Capmatinib is a new drug to treat non-small cell lung cancer. 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. Capmatinib is taken as a tablet and may offer a new treatment option for people whose cancer has returned after their previous treatments.

NIHR HSRIC ID: 7920

Lay summary

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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.

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.
TARGET GROUP

- Non-small cell lung cancer: advanced; epidermal growth factor receptor (EGFR) wild-type; c-Met amplified – second or third line.

TECHNOLOGY

DESCRIPTION

Capmatinib (INC-280; INCB028060) is a small-molecule proto-oncogene protein c-Met inhibitor. The c-Met pathway triggers cell migration, invasion, and proliferation. Dysregulation of the c-Met signaling pathway, due to abnormalities with the c-Met receptor or over-expression of its ligand, have been associated with an aggressive cancer phenotype. c-Met over-expression has also been associated with resistance to EGFR inhibitors. Capmatinib is intended for second or third line treatment of advanced, c-Met amplified non-small cell lung cancer (NSCLC). In the phase II clinical trial, capmatinib is administered orally at 400mg twice daily until disease progression.

Capmatinib does not currently have Marketing Authorisation in the EU for any indication.

Capmatinib is also in phase II development for advanced hepatocellular carcinoma.

INNOVATION and/or ADVANTAGES

If licensed, capmatinib will offer an additional oral treatment option for a subset of patients with advanced NSCLC who currently have few effective therapies available.

DEVELOPER

Novartis Oncology.

AVAILABILITY, LAUNCH OR MARKETING

Capmatinib is currently in phase II clinical trials.

PATIENT GROUP

BACKGROUND

Approximately 85-90% of all lung cancers are of the non-small cell type, which can be further classified into three histological sub-types, namely large-cell undifferentiated carcinoma, squamous cell carcinoma, and adenocarcinoma. The symptoms of NSCLC include haemoptysis, malaise, significant weight loss, dyspnoea and voice loss. Smoking is the main cause of lung cancer, responsible for in excess of 80% of cases. Other known risk factors include exposure to asbestos, arsenic, radon, and non-tobacco-related polycyclic aromatic hydrocarbons. NSCLC has often metastasised by the time of diagnosis, resulting in a poor prognosis.
In the UK, lung cancer is the second most common diagnosed cancer after breast cancer, but is the most common cause of cancer death in the UK, accounting for more than 1 in 5 cancer deaths. In England there were 36,630 cases of lung cancer in 2013 (representing 67.1 cases per 100,000 population) (ICD-10 C34). Incidence of lung cancer is higher in lower socioeconomic groups, and survival is poorer in these groups compared to higher socioeconomic groups. The majority of lung cancers are diagnosed in the later stages of the disease, with 21% presenting with locally and regionally advanced disease (stage IIIIB) and 48% presenting with metastases (stage IV). Median survival for patients with stage IV NSCLC treated with platinum-based therapy is 8 to 12 months, and for people presenting with stage IV NSCLC, the 5-year survival rate varies from 2 to 13%. Around 23% of patients with advanced NSCLC receive first line chemotherapy. Around 30-40% of these patients may subsequently become candidates for second-line therapy (approximately 1,256-1,675 patients in England). Amplification of c-Met is present in 20% of tumours that are resistant to EGFR inhibitor treatment.

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. In 2014, there were 30,851 deaths from lung cancer (ICD-10 C34) registered in England and Wales. The population likely to be eligible to receive capmatinib could not easily be estimated from available routine published sources.

RELEVANT PATHWAY

NICE Guidance

- NICE technology appraisal. Erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed after prior chemotherapy (TA374). December 2015.

**NHS England Policies and Guidance**


**Other Guidance**


**CURRENT TREATMENT OPTIONS**

The aim of treatment for locally advanced or metastatic NSCLC is to prolong survival, improve quality of life, and control disease-related symptoms. Treatment strategies should take into account the tumour histology and molecular pathology, as well as the patient’s age,
performance status, comorbidities, and preferences\textsuperscript{4}. Patients who smoke should be encouraged to cease, as cessation improves treatment outcomes\textsuperscript{4}.

Current guidelines for first line treatment of NSCLC recommend that chemotherapy should be offered to patients with stage IV NSCLC and good performance status (WHO 0 or 1, or a Karnofsky score of 80–100)\textsuperscript{20}. Induction chemotherapy for advanced NSCLC should be a combination of a single third generation drug (docetaxel, gemcitabine, paclitaxel, or vinorelbine) plus a platinum drug (either carboplatin or cisplatin)\textsuperscript{21}. If patients cannot tolerate a platinum combination (or are WHO performance status 2)\textsuperscript{22}, single agent chemotherapy with a third generation drug is recommended\textsuperscript{21}. In the first and subsequent treatment line setting, afatinib, erlotinib and gefitinib are all options for epidermal growth factor receptor tyrosine kinase mutation (EGFR-TK) positive metastatic NSCLC patients\textsuperscript{22,23}.

Pemetrexed in combination with cisplatin is recommended if the tumour has been confirmed as adenocarcinoma or large-cell carcinoma\textsuperscript{21}. Pemetrexed is recommended as maintenance therapy after treatment with platinum-based chemotherapy in combination with gemcitabine, paclitaxel and docetaxel (switch maintenance) if the tumour is adenocarcinoma or large-cell carcinoma\textsuperscript{21,22}.

It is recommended that patients progressing after first line chemotherapy be offered docetaxel or erlotinib monotherapy as a second line treatment option\textsuperscript{21}, or crizotinib for previously treated ALK-positive advanced NSCLC, though this is not currently recommended by NICE\textsuperscript{24}.

### EFFICACY and SAFETY

<table>
<thead>
<tr>
<th>Trial</th>
<th>NCT02414139, CINC280A2201, 2014-003850-15; capmatinib; phase II.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>Novartis Pharmaceuticals.</td>
</tr>
<tr>
<td>Status</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry\textsuperscript{1}, manufacturer.</td>
</tr>
<tr>
<td>Location</td>
<td>EU (not UK), USA, Canada and other countries.</td>
</tr>
<tr>
<td>Design</td>
<td>Non-randomised, uncontrolled.</td>
</tr>
<tr>
<td>Participants</td>
<td>n=276 (planned); aged ≥18 years; NSCLC; advanced stage; EGFR wildtype; ALK-negative; c-Met amplified; 1 or 2 prior systemic therapies; no prior c-Met inhibitor treatment.</td>
</tr>
<tr>
<td>Schedule</td>
<td>Capmatinib 400mg oral twice daily.</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Active treatment until disease progression, follow up until death.</td>
</tr>
<tr>
<td>Primary outcome/s</td>
<td>Overall response rate.</td>
</tr>
<tr>
<td>Secondary outcome/s</td>
<td>Duration of response, time to response, progression free survival, overall survival, adverse events, pharmacokinetics, quality of life (EORTC QLQ-C30 &amp; LC13 and EuroQoL-5 EQ-5D-5L questionnaires).</td>
</tr>
<tr>
<td>Expected reporting date</td>
<td>Study completion date reported as January 2019.</td>
</tr>
</tbody>
</table>
ESTIMATED COST and IMPACT

COST

The cost of capmatinib is not yet known. The costs of selected comparators for the second and subsequent lines of treatment of NSCLC are as follows:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Unit cost (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Docetaxel</td>
<td>75mg/m² intravenous (IV) on day 1 of each 21 day cycle for up to 6 cycles.</td>
<td>A 1-mL vial (at 20mg/mL) costs £160.00</td>
</tr>
<tr>
<td>Pemtrexed</td>
<td>500mg/m² IV on first day of 21 day cycle</td>
<td>500mg vial costs £800</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>150mg/day oral</td>
<td>A pack of 30 x 150mg costs £1,631.53</td>
</tr>
</tbody>
</table>

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: uncertain unit cost compared to existing treatments. ☐ None identified

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

REFERENCES

1 ClinicalTrials.gov. Clinical study of oral cMET inhibitor INC280 in adult patients with advanced non-small cell lung cancer who have received one or two prior lines of therapy. www.clinicaltrials.gov/ct2/show/NCT02414139 Accessed 03 June 2016.
Horizon Scanning Research & Intelligence Centre

   http://publications.cancerresearchuk.org/downloads/Product/CS_KF_LUNG.pdf

   www.hscic.gov.uk/hes


9 NIHR Horizon Scanning Research and Intelligence Centre. Ramucirumab (Cyramza) in combination with docetaxel for locally advanced or metastatic non-small cell lung cancer – second line. University of Birmingham, November 2014. www.hsc.nihr.ac.uk/


22 NIHR Horizon Scanning Research and Intelligence Centre. Crizotinib (Xalkori) for ALK-positive, locally advanced or metastatic, non-small cell lung cancer – first line. University of Birmingham, January 2015. www.hsc.nihr.ac.uk/

