

**NIHR Innovation Observatory
Evidence Briefing: May 2017****Veliparib (ABT-888) with carboplatin and paclitaxel
for advanced or metastatic non-squamous (current
of former smokers) non-small cell lung cancer**

NIHR (HSRIC) ID: 11710

NICE ID: 8480

LAY SUMMARY

Lung cancer is the third most common cancer in the UK. It has two main types, small cell lung cancer and non-small cell lung cancer. The latter type accounts for approximately 90% of all lung cancers. There are three main types of non-small cell lung cancer: adenocarcinoma, squamous cell carcinoma and large cell carcinoma. They usually develop in the cells that line the airways or outer parts of the lungs. Symptoms of non-small cell lung cancer include painful cough, bringing up mucus or phlegm, being short of breath, coughing up blood, ache or pain in the chest or shoulder, loss of appetite, losing weight or feeling very tired. Causes or risk factors include exposure to radon gas or certain chemicals in the workplace, history of other lung diseases such as tuberculosis, family history of lung cancer, cancer treatment for other types of cancer or a lowered immune system and smoking.

Current treatments of non-small cell lung cancer aim to prolong the life of patients. Most early stage cancers are treated with surgery in order to remove the tumour. Chemotherapy or radiotherapy may alternatively be used.

Veliparib is being developed as an improvement on previous drugs, for the treatment of advanced or metastatic non-squamous non-small cell lung cancer. In combination with carboplatin and paclitaxel it will, if licenced, offer an additional treatment option for patients with this indication.

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

Veliparib (ABT-888) with carboplatin and paclitaxel for advanced or metastatic non-squamous (current or former smokers) non-small-cell lung cancer (NSCLC).

TECHNOLOGY

DESCRIPTION

Veliparib [ABT-888; NSC-737664] is a poly (ADP-ribose) polymerase (PARP) inhibitor, for the treatment of cancer. Veliparib is orally administered. It was optimised from a prior lead compound (A 620223) and has an improved pharmacokinetic profile compared with its predecessor. Veliparib inhibits both PARP-1 and PARP-2 enzymes; PARP enzymes recognise DNA damage and facilitate DNA repair. Research has shown that inhibition of PARP enzymes can potentiate the cytotoxicity of common DNA-damaging cancer therapies such as radiation and alkylating chemotherapeutics.

Clinical trials for veliparib are underway worldwide, investigating the technology primarily as part of a combination therapy in oncology indications such as brain, colorectal, melanoma, ovarian, prostate and pancreatic cancers. Phase III development is underway worldwide in patients with breast cancer, and phase III development is underway in the US, the EU, Norway, Canada, Russia and Australia in patients with non-small cell lung cancer. Development is at the phase II/III stage for glioblastoma in the US and Puerto Rico. Phase II development as a combination therapy for germ cell tumours is in progress in Slovakia. Phase II development as a combination therapy for rectal cancer is underway in the US. Phase I/II development in small cell lung cancer is ongoing in the US and for ovarian cancer in Denmark. Phase I development in solid tumours is ongoing in the US, Spain, the Netherlands, South Korea and Japan.¹

In a phase III clinical trial veliparib is administered on day -2 through 5 of a 21-day cycle and carboplatin and paclitaxel on day 1 of a 21 day cycle.¹

INNOVATION and/or ADVANTAGES

If licenced, veliparib (ABT-888) with carboplatin and paclitaxel will offer an additional treatment option for patients with advanced or metastatic non-squamous (current or former smokers) non-small-cell lung cancer.

DEVELOPER

AbbVie

AVAILABILITY, LAUNCH or MARKETING

Veliparib is currently in phase III clinical trials in combination with carboplatin and paclitaxel for (current or former smokers) advanced or metastatic non-squamous non-small-cell lung cancer.¹

PATIENT GROUP

BACKGROUND

Lung cancer has two main types, which behave in different ways and require different treatment. NSCLC is the most common type, accounting for approximately 90% of all lung cancers; small cell lung cancer (SCLC) makes up to about a tenth of all lung cancers. The latter type gets its name from how the cancer cells look when examined under a microscope and is usually caused by smoking and grows and spreads rapidly. There are three main types of NSCLC: adenocarcinoma, which develops from mucus-producing cells that line the airways; squamous cell carcinoma, which is usually caused by smoking and also develops in the cells that line the airways; and large cell carcinoma² that spreads more quickly than other types and is usually found in outer parts of the lungs – which means usual symptoms of lung cancer may not be present until much later on in the progression of the disease.³

Usually symptoms of lung cancer include having a cough for a long period of time (often becoming painful, and bringing up mucus or phlegm), being short of breath, coughing up blood, an ache or pain in the chest or shoulder, loss of appetite, losing weight and feeling very tired.⁴ Causes or risk factors include exposure to radon gas or certain chemicals in the workplace, history of other lung diseases such as tuberculosis, family history of lung cancer, cancer treatment for other types of cancer or a lowered immune system.⁵

CLINICAL NEED and BURDEN OF DISEASE

Lung cancer is the third most common cancer in the UK. About 46,400 people are diagnosed with the condition each year. More than 4 out of 10 people (44%) diagnosed with lung cancer in the UK are aged 75 and older. About half of lung cancer deaths in the UK each year are in people aged 75 and over. Lung cancer accounts for 13% of all new cancer cases in the UK (2014). 1 in 13 men and 1 in 17 women will be diagnosed with lung cancer during their lifetime. Incidence rates are highest in people aged 85-89.⁶ Smoking can be linked to 86% of people who are diagnosed.⁵ Furthermore about 87 out of every 100 lung cancers in the UK (87%) are non-small cell lung cancer (NSCLC).⁷

Lung cancer caused about 35,900 deaths in England in 2014. The median survival with lung cancer (all stages) is approximately 6 months.

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal in development. Lung cancer (non-small-cell, untreated) - paclitaxel formulated as albumin-bound nanoparticles (with carboplatin) [ID553]. Expected TBC.
- NICE technology appraisal. Crizotinib for untreated anaplastic lymphoma kinase-positive advanced non-small-cell lung cancer [TA406]. September 2016.
- NICE technology appraisal. Necitumumab for untreated advanced or metastatic squamous non-small-cell lung cancer [TA411]. September 2016.
- NICE technology appraisal. Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin [TA402]. August 2016.
- NICE technology appraisal. Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer [TA403]. August 2016.
- NICE technology appraisal. Paclitaxel as albumin-bound nanoparticles with carboplatin for untreated non-small-cell lung cancer (terminated appraisal) [TA362]. October 2015.
- NICE technology appraisal. Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer [TA347]. July 2015.

- NICE technology appraisal. Pemetrexed for the maintenance treatment of non-small-cell lung cancer [TA190]. June 2010.
- NICE clinical guidance. Lung cancer: diagnosis and management [CG121]. April 2011.

NHS ENGLAND and POLICY GUIDANCE

- NHS England. 2016 Clinical Commissioning Policy: Robotic assisted lung resection for primary lung cancer. 16024/P
- NHS England. 2013 Clinical Commissioning Policy: Stereotactic Ablative Body Radiotherapy for Non-Small-Cell Lung Cancer. NHSCB/B01/P/a

OTHER GUIDANCE

No other guidance was identified.

CURRENT TREATMENT OPTIONS

Most stage I and stage II non-small cell lung cancers are treated with surgery to remove the tumour. Video-assisted thoracoscopic surgery is sometimes used. Adjuvant chemotherapy after surgery may help prevent the cancer from returning. This is particularly true for patients with stage II and IIIA disease. In cases the tumour cannot be removed with surgery, chemotherapy in combination with radiation treatments are recommended.

Chemotherapy treatment plan consists of a combination of drugs – those most commonly used are: cisplatin or carboplatin plus docetaxel, gemcitabine, paclitaxel, vinorelbine, or pemetrexed. Neoadjuvant chemotherapy may shrink the tumour enough to make it easier to remove with surgery, increasing the effectiveness of radiation and destroying hidden cancer cells at the earliest possible time. Targeted treatments have recently been used, which are designed specifically to attack cancer cells (unlike chemotherapy) by attaching to or blocking targets that appear on the surfaces of those cells. These include erlotinib, afatinib, gefitinib, bevacizumab, crizotinib and ceritinib. Immunotherapy has recently emerged as a new treatment option for certain lung cancers.⁸

EFFICACY and SAFETY

Trial	GDCT0225995, NCT02264990; phase III
Sponsor	AbbVie
Status	Open
Source of Information	Trial registry ¹
Location	Europe (incl.UK), Canada, USA and other countries
Design	Randomized, open-Label, multicentre, phase III parallel assignment
Participants	Estimated N= 525, aged > or = 18; Life expectancy > 12 weeks. Subject must have cytologically or histologically confirmed advanced or metastatic non-squamous NSCLC and are current (defined as having > 100 smoking events lifetime and having smoked within the past year) or former smokers (defined as having > 100 smoking events lifetime and having not smoked within the past year). Subject must have NSCLC that is not amenable to surgical resection or

	radiation with curative intent at time of screening. Subject must have at least 1 unidimensional measurable NSCLC lesion on a CT scan as defined by Response Evaluation Criteria In Solid Tumors.
Schedule	Experimental: veliparib/carboplatin/paclitaxel Veliparib is administered on day -2 through 5 of a 21-day cycle and carboplatin and paclitaxel on day 1 of a 21 day cycle. Active Comparator: Investigator's choice of platinum doublet: either carboplatin and paclitaxel, cisplatin and pemetrexed, or carboplatin and pemetrexed on Day 1 of a 21 day cycle.
Follow-up	Not reported.
Primary Outcomes	Overall survival (OS) in current smokers. Overall survival is defined as the number of days from the date that the participant was randomised to the date of the participant's death.
Secondary Outcomes	Overall survival (OS) in all participants. Progression free survival (PFS) in current smokers and all participants. Objective response rate (ORR) in current smokers and all participants.
Key Results	Not reported
Adverse effects (AEs)	Not reported
Expected reporting date	Estimated study completion date July 31, 2017.

ESTIMATED COST and IMPACT

COST

The cost of veliparib is not yet known.

IMPACT – SPECULATIVE

IMPACT ON PATIENTS and CARERS

- Reduced mortality/increased length of survival Reduced symptoms or disability
 Other: *improved patient convenience, wider societal benefits* 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

INFORMATION FROM

UK PharmaScan ID: 641058

REFERENCES

- 1 AdisInsight. Veliparib. 2017 [cited 2017 02.05.]; Available from: <http://adisinsight.springer.com/drugs/800028802>
- 2 Macmillan Cancer Support. Types of Lung Cancer 2015 [cited 2017 03.05.]; Available from: <http://www.macmillan.org.uk/information-and-support/lung-cancer/understanding-cancer/types-of-lung-cancer.html#159860>
- 3 Lung Health UK. Non small cell lung cancer. 2017 [cited 2017 03.05.]; Available from: <https://www.lunghealthuk.com/what-is-lung-cancer/non-small-cell-lung-cancer>
- 4 Cancer Research UK. Lung cancer- symptoms. 2015 [cited 2017 03.05.]; Available from: <http://www.cancerresearchuk.org/about-cancer/lung-cancer/symptoms>
- 5 Cancer Research UK. About lung cancer. 2016 [cited 2017 02.05.]; Available from: <http://www.cancerresearchuk.org/about-cancer/lung-cancer/about>
- 6 Cancer Research UK. Lung cancer statistics. 2014 [cited 2017 03.05.]; Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer#heading-One>
- 7 Cancer Research UK. Lung cancer - types. 2016 [cited 2017 02.05.]; Available from: <http://www.cancerresearchuk.org/about-cancer/lung-cancer/stages-types-grades/types>
- 8 LungCancer.org. Non-small cell lung cancer treatment. 2017 [cited 2017 03.05.]; Available from: http://www.lungcancer.org/find_information/publications/163-lung_cancer_101/269-non-small_cell_lung_cancer_treatment