National Institute for Health Research

NIHR Innovation Observatory
Evidence Briefing: July 2018

Atezolizumab in addition to chemotherapy for stage IV non-squamous non-small-cell lung cancer – first line

NIHRIO (HSRIC) ID: 12879 NICE ID: N/A

LAY SUMMARY

Non-small-cell lung cancer (NSCLC) comprise the majority of lung cancers in the UK. NSCLC has two types, squamous and non-squamous (which includes adenocarcinoma and large cell) cancers. Adenocarcinoma and large cell cancers both involve the outer areas of the lungs and are difficult to detect in early stages. Stage IV (or advanced/metastatic) NSCLC is when the cancer has spread beyond the lung which was initially affected, most often to the liver, the adrenal glands, the bones, and the brain. Symptoms may include a persistent cough, hoarseness, shortness of breath, weight-loss or lack of appetite, feeling weak or tired, coughing up blood and pneumonia or infections that keep coming back.

Atezolizumab is a monoclonal antibody designed to recognise and attach to a protein called 'programmed death-ligand 1' (PD-L1), which is present on the surface of many cancer cells. PD-L1 switches off immune cells that would otherwise attack cancer cells. By attaching to PD-L1 and reducing its effect, atezolizumab increases the ability of the immune system to attack the cancer cells and thereby slow down the progression of the disease. Atezolizumab is administered by intravenous infusion. If licensed, atezolizumab in addition to current chemotherapy will offer an additional first line treatment option for patients with untreated, advanced, non-squamous non-small cell lung cancer.

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 (NSCLC) (non-squamous, stage IV) – first line; in combination with chemotherapy (carboplatin and nab-paclitaxel).

TECHNOLOGY

DESCRIPTION

Atezolizumab (Tecentriq) is an Fc-engineered, humanised immunoglobulin G1 (IgG1) monoclonal antibody that directly binds to programmed death-ligand 1 (PD-L1) and provides a dual blockade of the PD-1 and B7.1 receptors. It releases PD-L1/PD-1 mediated inhibition of the immune response, including reactivating the anti-tumour immune response without inducing antibody-dependent cellular cytotoxicity. Atezolizumab spares the PD-L2/PD-1 interaction allowing PD-L2/PD-1 mediated inhibitory signals to persist. PD-L1 may be expressed on tumour cells and/or tumour-infiltrating immune cells, and can contribute to the inhibition of the anti-tumour immune response in the tumour microenvironment. Binding of PD-L1 to the PD-1 and B7.1 receptors found on T-cells and antigen presenting cells suppresses cytotoxic T-cell activity, T-cell proliferation and cytokine production.[1]

In the phase III clinical trial (IMpower130, NCT02367781), the two treatment arms being studied are atezolizumab with nab-paclitaxel and carboplatin (Arm A), versus nab-paclitaxel and carboplatin (Arm B) in the treatment of naïve stage IV non-squamous NSCLC. Within the study atezolizumab and carboplatin are administered by intravenous (IV) infusion on day 1 of each 21-day cycle, and nab-paclitaxel on days 1, 8, and 15 of each 21-day cycle for four or six cycles or until loss of clinical benefit (whichever occurs first during induction treatment phase). During maintenance treatment IV infusion of atezolizumab is given until loss of clinical benefit.[2]

Atezolizumab is already licensed in the EU as monotherapy for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma after prior platinum-containing chemotherapy, or who are considered cisplatin ineligible. It is also licensed as monotherapy for the treatment of adult patients with locally advanced or metastatic NSCLC after prior chemotherapy. Patients with EGFR activating mutations or ALK-positive tumour mutations should also have received targeted therapy before receiving atezolizumab.[1,3] The most common side effects with atezolizumab (which may affect more than 1 in 10 people) are tiredness, reduced appetite, nausea and vomiting, difficulty breathing, diarrhoea, rash, fever, joint pain, weakness and itching.[3]

Atezolizumab is in phase II and phase III clinical development, as monotherapy or in combination with other drugs, for the treatment of a range of cancers such as breast cancer, hepatocellular carcinoma, ovarian cancer and solid tumours.[4]

INNOVATION and/or ADVANTAGES

Non-squamous NSCLC is a heterogeneous disease with multiple treatment options dependent upon staging, presence of metastasis, and patient factors including presence of comorbidities among other considerations. Current treatment options include surgical resection, chemotherapy, radiation, immunotherapy, and targeted therapy.[5]

Results from the phase III IMpower130 study where atezolizumab is added to standard chemotherapies have shown improvement in overall survival (OS) and progression-free survival (PFS).[6]

If licensed, atezolizumab in addition to chemotherapy will offer a first line treatment option for patients with advanced non-squamous NSCLC not previously treated.

DEVELOPER

Roche Products Ltd.

PATIENT GROUP

BACKGROUND

Lung cancer is classified as one of two main histologic types: small-cell lung cancer (SCLC) or non-small-cell lung cancer (NSCLC).[7] NSCLC comprises approximately 87% of lung cancers in the UK.[8] NSCLC can further be sub-classified as squamous (~30%) or non-squamous (~70%; includes adenocarcinoma and large-cell histologies).[9]

The most common type of lung cancer is adenocarcinoma; it comprises around 40% of all lung cancer. It arises from small airway epithelial, type II alveolar cells, which secrete mucus and other substances. Adenocarcinoma is the most common type of lung cancer in smokers and non-smokers in men and women regardless of their age. Compared to other types of lung cancer, adenocarcinoma tends to grow slower and has a greater chance of being found before it has spread outside of the lungs.[10]

Large cell (undifferentiated) carcinoma accounts for 5–10% of lung cancers. This type of carcinoma shows no evidence of squamous or glandular maturation and as a result is often diagnosed by default through exclusion of other possibilities. Large cell carcinoma often begins in the central part of the lungs, sometimes into nearby lymph nodes and into the chest wall as well as distant organs. Large cell carcinoma tumours are strongly associated with smoking.[10]

Symptoms of lung cancer include a persistent cough (which may be more painful, have a different sound or bring up coloured mucus), shortness of breath, coughing up blood, aches and pains in the chest or shoulder, loss of appetite, weight loss and fatigue.[11]

NSCLC can be graded to give an idea of how quickly the cancer may grow and whether it is likely to spread. NSCLC is graded from stages 1 to 4. Stage 4 is advanced lung cancer which had spread and can further subdivide into stage 4A and 4B. Stage 4A NSCLC described cancer in both the lungs, cancer covering the pleura or pericardium, fluid around the lungs or heart that contain cancer cells or cancer which has spread from the chest to a lymph node or other organ. Stage 4B NSCLC means cancer has spread to several areas in one or more organs.[12] NSCLC is often asymptomatic until it has become well advanced. Upon initial NSCLC diagnosis, 20% of patients have localized disease, 25% of patients have regional metastasis, and 55% of patients have distant metastasis.[13] Once lung cancer has metastasised (spread to other distant organs), the 5-year overall survival is less than 5%. Symptoms of metastatic lung tumours depend on the location and size. Lung cancer most often spreads to the liver, the adrenal glands, the bones, and the brain.[14]

CLINICAL NEED and BURDEN OF DISEASE

NSCLC is the most common type of lung cancer with approximately 88% of all cases having this type. There are three common types: adenocarcinoma, squamous cell cancer and large cell carcinoma.[8, 9]

In England in 2016 there were 38,363 registrations of newly diagnosed cases of malignant neoplasm of bronchus and lung (ICD-10 code C34).[15] Across the UK, the incidence rate for lung cancer (ICD-10 codes C33-34) is expected to decrease from 94.41 per 100,000 European age-standardised rate (EASR) (46,400 cases) in 2014 to 87.99 per 100,000 EASR (62,832 cases) in 2035.[16]

In England and Wales in 2016 there were 30,570 deaths with malignant neoplasm of trachea, bronchus and lung (ICD-10 codes C33-34) recorded as the underlying cause.[17]

Stage IV adenocarcinoma patients have a 5-year survival rate of 1.5% while the 5-year survival rate for stage IV large cell carcinoma is 1.1%.[18] In England in 2016-17, there were 91,902 hospital admissions with a primary diagnosis of malignant neoplasm of bronchus and lung (ICD-10 C34), resulting in 267,931 FCE bed days and 64,257 day cases.[19]

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal in development. Nivolumab in combination with platinum-doublet chemotherapy for untreated PD-L1-negative non-small-cell lung cancer (ID1135). Expected publication date TBC.
- NICE technology appraisal in development. Atezolizumab for untreated non-squamous non-small-cell lung cancer (ID1210). Expected publication date TBC.
- NICE technology appraisal in development. Veliparib with carboplatin and paclitaxel for untreated non-squamous non-small-cell lung cancer (ID1277). Expected publication date TBC.
- NICE technology appraisal in development. Nivolumab in combination with ipilimumab for untreated PD-L1-positive non-small-cell lung cancer (ID1187). Expected publication date: May 2019.
- NICE technology appraisal in development. Avelumab for untreated PD-L1 positive non-small cell lung cancer (ID1261). Expected publication date TBC.
- NICE technology appraisal in development. Pembrolizumab for untreated PD-L1 positive metastatic non-small-cell lung cancer (CDF Review of TA447) (ID1349). July 2018.
- NICE technology appraisal. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (TA447). June 2017.
- NICE technology appraisal. Necitumumab for untreated advanced or metastatic squamous non-small-cell lung cancer (TA411). September 2016.
- NICE technology appraisal. Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer (TA192). July 2010.
- NICE technology appraisal. Pemetrexed for the first-line treatment of non-small-cell lung cancer (TA181). September 2009.
- NICE technology appraisal. Pemetrexed for the treatment of non-small-cell lung cancer (TA124). August 2007.
- NICE clinical guideline. Lung cancer: diagnosis and management (CG121). April 2011.
- NICE quality standards. Lung cancer in adults (QS17). March 2012.

NHS ENGLAND and POLICY GUIDANCE

- 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. 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 (Adult). B01/P/a.

OTHER GUIDANCE

- European Society for Medical Oncology. Metastatic non-small cell lung cancer (NSCLC): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. 2014.[20]
- Scottish Intercollegiate Guidelines Network. Management of lung cancer (SIGN 137). 2014.[21]
- National Comprehensive Cancer Network. The NCCN clinical practice guidelines in oncology. Non-small cell lung cancer. 2013.[22]

CURRENT TREATMENT OPTIONS

Treatment of non-squamous NSCLC varies by location within the lung and/or body, how far the cancer has spread (the stage), abnormality of cells (the grade), and the general health and level of fitness of the patient. Treatment options may include surgery, chemotherapy and/or radiotherapy, and a variety of symptom control management treatments. NSCLC is referred to as metastatic or stage IV disease when it has spread beyond the lung which was initially affected. It is rarely possible to remove metastatic NSCLC with surgery or to treat it radically with chemotherapy.[23]

Intravenous chemotherapy with a two-drug combination (with or without the addition of the targeted therapy called bevacizumab) is the main treatment option for patients with metastatic or stage IV NSCLC. New options using first-line immunotherapy are under evaluation and pembrolizumab has recently been approved in the EU for use in this setting. Immunotherapy is likely to replace or complement first-line chemotherapy in selected patients in the next few years.[23]

In the clinical management of treatment-naïve non-squamous NSCLC, platinum therapy may be given as an initial treatment in people whose disease is not epidermal growth factor receptor mutation (EGFR) or anaplastic lymphoma kinase (ALK) positive.[24] In patients whose tumours express high amounts of PD-L1, pembrolizumab may be given.[25] For those with EGFR-positive disease, treatment may start with a targeted tyrosine kinase inhibitor (TKI) such as erlotinib, followed by a platinum therapy option after the disease stops responding to TKI therapy.[24] For people with ALK-positive NSCLC, an ALK-inhibitor such as alectinib, ceritinib or crizotinib are typically the standard treatment of choice.[26,24]

Updates to NICE clinical guideline (CG121) for the diagnosis and management of lung cancer are expected in March of 2019.[27] NICE technology appraisal guidance for the use of atezolizumab for untreated non-squamous non-small-cell lung cancer (ID1210) is also in development, with expected publication date to be confirmed.[28]

EFFICACY and SAFETY

Trial	IMpower130, NCT02367781, GO29537; adults; atezolizumab in combination with carboplatin plus nab-paclitaxel vs carboplatin plus nab-paclitaxel; phase III
Sponsor	Hoffmann-La Roche
Status	Ongoing

Source of Information	Trial registry[2]
Location	5 EU countries (not including UK), USA, Canada, Hong Kong and Israel
Design	Randomised, crossover
Participants	n=724 (enrolled); aged 18 years and older; non-small-cell lung cancer; non-squamous; stage IV; no prior treatment
Schedule	Patients will be randomised to intravenous infusion (IV) of atezolizumab and carboplatin on day 1 of each 21-day cycle, and nab-paclitaxel on days 1, 8, and 15 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first during induction treatment phase. Participants will receive IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.
Follow-up	Not reported
Primary Outcomes	• Progression-Free Survival (PFS) as determined by the investigator using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) [Time frame: Baseline until disease progression or death, whichever occurs first (up to approximately 31 months)] • Overall Survival (OS) [Time frame: Baseline until death (up to approximately 31 months)]
Secondary Outcomes	• Duration of Response (DOR) as determined by the investigator using RECIST v1.1 [Time frame: From first occurrence of a documented OR to the time of disease progression or death, whichever occurs first (up to approximately 41 months)] • Percentage of participants who are alive at year 1 and 2 [Time frame: years 1 and 2] • Time to deterioration (TTD) in patient-reported lung cancer symptoms as determined by European Organization for Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire-Core 30 (QLQ-C30) score [Time frame: Baseline up to approximately 41 months] • TTD in patient-reported lung cancer symptoms as determined by EORTC Quality-of-Life Questionnaire-Core Lung Cancer module 13 (QLQ-LC13) [Time frame: Baseline up to approximately 41 months] • Change From baseline in patient-reported lung cancer symptoms score using the Symptoms in Lung Cancer (SILC) Scale [Time frame: Baseline up to approximately 41 months] • Percentage of participants with adverse events [Time frame: Baseline up to approximately 41 months] • Percentage of participants with Anti-Therapeutic Antibodies (ATAs) to atezolizumab [Time frame: Baseline up to approximately 41 months] • Maximum observed serum concentration (Cmax) of atezolizumab [Time frame: Arm A: predose on day (D) 1 of cycle (Cy) 1,2,3,4,8,16 and every 8 cycles thereafter up to end of treatment (EOT) (approximately 41 months), 0.5 hours (h) post-infusion on D1 of Cy1,3, at 120 days after EOT (up to approximately 41 months)] • Minimum observed serum concentration (Cmin) of atezolizumab prior to Infusion [Time frame: Arm A: predose on D1 of Cy 1, 2, 3, 4, 8, 16 and every 8 cycles thereafter up to EOT (approximately 41 months), at 120 days after EOT (up to approximately 41 months)] • Plasma concentrations of carboplatin [Time frame: predose (same day of treatment administration), 5-10 minutes before end of carboplatin infusion,

	1 h after carboplatin infusion (infusion duration=15 to 30 minutes) on D1 of Cy1,3 (1Cy=21 days)] • Plasma concentrations of nab-paclitaxel reported as total paclitaxel [Time frame: predose (same day of treatment administration), 5-10 minutes before end of nab-paclitaxel infusion, 1 h after nab-paclitaxel infusion (infusion duration=30 minutes) on D1 of Cy1,3 (1Cy=21 days)] • Cmax of atezolizumab in arm B participants who received atezolizumab during maintenance phase [Time frame: Arm B: predose on D1 of Cy 1A,2A,3A,4A,8A,16A and every 8 cycles thereafter up to EOT (approximately 41 months), 0.5 h post-infusion on D1 of Cy1A,3A, at 120 days after EOT (up to approximately 41 months)] • Cmin of atezolizumab prior to infusion in arm B participants who received atezolizumab during maintenance phase [Time frame: Arm B: predose on D1 of Cy 1A,2A,3A,4A,8A,16A and every 8 cycles thereafter up to EOT (approximately 41 months), at 120 days after EOT (up to approximately 41 months)]
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Estimated study completion date reported as December 2019.

ESTIMATED COST and IMPACT

COST

Atezolizumab is already marketed in the UK for the treatment of urothelial carcinoma and non-small-cell lung cancer (specialist use only). The cost of atezolizumab 60mg/1ml concentrate for solution for infusion vial is £3,807.[29]

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: When compared to chemotherapy comparators that some patients may get.

☐ 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

[1] Electronic Medicines Compendium. *Tecentriq 1,200 mg concentrate for solution for infusion*. Available from: https://www.medicines.org.uk/emc/product/8442/smpc%23PHARMACOLOGICAL_PROPS#PHARMACODYNAMIC_PROPS [Accessed on 03 July 2018]

[2] ClinicalTrials.gov. *A Study of Atezolizumab in Combination With Carboplatin Plus (+) Nab-Paclitaxel Compared With Carboplatin+Nab-Paclitaxel in Participants With Stage IV Non-Squamous Non-Small Cell Lung Cancer (NSCLC) (IMpower130).* Available from: https://clinicaltrials.gov/ct2/show/record/NCT02367781 [Accessed on 03 July 2018]

[3] European Medicines Agency. *Tecentriq (atezolizumab).* Available from: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/004143/WC500235781.pdf [Accessed on 03 July 2018]

[4] Roche. *Product Development Portfolio*. Available from: https://www.roche.com/de/research_and_development/who_we_are_how_we_work/pipeline.htm [Accessed on 03 July 2018]

[5] Targeted Oncology. *Current Treatment Strategies in Nonsquamous Non-Small Cell Lung Cancer*. Available from: https://www.targetedonc.com/publications/evolving-paradigms/2017/immunotherapy-nsclc/current-treatment-strategies-in-nonsquamous-nonsmall-cell-lung-cancer [Accessed on 03 July 2018]

[6] Roche. *Media Release.* Available from: https://www.roche.com/media/releases/med-cor-2018-05-29.htm [Accessed on 03 July 2018]

[7] American Cancer Society. *What Is Non-Small Cell Lung Cancer?* Available from: https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lung-cancer.html [Accessed on 03 July 2018]

[8] Cancer Research UK. *Lung cancer: Types*. Available from: https://about-cancer.cancerresearchuk.org/about-cancer/lung-cancer/stages-types-grades/types [Accessed on 03 July 2018]

[9] McKeage MJ, Jameson MB and AS1404-201 Study Group Investigators. Comparative outcomes of squamous and non-squamous non-small cell lung cancer (NSCLC) patients in phase II studies of ASA404 (DMXAA) – retrospective analysis of pooled data. *J Thorac Dis*. 2010 Dec; 2(4): 199–204. Available from: https://dx.doi.org/10.3978%2Fj.issn.2072-1439.2010.02.04.1

[10] Zappa C and Mousa SA. Non-small cell lung cancer: current treatment and future advances. *Transl Lung Cancer Res*. 2016 Jun; 5(3): 288–300. Available from: https://dx.doi.org/10.21037%2Ftlcr.2016.06.07

[11] Cancer Research UK. *Lung cancer – Symptoms.* Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/symptoms [Accessed 26 July 2018]

[12] Cancer Research UK. *Lung cancer – Stage 4.* Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/stages-types-grades/stage-4 [Accessed 26 July 2018]

[13] Medscape. *Non-Small Cell Lung Cancer*. Available from: https://emedicine.medscape.com/article/279960-overview [Accessed on 03 July 2018]

[14] Emedicine health. *Lung cancer*. Available from: https://www.emedicinehealth.com/lung_cancer/article_em.htm#lung_cancer_quick_overview [Accessed on 03 July 2018]

[15] Office for National Statistics. *Cancer Registration Statistics, England, 2016.* Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancerregistrationstatisticscancerregistrationstatisticsengland. [Downloaded 06 February 2018] [Accessed 04 July 2018]

[16] Cancer Research UK. *Selected Cancers, Number of Projected and Observed Cases and European Age-Standardised Incidence Rates per 100,000 people by Cancer Type and Sex*. Available from: http://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/common-cancers-compared#heading-Four [Downloaded 09 March 2018] [Accessed 04 July 2018]

[17] Office for National Statistics. *Death Registrations Summary Statistics, England and Wales, 2016*. Available from:https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathregistrationssummarytablesenglandandwalesreferencetables. [Downloaded 06 February 2018] [Accessed 04 July 2018]

[18] Cetin K, Ettinger DS, Hei YJ, O'Malley CD. Survival by histologic subtype in stage IV nonsmall cell lung cancer based on data from the Surveillance, Epidemiology and End Results Program. *Clin Epidemiol.* 2011; 3:139-48. Available from: https://dx.doi.org/10.2147%2FCLEP.S17191

[19] NHS Digital, Hospital Episode Statistics for England. *Admitted Patient Care statistics, 2016-17*. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2016-17 [Accessed on 03 July 2018]

[20] Azzoli CG, Temin S, Aliff T , Baker Jr S, Brahmer J, Johnson DH et al. New ASCO focused update recommendation on Maintenance treatment of
Stage IV non-small cell lung cancer. *Journal of Clinical Oncology.* 2011;29:3825-3831. Available from: https://doi.org/10.1200/JCO.2010.34.2774

[21] Scottish Intercollegiate Guidelines Network. Management of Lung cancer (SIGN 137). Available from http://www.sign.ac.uk/assets/sign137.pdf [Accessed on 03 July 2018]

[22] National Comprehensive Cancer Network. *Clinical Practice Guidelines in Oncology. Non-small cell lung cancer. Version 1. 2015.* Available from http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf [Accessed on 03 July 2018]

[23] European Society for Medical Oncology. *What is non-small-cell lung cancer?* Available from: https://www.esmo.org/content/download/7252/143219/file/EN-Non-Small-Cell-Lung-Cancer-Guide-forPatients.pdf [Accessed 20 July 2018]

[24] Toschi L, Rossi S, Finocchiaro G and Santoro A. Non-small cell lung cancer treatment (r)evolution: ten years of advances and more to come. *eCancer Medical Science*. 2017; 11: 787. Available from: https://dx.doi.org/10.3332%2Fecancer.2017.787

[25] Ernani V and Ganti AK. Immunotherapy in treatment naïve advanced non-small cell lung cancer. *Journal of Thoracic Disease*. 2018 Feb; 10(Suppl 3): S412-S421. Available from: https://dx.doi.org/10.21037%2Fjtd.2017.12.94

[26] National Institute for Health and Care Excellence. *Technology appraisal guidance: Nivolumab for previously treated non-squamous non-small-cell lung cancer [TA484].* Available from: https://www.nice.org.uk/guidance/ta484/resources/nivolumab-for-previously-treated-nonsquamousnonsmallcell-lung-cancer-pdf-82605026489029 [Accessed 20 July 2018]

[27] National Institute for Health and Care Excellence. *Lung cancer: diagnosis and management (update).* Available from: https://www.nice.org.uk/guidance/indevelopment/gid-ng10061 [Accessed 20 July 2018]

[28] National Institute for Health and Care Excellence. *Atezolizumab for untreated non-squamous non-small-cell lung cancer [ID1210].* Available from: https://www.nice.org.uk/guidance/indevelopment/gid-ta10340 [Accessed 20 July 2018]

[29] National Institute for Health and Care Excellence BNF. *Atezolizumab*. Available from: https://bnf.nice.org.uk/medicinal-forms/atezolizumab.html [Accessed on 03 July 2018]