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

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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.

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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.  

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.  

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. 

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 carcinoma 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.

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. 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.

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. Smoking can be linked to 86% of people who are diagnosed. Furthermore about 87 out of every 100 lung cancers in the UK (87%) are non-small cell lung cancer (NSCLC).

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. Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer [TA403]. August 2016.
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**

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<th>Trial</th>
<th>GDCT0225995, NCT02264990; phase III</th>
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<td>Source of Information</td>
<td>Trial registry¹</td>
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<td>Location</td>
<td>Europe (incl.UK), Canada, USA and other countries</td>
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<td>Design</td>
<td>Randomized, open-Label, multicentre, phase III parallel assignment</td>
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<td>Participants</td>
<td>Estimated N= 525, aged ≥ 18; Life expectancy &gt; 12 weeks. Subject must have cytologically or histologically confirmed advanced or metastatic non-squamous NSCLC and are current (defined as having &gt; 100 smoking events lifetime and having smoked within the past year) or former smokers (defined as having &gt; 100 smoking events lifetime and having not smoked within the past year). Subject must have NSCLC that is not amenable to surgical resection or</td>
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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
4 Cancer Research UK. Lung cancer- symptoms. 2015 [cited 2017 03.05. ]; Available from: http://www.cancerresearchuk.org/about-cancer/lung-cancer/symptoms