans** | Currently in phase III trial. |

## SUMMARY


Avelumab is in clinical development for gastric or gastro-oesophageal cancer. Gastric cancer is cancer that starts anywhere inside the stomach or the stomach wall. Advanced gastric cancer can be locally advanced (has spread into the tissues around the stomach) or metastatic (has spread to at least one other part of the body such as the liver). Advanced or metastatic cancers have poor prognosis and often have no cure (surgically), but treatment may control further growth of the disease, relieve symptoms and give the patient a good quality of life. Treatment strategy often involve an induction phase to preserve patient quality of life and a maintenance phase to prolong treatment benefit.

Avelumab is a human monoclonal antibody designed to recognise and attach to a protein called 'programmed death-ligand-1' (PD-L1). PD-L1 is a protein produced by several cancers and prevents the activation of T cells, which are part of the body's immune (defence) system. Avelumab blocks PD-L1 which prevents the cancer cells from switching off the T cells, increasing the ability of the T cells to kill the cancer cells. Early results have shown that avelumab was well tolerated and showed promising clinical activity with good response rate when given as first line maintenance in patients with advanced or metastatic gastric or gastro-oesophageal junction cancer.

# PROPOSED INDICATION

First line maintenance for unresectable, locally advanced or metastatic, adenocarcinoma of the stomach, or gastro-esophageal junction.[a]

# TECHNOLOGY

## DESCRIPTION

Avelumab (Bavencio) is a human immunoglobulin G1 (IgG1) monoclonal antibody directed against programmed death ligand 1 (PD-L1). Avelumab binds PD-L1 and blocks the interaction between PD-L1 and the programmed death 1 (PD-1) and B7.1 receptors. This removes the suppressive effects of PD-L1 on cytotoxic $CD8^+$ T-cells, resulting in the restoration of anti-tumour T-cell responses. Avelumab has also shown to induce natural killer (NK) cell-mediated direct tumour cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC).[1]

Avelumab is in clinical development for the treatment of patients with unresectable, locally advanced or metastatic, adenocarcinoma of the stomach, or gastro-esophageal junction. In the phase III clinical trial (NCT02625610; JAVELIN Gastric 100), participants will receive oxaliplatin and either 5-Fluorouracil (5-FU) or capecitabine for 12 weeks for the induction phase. For the maintenance phase, participants will be administered intravenous (IV) infusion of avelumab (10 mg/kg over 1 hour) once every 2 weeks until disease progression, significant clinical deterioration, unacceptable toxicity, or discontinuation.[2]

## INNOVATION AND/OR ADVANTAGES

Despite improvements in chemotherapy for patients with advanced gastric or gastro-oesophageal junction cancer, the median overall survival (OS) remains short. Because patients with advanced gastric or gastro-oesophageal junction cancer often have poor prognostic factors that limit long-term use of standard combination chemotherapy regimens, an optimal continuation of care with maximised overall benefit without added toxicity is needed.[3,4] Maintenance therapy is an established strategy for treatment of various advanced tumours based on studies showing prolonged antitumour responses and extended remissions.[4]

Avelumab, which is a human IgG1 anti-PD-L1 monoclonal antibody, has shown durable clinical activity in a range of tumours. Results from clinical study has shown that avelumab was well tolerated and showed promising clinical activity with good response rate when given as first line maintenance in patients with advanced or metastatic gastric or gastro-oesophageal junction cancer. Maintenance treatment with avelumab after first line induction chemotherapy may provide an alternative treatment strategy to first line combination treatment, with the aim of enabling patients with advanced gastric or gastro-oesophageal junction cancer obtain the efficacy benefits of checkpoint inhibitor therapy without the increased toxicity burden of combination treatment. This treatment strategy might also better preserve patient quality of life and enable a longer duration of treatment benefit.[4]

[a] Information provided by Merck Serono Ltd on UK PharmaScan

## DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Avelumab is licenced in the UK for the treatment of metastatic Merkel cell carcinoma. The most common adverse reactions with avelumab were fatigue, nausea, diarrhoea, decreased appetite, constipation, infusion-related reactions, weight decreased and vomiting.[5]

Avelumab is currently in phase II and III clinical trials for the treatment of multiple malignant conditions such as breast cancer, colorectal cancer, prostate cancer, urothelial cancer, non-small cell lung cancer, locally advanced head and neck cancer etc.[6]

Avelumab has been granted an orphan designation in the EU in 2016 for treatment of gastric cancer.[7]

# PATIENT GROUP

## DISEASE BACKGROUND

Gastric cancer is a malignant tumour originating in the cells of the stomach. There are several different types of stomach cancer. More than 95% of stomach cancers develop in the cells of the stomach lining and are known as adenocarcinomas.[8,9] Most gastric cancers originate in the gland cells in the inner stomach lining.[10] Advanced gastric cancer begins in the stomach and spread into the tissues around the stomach, either as locally advanced disease, or it can metastasise to other areas of the body such as the liver, lungs, lymph nodes, or the oesophagus. Advanced cancer cannot usually be cured, but treatment may control further growth of the disease, relieve symptoms and give the patient a good quality of life.[8] Gastric cancer begins with a mutation in the structure of the DNA in cells, which can affect how they grow. This means cells grow and reproduce uncontrollably, resulting in a tumour. It is not known what triggers the changes in DNA that lead to gastric cancer.[11] Gastric cancer can involve loss of the tumour suppression gene, p53.[12]

Several factors which increase the risk of gastric cancer include aging (55 years and older), male gender, smoking, severe chronic atrophic gastritis, peptic ulcers caused by Helicobacter pylori infection, diet, family history of gastric cancer, having another type of cancer, vitamin B12 deficiency, and history of stomach surgery.[11]

The initial diagnosis of gastric carcinoma is often delayed because up to 80 percent of patients are asymptomatic during the early stages of stomach cancer. Weight loss, abdominal pain, nausea and vomiting, early satiety, and peptic ulcer symptoms may accompany late-stage gastric cancer. Signs may include a palpably enlarged stomach, a primary mass (rare), an enlarged liver, Virchow's node, metastatic tumour felt on rectal examination, with growth in the rectouterine space.[13]

## CLINICAL NEED AND BURDEN OF DISEASE

In 2016, gastric cancer was the 17th most common cancer in the UK. There were around 6,700 new cases of stomach cancer in the UK in 2014-2016. The age-standardised incidence rate in England for malignant neoplasm of the stomach, in 2016, was 15.4 per 100,000 in males and 6.4 per 100,000 in females.[14]

Stomach cancer patients with a known stage are often diagnosed at stage IV (46-57%). More patients with a known stage are diagnosed at a late stage (69-75% are diagnosed at stage III

or IV), than an early stage (25-31% are diagnosed at stage I or II).[14] There were 5,712 diagnosis for stage IV stomach cancer in England between 2013 and 2015.[15]

In the UK, 34% of stomach cancer cases in the UK are in females, and 66% are in males. According to 2010-2012 data in the UK, the largest proportion of gastric cancer cases (occur in the cardia (next to the oesophagus).[14] In England, cancers of the gastro-oesophageal junction account for 40% of all cancers arising in the upper gastro-intestinal tract.[16]

In England, in 2017-2018, there were 25,409 finished consultant episodes (FCE) for malignant neoplasm of stomach (ICD 10: C16), resulting in 19,873 hospital admissions and 60,252 FCE bed days.[17]

According to 2010-2011 data, 19% of people diagnosed with stomach cancer in England and Wales survive their disease for five years or more.[18] Five year survival rates for stage III (A, B, C) gastric cancer were 25%, 20%, and 10% respectively; whereas stage IV was 5%.[19]

Gastric cancer was the 14th most common cause of cancer death in the UK in 2016. Crude mortality rate in England was 6.6 per 100,000 in 2014. Gastric cancer was the 14th most common cause of cancer death in the UK in 2016. Crude mortality rate in England was 6.6 per 100,000 in 2014. Gastric cancer mortality is strongly related to age, with the highest mortality rates being in older males and females.[20] In the 2017 death registration in England and Wales, there were 3,772 deaths (2,444 males, 1,328 males) due to malignant neoplasm of stomach (C16) with the higher proportions in aged 65 years and above.[21]

# PATIENT TREATMENT PATHWAY

## TREATMENT PATHWAY

The most common treatments for gastric cancers are surgery, radiotherapy, and chemotherapy. The patient may have one of these treatments or a combination. If the tumour is in the upper part of the stomach, the patient may also have radiotherapy prior to surgery. If surgery is recommended, the patient may have chemotherapy beforehand. If it is not possible to remove the tumour completely, then the treatment focus will be on preventing the tumour from getting any bigger and causing further harm to the body. This can be done by surgery (palliative surgery) or by chemotherapy.[22,23]

Palliative chemotherapy is recommended as first and second line treatment in locally advanced or metastatic oesophago-gastric cancer. The aim of treatment is to prevent progression, extend survival and relieve symptoms with minimal adverse effects.[24,25]

## CURRENT TREATMENT OPTIONS

There is no standard treatment for previously treated advanced or metastatic disease. Best supportive care is commonly used at this stage. Taxane (docetaxel or paclitaxel) monotherapy may be an option or combination therapy may be given once again.[25]

Treatment options may be used sequentially in second and third line, but there is no clear evidence for a benefit beyond second line treatment.[26]

## PLACE OF TECHNOLOGY

If licensed, avelumab will offer a treatment option as first-line maintenance in patients with unresectable, locally advanced or metastatic, adenocarcinoma of the stomach, or gastro-esophageal junction.

# CLINICAL TRIAL INFORMATION

| | |
|---|---|
| **Trial** | **JAVELIN Gastric 100; NCT02625610; EudraCT-2015-003300-23; adult aged 18 years and older; avelumab vs oxaliplatin-fluoropyrimidine doublet; phase III** |
| **Sponsor** | EMD Serono Research & Development Institute, Inc |
| **Status** | Ongoing |
| **Source of Information** | Trial registry[27,28] |
| **Location** | 7 EU (incl UK), USA, Canada and other countries |
| **Design** | Randomised; parallel assignment; open label |
| **Participants** | N=499; 18 years and older; disease measurable by Response Evaluation Criteria in Solid Tumours version 1.1 (RECIST 1.1); histologically confirmed unresectable locally advanced or metastatic adenocarcinoma of the stomach or gastro-esophageal junction (GEJ); Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 to 1 at trial entry; estimated life expectancy of more than 12 weeks |
| **Schedule** | Randomised to:<br>• Avelumab<br>- Induction phase: subjects will be administered with oxaliplatin and either 5-Fluorouracil (5-FU) or capecitabine for 12 weeks.<br>- Maintenance phase: Subjects will be administered with intravenous (IV) infusion of avelumab (10mg/kg over 1 hour) once every 2 weeks until disease progression, significant clinical deterioration, unacceptable toxicity, or discontinuation.<br>• Oxaliplatin-fluoropyrimidine doublet<br>- Induction phase: subjects will be administered with oxaliplatin and either 5-FU or capecitabine for 12 weeks.<br>- Maintenance phase: subjects will continue the same regimen of oxaliplatin-fluoropyrimidine doublet chemotherapy (oxaliplatin + 5-FU/Leucovorin (LV) or oxaliplatin + capecitabine) as they received during the Induction Phase until disease progression, significant clinical deterioration, unacceptable toxicity, or discontinuation. Subjects who are not deemed eligible to receive further chemotherapy will receive best supportive care (BSC) alone with no active therapy.<br>Oxaliplatin will be administered at a dose of 85 mg per square meter (mg/m^2) as a continuous intravenous (IV) infusion on Day 1 along with leucovorin followed by 5-Fluorouracil every 2 weeks up to 12 weeks (or) Oxaliplatin at 130 mg/m^2 IV on Day 1 along with capecitabine twice |

| | |
|---|---|
| | daily for 2 weeks followed by a 1-week rest period given every 3 weeks up to 12 weeks.<br><br>5-Fluorouracil will be administered at a dose of 2600 mg/m^2 IV continuous infusion over 24 hours on Day 1 (or) 5-FU at 400 mg/m^2 IV push on Day 1 and 2400 mg/m^2 IV continuous infusion over 46-48 hours (Days 1 and 2) along with oxaliplatin and leucovorin every 2 weeks up to 12 weeks.<br>Leucovorin will be administered at a dose of 200 mg/m^2 IV (or) Leucovorin 400 mg/m^2 IV on Day 1 along with oxaliplatin and 5-FU every 2 weeks up to 12 weeks.<br><br>Capecitabine will be administered at a dose of 1000 mg/m^2 twice daily for 2 weeks followed by a 1-week rest period given every 3 weeks along with oxaliplatin up to 12 weeks. |
| **Follow-up** | Until disease progression, significant clinical deterioration, unacceptable toxicity, or discontinuation. |
| **Primary Outcomes** | • Overall survival (OS) [ Time frame: from the start of randomisation to a minimum of 36 months ] |
| **Secondary Outcomes** | Time frame: from the start of randomization to a minimum of 36 months<br>• Progression-Free Survival (PFS)<br>• Best Overall Response (BOR) in maintenance phase<br>• Change from baseline in European quality of life 5-dimensions-5 levels (EQ-5D-5L) health outcome questionnaire<br>• Change from baseline in European Organization for the Research and Treatment of Cancer Quality of Life (EORTC QLQ-C30)<br>• Change from baseline in European organization for research and treatment of cancer gastric cancer module QLQ-STO22<br>• Number of subjects with treatment-emergent adverse events (TEAEs) |
| **Key Results** | - |
| **Adverse effects (AEs)** | - |
| **Expected reporting date** | Primary completion date reported as November 2019 |

# ESTIMATED COST

Avelumab is already marketed in the UK; The cost of avelumab 20 mg per 1 mL for the current licensed indication is £768.00.[5]

# RELEVANT GUIDANCE

## NICE GUIDANCE

- NICE technology appraisal in development. Nivolumab for previously treated gastric or gastro-oesophageal junction cancer (ID1118). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Trifluridine–tipiracil for treating metastatic gastric or gastro-oesophageal junction cancer after 2 or more therapies (ID1507). Expected date of issue to be confirmed

- NICE technology appraisal in development. Pembrolizumab for previously treated metastatic gastric or gastro-oesophageal junction cancer (ID1168). Expected date of issue to be confirmed
- NICE technology appraisal. Capecitabine for the treatment of advanced gastric cancer (TA191). July 2010.
- NICE guideline. Oesophago-gastric cancer: assessment and management in adults (NG83). January 2018.
- NICE quality standard. Oesophago-gastric cancer (QS176). December 2018.
- NICE interventional procedure guidance. Endoscopic submucosal dissection of gastric lesions (IPG360). October 2010.
- NICE interventional procedure guidance. Laparoscopic gastrectomy for cancer (IPG269). July 2008.
- NICE interventional procedure guidance. Laparo-endogastric surgery (IPG25). December 2003.

## NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Cancer: Oesophageal and gastric (Adult). B11/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a.
- NHS England. Clinical Commissioning Policy: Robotic assisted surgery for oesophago-gastric cancers. 16006/P. July 2016

## OTHER GUIDANCE

- National Comprehensive Cancer Network (NCCN). Gastric Cancer, Version 3.NCCN Clinical Practice Guidelines in Oncology. 2016.[29]
- European Society for Medical Oncology (ESMO) Guidelines Committee. Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up .2016.[26]
- London Cancer Alliance (LCA). LCA Oesophageal and Gastric Cancer Clinical Guidelines. 2014.[30]
- Britain and Ireland, the British Society of Gastroenterology and the British Association of Surgical Oncology. Guidelines for the management of oesophageal and gastric cancer. 2011.[31]

# ADDITIONAL INFORMATION

# REFERENCES


1 Electronic Medicines Compendium (emc). *Bavencio 20 mg/mL concentrate for solution for infusion.* Available from: https://www.medicines.org.uk/emc/product/8453#PHARMACOLOGICAL_PROPS [Accessed 23 July 2019].

2 ClinicalTrials.gov. *Avelumab in First-Line Maintenance Gastric Cancer (JAVELIN Gastric 100). Trial ID: NCT02625610*. Status: Ongoing. Available from: https://clinicaltrials.gov/ct2/show/NCT02625610 [Accessed 09 July 2019].
3 Moehler MH, Ryu M-H, Lee K-W, Coskun HS, Wong R, Ozguroglu M, et al. JAVELIN Gastric 100: Phase 3 trial of avelumab (anti-PD-L1) maintenance therapy versus continuation of first-line chemotherapy in patients with advanced gastric or gastroesophageal junction cancer (GC/GEJC). *Journal of Clinical Oncology*. 2018 2018/02/01;36(4_suppl):TPS195-TPS. Available from: https://doi.org/10.1200/JCO.2018.36.4_suppl.TPS195.
4 Moehler M, Ryu M-H, Dvorkin M, Lee K-W, Coşkun HŞ, Wong R, et al. Maintenance avelumab versus continuation of first-line chemotherapy in gastric cancer: JAVELIN Gastric 100 study design. *Future Oncology*. 2018 2019/02/01;15(6):567-77. Available from: https://doi.org/10.2217/fon-2018-0668.
5 British Medical Formulary (BNF). *Avelumab*. Available from: https://doi.org/10.18578/BNF.229907442 [Accessed
6 Merck Sharp & Dohme Corp. *Merck Pipeline*. Available from: https://www.merck.com/research/pipeline/home.html [Accessed 22 May 2019].
7 European Medicines Agency. *Orphan designation: EU/3/16/1798*. Available from: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu3161798 [Accessed 09 July 2019].
8 Cancer Research UK. *About advanced cancer*. Available from: https://www.cancerresearchuk.org/about-cancer/stomach-cancer/advanced-cancer/about-advanced-cancer [Accessed 20 June 2019].
9 National Health Service. *Overview - Stomach cancer*. Available from: https://www.nhs.uk/conditions/stomach-cancer/ [Accessed 20 June 2019].
10 Cancer Research UK. *About stomach cancer*. Available from: https://www.cancerresearchuk.org/about-cancer/stomach-cancer/about-stomach-cancer [Accessed 20 June 2019].
11 National Health Service. *Causes - Stomach cancer*. Available from: https://www.nhs.uk/conditions/stomach-cancer/causes/ [Accessed 20 June 2019].
12 Zheng L, Wang L, Ajani J, Xie K. Molecular basis of gastric cancer development and progression. *Gastric Cancer*. 2004;7(2):61-77. Available from: https://dx.doi.org/10.1007/s10120-004-0277-4.
13 Layke JC, Lopez PP. Gastric cancer: diagnosis and treatment options. *Am Fam Physician*. 2004 Mar 1;69(5):1133-40. Available from: https://www.ncbi.nlm.nih.gov/pubmed/15023013.
14 Cancer Research UK. *Stomach cancer incidence statistics*. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/stomach-cancer/incidence [Accessed 20 June 2019].
15 Public Health England. *Chemotherapy, Radiotherapy and Surgical Tumour Resections in England*. Available from: http://www.ncin.org.uk/cancer_type_and_topic_specific_work/topic_specific_work/main_cancer_treatments [Accessed 21 March 2019].
16 National Cancer Registration and Analysis Service (NCRAS). *Gastro-oesophageal junction cancers (ICD10 C15.2, C15.5, C16.0)*. Available from: https://www.google.com/search?q=Gastro-oesophageal+junction+cancers+(ICD10+C15.2%2C+C15.5%2C+C16.0)1&rlz=1C1GCEB_enGB844GB844&oq=Gastro-oesophageal+junction+cancers+(ICD10+C15.2%2C+C15.5%2C+C16.0)1&aqs=chrome..69i57&sourceid=chrome&ie=UTF-8# [Accessed 20 June 2019].
17 NHS Digital. *Hospital Admitted Patient Care Activity, 2017-18*. 2017. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2017-18 [Accessed 17 December 2018].
18 Cancer Research UK. *Stomach cancer statistics*. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/stomach-cancer [Accessed 20 June 2019].
19 Cancer Research UK. *Stomach cancer survival*. Available from: https://www.cancerresearchuk.org/about-cancer/stomach-cancer/survival#collapse-182552 [Accessed 20 June 2019].
20 Cancer Research UK. *Stomach cancer mortality statistics*. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/stomach-cancer/mortality#heading-One [Accessed 10 July 2019].

21 Office for National Statistics (ONS). *21st Office for National Statistics. Death Registrations Summary Statistics, England and Wales, 2017*. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathregistrationssummarytablesenglandandwalesreferencetables [Downloaded 18 December 2018].
22 National Health Service. *Treatment - Stomach cancer*. Available from: https://www.nhs.uk/conditions/stomach-cancer/treatment/ [Accessed 26 June 2019].
23 American Cancer Society. *Surgery for Stomach Cancer*. Available from: https://www.cancer.org/cancer/stomach-cancer/treating/types-of-surgery.html [Accessed 26 June 2019].
24 National Institute for Health and Care Excellence. *Palliative management for people with oesophageal and gastric cancer*. Available from: https://pathways.nice.org.uk/pathways/oesophageal-and-gastric-cancer/palliative-management-for-people-with-oesophageal-and-gastric-cancer.pdf [Accessed 10 July 2019].
25 National Institute for Health and Care Excellence. *Trifluridine–tipiracil for treating metastatic gastric or gastrooesophageal junction cancer after 2 or more therapies; Final scope.* Available from: https://www.nice.org.uk/guidance/gid-ta10456/documents/final-scope [Accessed 10 July 2019].
26 Smyth EC, Committee obotEG, Verheij M, Committee obotEG, Allum W, Committee obotEG, et al. Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. *Annals of Oncology*. 2016;27(suppl_5):v38-v49. Available from: https://doi.org/10.1093/annonc/mdw350.
27 ClinicalTrials.gov. *Study of Pembrolizumab (MK-3475) Plus Chemotherapy Versus Placebo Plus Chemotherapy in Participants With Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma (MK-3475-585/KEYNOTE-585). Trial ID: NCT03221426.* Available from: https://clinicaltrials.gov/ct2/show/NCT03221426 [Accessed 20 June 2019].
28 EU Clinical Trials Register. *Avelumab in First-Line Gastric Cancer*. Available from: https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-003300-23/GB [Accessed 10 July 2019].
29 Jaffer AA, Thomas ADA, Khaldoun A, David JB, Joseph C, Prajnan D, et al. Gastric Cancer, Version 3.2016, NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network J Natl Compr Canc Netw*. 2016;14(10):1286-312. Available from: https://jnccn.org/view/journals/jnccn/14/10/article-p1286.xml.
30 London Cancer Alliance (LCA). *LCA Oesophageal and Gastric Cancer Clinical Guidelines.* Available from: http://www.londoncanceralliance.nhs.uk/media/71819/LCA%20OG%20Cancer%20Clinical%20Guidelines%20April%202014.pdf [Accessed 26 June 2019].
31 Allum WH, Blazeby JM, Griffin SM, Cunningham D, Jankowski JA, Wong R. Guidelines for the management of oesophageal and gastric cancer. *Gut*. 2011;60(11):1449-72. Available from: https://gut.bmj.com/content/gutjnl/60/11/1449.full.pdf.

***NB: This briefing presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.***