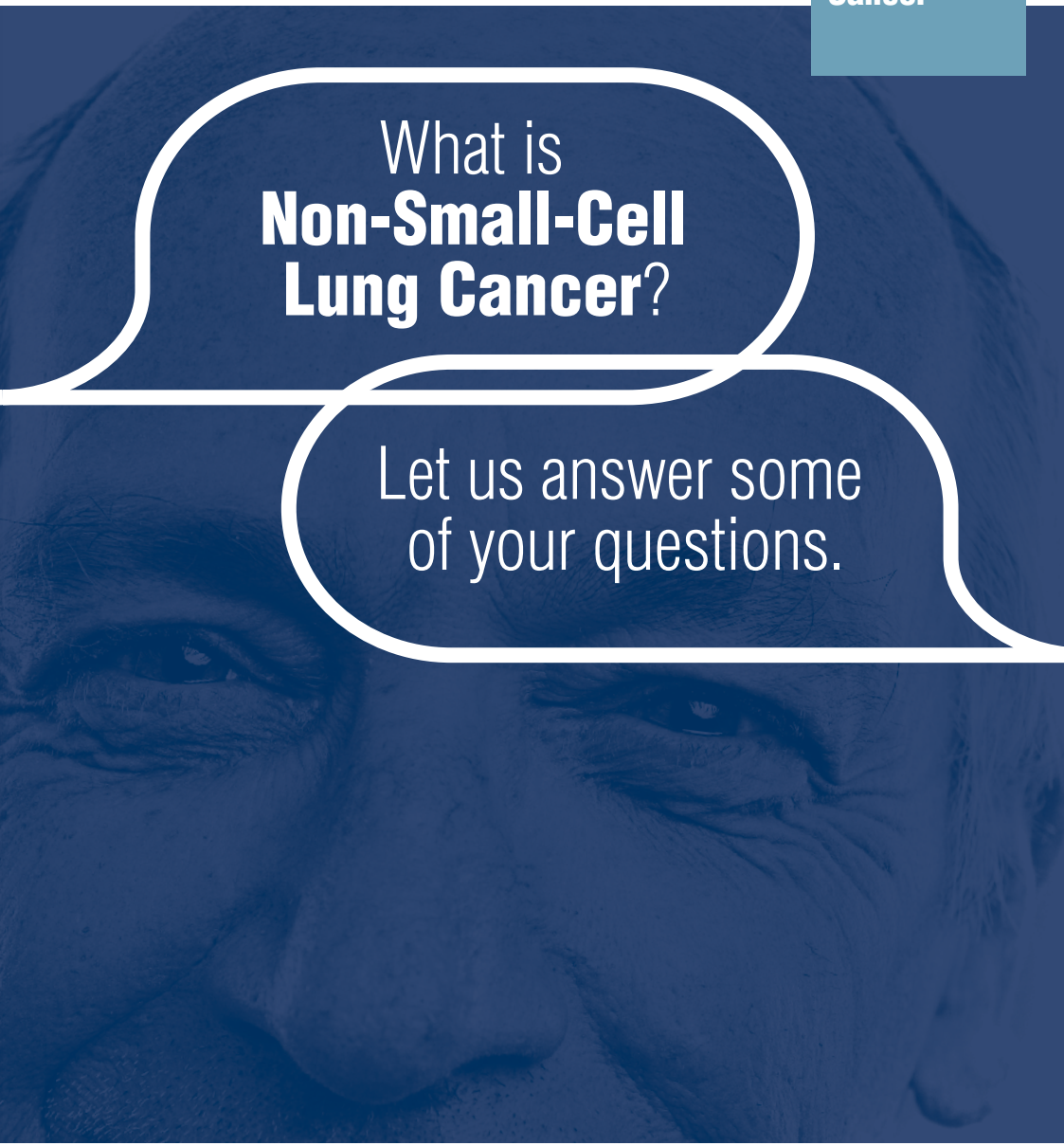
ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

Non-Small-Cell Lung Cancer

What is **Non-Small-Cell Lung Cancer**?

Let us answer some of your questions.



ESMO Patient Guide Series

based on the ESMO Clinical Practice Guidelines

esmo.org

Non-small-cell lung cancer (NSCLC)

An ESMO guide for patients

Patient information based on ESMO Clinical Practice Guidelines

This guide has been prepared to help you, as well as your friends, family and caregivers, better understand non-small-cell lung cancer (NSCLC) and its treatment. It contains information on the different subtypes of NSCLC, the causes of the disease and how it is diagnosed, up-to-date guidance on the types of treatments that may be available and any possible side effects of treatment.

The medical information described in this document is based on the ESMO Clinical Practice Guidelines for NSCLC, which are designed to help clinicians with the diagnosis and management of early-stage, locally advanced and metastatic NSCLC. All ESMO Clinical Practice Guidelines are prepared and reviewed by leading experts using evidence gained from the latest clinical trials, research and expert opinion.

The information included in this guide is not intended as a replacement for your doctor's advice. Your doctor knows your full medical history and will help guide you regarding the best treatment for you.

Words highlighted in **colour** are defined in the glossary at the end of the document.

This guide has been developed and reviewed by:

Representatives of the European Society for Medical Oncology (ESMO): David Planchard; Silvia Novello; Solange Peters; Raffaele Califano; Jean-Yves Douillard; Francesca Longo; Claire Bramley; and Svetlana Jezdic

Representatives of the European Oncology Nursing Society (EONS): Anita Margulies; Roisin Lawless

Patient advocate from Lung Cancer Europe (LuCE) and Women Against Lung Cancer in Europe (WALCE): Stefania Vallone

WHAT'S INSIDE

Lung cancer: A summary of key information

This summary is an overview of the key information provided within the NSCLC guide. The following information will be discussed in detail in the main pages of the guide.

Introduction to lung cancer

- Lung cancer arises from cells in the lung that have grown abnormally and multiplied to form a lump or **tumour**.
- Non-small-cell lung cancer (NSCLC) is a type of lung cancer, which is differentiated from small-cell lung cancer (SCLC) because of the way the **tumour** cells look under a microscope. The three main types of NSCLC are **adenocarcinoma, squamous cell carcinoma**, and **large cell (undifferentiated) carcinoma** of the lung. They are diagnosed in the same way, but may be treated differently.
- Lung cancer is the third most common cancer in Europe; NSCLC represents 85–90% of all lung cancers. Smoking is the biggest **risk factor** for the development of lung cancer.
- In Europe, there has been a decrease in lung cancer mortality among men, while it is increasing in women – this reflects a difference in smoking trends between the sexes.

Diagnosis of NSCLC

- Lung cancer may be suspected if a person has symptoms such as persistent cough or chest infection, breathlessness, hoarseness, chest pain or coughing up blood. Other symptoms may be fever, appetite loss, unexplained weight loss and **fatigue**.
- Following a clinical examination, your doctor will arrange for an **x-ray** and/or **computed tomography** (**CT**) scan (or might use other technologies, such as **positron emission tomography** [**PET**] **CT** scan or **magnetic resonance imaging** [**MRI**]) to evaluate the position and extent of the cancer. Examination of a **biopsy** (cells or tissue taken from the **tumour**) will confirm a diagnosis of NSCLC.

Treatment options for NSCLC

- Types of treatment include:
  - Surgery
  - **Chemotherapy** – the use of anti-cancer drugs to destroy cancer cells. **Chemotherapy** can be given alone or with other treatments.
  - **Targeted therapy** – newer drugs that work by blocking the signals that tell cancer cells to grow.
  - **Immunotherapy** – a type of treatment designed to boost the body's natural defences to fight cancer.
  - **Radiotherapy** – the use of measured doses of radiation to damage cancer cells and stop them growing.
- Combinations of different treatment types are frequently offered based on the stage and type of NSCLC and on the patient's condition and **comorbidities** (additional diseases or disorders experienced at the same time).

- Cancer is 'staged' according to **tumour** size, involvement of **regional lymph nodes** and whether it has spread outside the lung to other parts of the body. This information is used to help decide the best treatment.
- **Early-stage (Stage I-II) NSCLC**
  - Surgery is the main treatment for **early-stage** NSCLC.
  - **Chemotherapy** may be given after surgery (**adjuvant chemotherapy**) in patients with Stage II and Stage III NSCLC and in some patients with Stage IB disease.
  - **Radiotherapy** (either **stereotactic ablative radiotherapy [SABR]** or **conventional radiotherapy**) is an alternative to surgery in patients who are unable or unwilling to have surgery.
  - **Radiotherapy** may be given after surgery (**adjuvant radiotherapy**) in patients with Stage II and Stage III NSCLC.
- **Locally advanced (Stage III) NSCLC**
  - Treatment for **locally advanced** NSCLC is likely to involve different types of therapy (**multimodal therapy**).
  - If it is possible to remove the **tumour** (i.e. the **tumour** is **resectable**), treatment options can include:
    - **Induction therapy** (initial treatment[s] given to shrink the **tumour** before a second planned treatment) consisting of **chemotherapy** with or without **radiotherapy**, followed by surgery.
    - Surgery followed by **adjuvant chemotherapy** and/or **radiotherapy**.
    - **Chemoradiotherapy** (i.e. **chemotherapy** and **radiotherapy** given at the same time or sequentially).
  - The type of treatment – and sometimes the sequence of treatments – offered to patients with **resectable** Stage III NSCLC will depend on the general health of the patient and any **comorbidities**, as well as the extent and complexity of the surgery required to remove the **tumour**.
  - In **unresectable** Stage III NSCLC, **chemoradiotherapy** is the preferred treatment. Alternatively, **chemotherapy** and **radiotherapy** can be given **sequentially** (i.e. one after the other) in patients unable to tolerate **concurrent** treatment.
  - **Immunotherapy** may be offered to some patients with **unresectable locally advanced** NSCLC following treatment with **chemoradiotherapy**.
- **Metastatic (Stage IV) NSCLC**
  - 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 **radiotherapy**.
  - **Intravenous chemotherapy** with a two-drug combination (with or without the addition of the **targeted therapy** called **bevacizumab**) is the main treatment for patients with **metastatic** NSCLC.
  - The choice of drugs used will largely depend on the general health of the patient and the **histological subtype** of the **tumour**.

- Patients whose **tumours** express relatively high levels of **programmed death-ligand 1** (**PD-L1**) protein (determined by molecular testing using a **tumour biopsy**) may receive **first-line immunotherapy** with **pembrolizumab**.
- Patients whose **tumours** contain specific **mutations** (alterations) to the **epidermal growth factor receptor** (**EGFR**), **BRAF**, **anaplastic lymphoma kinase** (**ALK**) or **ROS1 genes** (determined by molecular testing using a **tumour biopsy**) are best treated with oral **targeted therapies** given continuously.
- After 4–6 cycles of **doublet chemotherapy** (i.e. two **chemotherapy** drugs given together), **maintenance treatment** (treatment to help keep the cancer from coming back) with a **chemotherapy** drug called **pemetrexed**, may be given to patients in good general health. The **targeted therapy erlotinib** may be offered as **maintenance treatment** in patients whose **tumours** have **EGFR mutations**.
- Should the cancer come back (**relapse** or **recurrence**), **second-** and **third-line** treatments may be offered. Suitable **second-** and **third-line** treatments depend on which **first-line** treatment has been received and on the general health of the patient. Treatment options include: **chemotherapy** (**pemetrexed** or **docetaxel**), **immunotherapy** (**nivolumab**, **pembrolizumab** or **atezolizumab**), when not given as **first-line** treatment, **antiangiogenic therapy** (**nintedanib** or **ramucirumab**) in combination with **docetaxel**, and **targeted therapies** (**afatinib**, **gefitinib**, **erlotinib**, **osimertinib**, **dabrafenib** in combination with **trametinib**, **crizotinib**, **ceritinib**, **alectinib**, **brigatinib** or **lorlatinib**) for patients with molecular alterations.
  - Patients whose **tumours** have **EGFR mutations** who have received **first-line** treatment with **erlotinib**, **gefitinib** or **afatinib**, and who have a confirmed **EGFR T790M mutation**, may be subsequently treated with **osimertinib**.
  - Patients with a confirmed **BRAF mutation** who have received **first-line** treatment with **dabrafenib** and **trametinib** may receive **second-line platinum-based chemotherapy**.
  - Patients whose **tumours** have **ALK rearrangements** and who have received **first-line** treatment with **crizotinib** may be treated with **second-line ceritinib**, **alectinib**, **brigatinib** or **lorlatinib** if available.

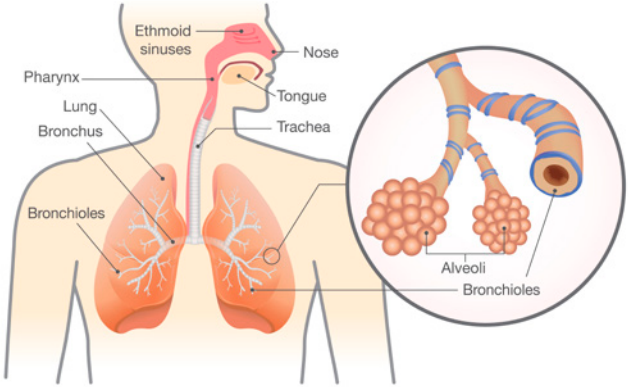
Follow-up after treatment

- Patients who have completed treatment for Stage I–III NSCLC are typically followed-up with clinical and **radiological examinations** every 6 months for the first 2 years and annually after that.
- Patients who have completed treatment for **metastatic** disease are typically followed up with **radiological examinations** every 6–12 weeks (depending on their suitability for further treatment) so that **second-line** therapy can be started if needed.

Anatomy of the lungs

The lungs form part of our respiratory (breathing) system, which includes:

- Nose and mouth.
- **Trachea** (windpipe).
- **Bronchi** (tubes that go to each lung).
- Lungs.



*Anatomy of the respiratory system, showing the **trachea**, **bronchi** and lungs. As we breathe in, air passes from our nose or mouth, through the **trachea**, **bronchi** and **bronchioles**, before it reaches tiny air sacs called **alveoli** – this is where oxygen from the air passes into the bloodstream (see inset image).*

What is lung cancer?

Lung cancers typically start in the cells that line the **bronchi** and parts of the lung such as the **bronchioles** or **alveoli**. There are two main types of **primary lung cancer**:

- Small-cell lung cancer (SCLC): This type gets its name from the small size of the cells that it is composed of when viewed under a microscope.
- Non-small-cell lung cancer (NSCLC): This is the more common type of lung cancer, and accounts for 80–90% of all lung cancers *(Planchard et al., 2018)*.
  - This guide will focus exclusively on NSCLC.

What subtypes of NSCLC are there?

The three main **histological subtypes** of NSCLC are:

- **Adenocarcinoma**: About 40% of all lung cancers are **adenocarcinomas**. These **tumours** start in mucus-producing cells that line the airways.
- **Squamous cell carcinoma** (**SCC**): About 25–30% of all lung cancers are **SCC**. This type of cancer develops in cells that line the airways and is usually caused by smoking.
- **Large cell (undifferentiated) carcinoma**: This type makes up around 10–15% of all lung cancers. It gets its name from the way that the cancer cells look when they are examined under a microscope.

What are the symptoms of lung cancer?

The most common symptoms of lung cancer, including NSCLC, are:

- Persistent cough.
- Chest infection that won't go away or keeps coming back.
- Difficulty breathing/breathlessness.
- Wheezing.
- Coughing blood.
- Chest or shoulder pain that won't go away.
- Hoarseness or lowering of the voice.

Other, non-specific symptoms, may include:

- Fever.
- Loss of appetite.
- Unexplained weight loss.
- Feeling extremely tired.

You should see your doctor if you experience any of these symptoms. However, it is important to remember that these symptoms are common in people who do not have lung cancer; they may also be caused by other conditions.

How common is NSCLC?

Lung cancer represents the third most common cancer in Europe

In 2018, the number of new cases of lung cancer diagnosed in Europe was estimated at more than 470,000 *(Ferlay et al., 2018)*:

- 312,000 new cases in men.
- 158,000 new cases in women.

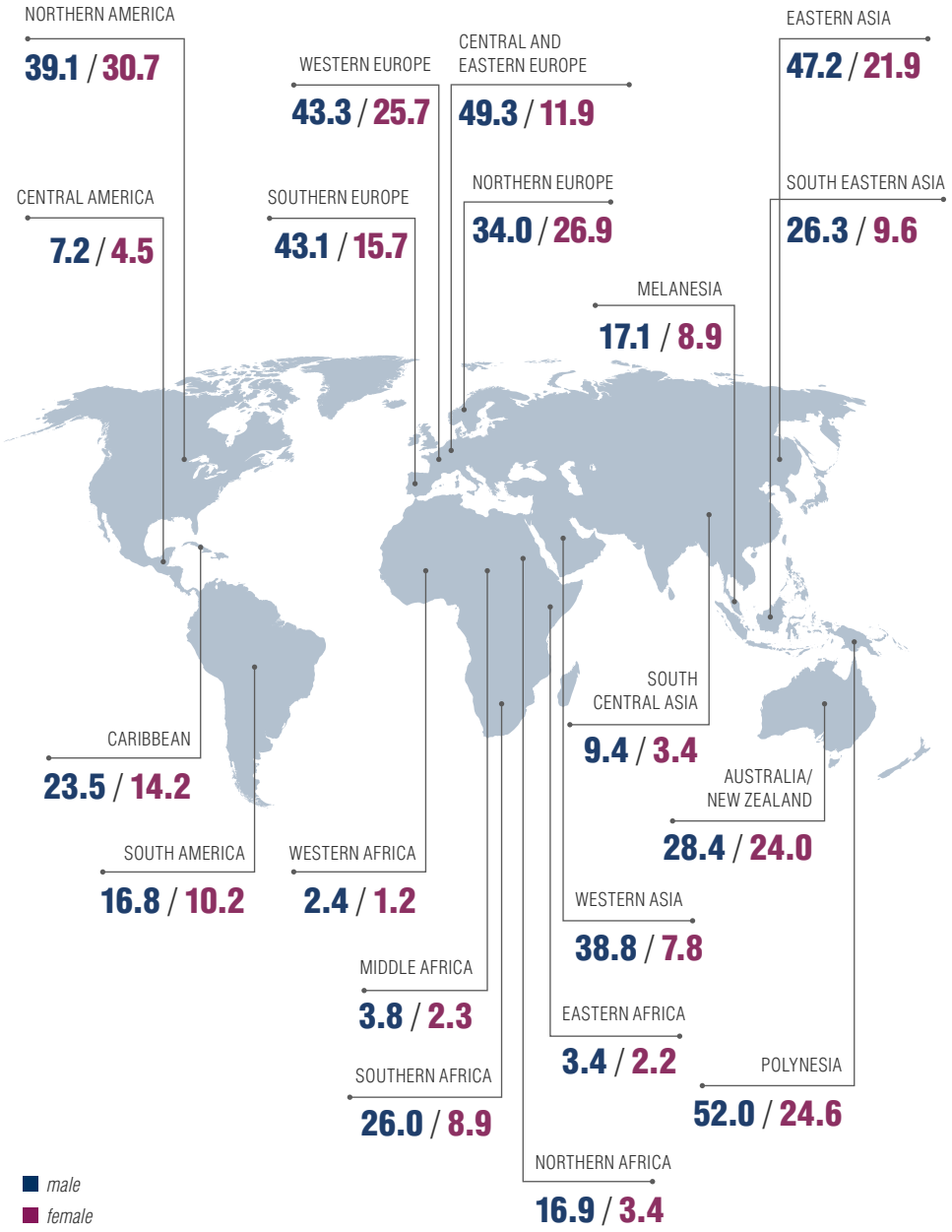
In Europe, lung cancer is the second most common cancer in men (after prostate cancer) and the third most common in women (after breast and colorectal cancer) *(Ferlay et al., 2018)*. Incidence rates of lung cancer are higher in more developed countries than in less developed countries; these variations largely reflect the differences in the stage and degree of the tobacco epidemic *(Torre et al., 2015)*.

In Europe, there has been a decrease in lung cancer mortality among men, while it is increasing in women – this reflects the difference in smoking prevalence trends between the sexes *(Malvezzi et al., 2016; Planchard et al., 2018)*.

The majority of cases of lung cancer are diagnosed in patients aged 65 years and over, and the median age at diagnosis is 70 years.

NSCLC is the most common type of lung cancer, representing 85–90% of all lung cancers

The map shows estimated numbers of new cases of lung cancer diagnosed in 2018 per 100,000 people of each region's population (Ferlay et al., 2018).



What causes NSCLC?

Smoking is the biggest **risk factor** for developing lung cancer. However, there are other **risk factors** that can also increase the chances of developing lung cancer. It is important to remember that having a **risk factor** increases the risk of cancer developing but it does not mean that you will definitely get cancer. Likewise, not having a **risk factor** does not mean that you definitely won't get cancer.

Smoking is the biggest risk factor for lung cancer

Smoking

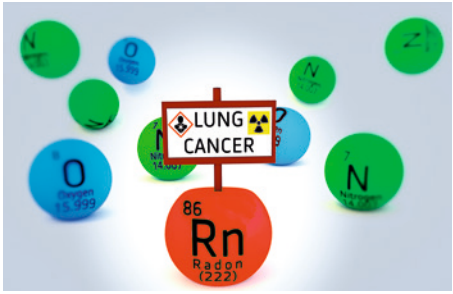
Tobacco smoking is the leading cause of lung cancer. In Europe, it is responsible for 90% of cases in men and 80% of cases in women *(Novello et al., 2016)*. The number of years that a person has been a smoker is more important than the number of cigarettes smoked per day; therefore, giving up smoking at any age can reduce the risk of developing lung cancer more than cutting down on the number of cigarettes smoked per day.

Passive smoking

Passive smoking, also referred to as 'second-hand smoke' or 'environmental tobacco smoke', increases the risk of developing NSCLC, but to a lesser extent than if you are a smoker.

Radon

Radon is a **radioactive** gas that is produced during the breakdown of naturally-occurring **uranium** in soil and rocks, particularly granite. It can pass through from the ground into homes and buildings. Exposure to excessive levels of radon is thought to be a significant causative factor in patients with lung cancer who have never smoked. This may be particularly relevant for underground miners who may be exposed to high levels of radon if the mines in which they work are in a particular geographical region.



Genetic susceptibility

It is thought that some people may be more likely to develop lung cancer based on their genetic makeup *(Bailey-Wilson et al., 2004)*. Having a family history of lung cancer, or other types of cancer, increases the risk of developing lung cancer to some degree. In people who are genetically predisposed to lung cancer, smoking further increases the risk.

Household and environmental pollutants

Other factors described as **risk factors** for the development of NSCLC include exposure to **asbestos** and **arsenic**. There is evidence that lung cancer rates are higher in cities than in rural areas, although factors other than outdoor air pollution may be responsible for this pattern. It has also been suggested that indoor air pollution from use of coal-fuelled stoves may be a factor in some countries *(Planchard et al., 2018)*. For example, in China there is an increased rate of lung cancer in women, despite the fact that a lower proportion of women are smokers in China compared with some European countries.

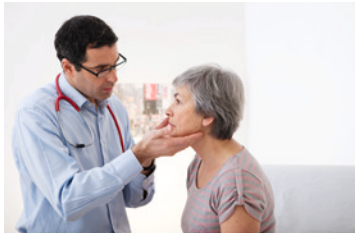
Recent results from a study using **computed tomography** (**CT**) to screen for lung cancer reported a 26% reduction in lung cancer deaths after 10 years of follow-up in men who had no symptoms of lung cancer but who were considered to be at high risk of developing the disease *(De Koning et al., 2018)*. However, at the present time, large-scale screening for NSCLC is not a routine procedure in people who are at a higher risk of developing the disease based on the above **risk factors**.

How is NSCLC diagnosed?

Most patients with NSCLC are diagnosed after seeing their doctor to report symptoms such as a persistent cough, a chest infection that won't go away, **dyspnoea**, wheezing, coughing blood, chest or shoulder pain that won't go away, hoarseness or lowering of the voice, unexplained weight loss, loss of appetite or extreme **fatigue**.

A diagnosis of lung cancer is based on the results of the following examinations and tests:

Clinical examination



Your doctor will carry out a clinical examination. He/she will examine your chest and check the **lymph nodes** in your neck. If there is a suspicion of lung cancer, he/she may arrange for a chest **x-ray**, or possibly a **CT** scan, and refer you to a specialist for further testing.

Imaging

Imaging is used to confirm a suspected diagnosis of lung cancer, and to investigate how far the cancer has progressed

Different imaging techniques include:

- **Chest x-ray:** A chest **x-ray** will enable the specialist to check your lungs for anything that looks abnormal. This is usually the first test that is carried out, based on your symptoms and the clinical examination.
- **CT scan of chest and upper abdomen:** A series of images are taken, which build up a three-dimensional picture of the inside of your body. This allows the specialist to gather more information about the cancer such as the exact location of the **tumour** in your lungs, whether nearby **lymph nodes** are affected, and whether the cancer has spread to other areas of the lungs and/or parts of your body. It is a painless procedure and usually takes about 10–30 minutes.
- **CT scan or magnetic resonance imaging (MRI) scan of the brain:** This test allows doctors to rule out or confirm whether the cancer has spread to your brain. An **MRI** scan uses powerful magnetism to build up detailed images. You may be given an injection of dye into a vein in your arm to help the images show up more clearly. The scan won't hurt but may be slightly uncomfortable as you will need to lie still inside the scanning tube for about 30 minutes. You will be able to hear and speak to the person doing the scan.

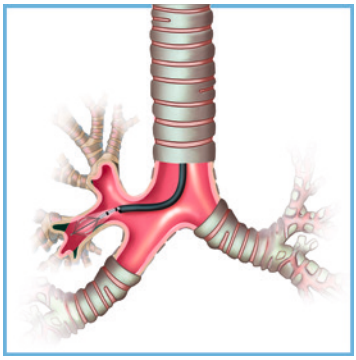
- **Positron emission tomography (PET)/CT scan:** A combination of a **CT** scan and a **PET** scan. **PET** uses low-dose radiation to measure the activity of cells in different parts of the body, so a **PET/CT** scan gives more detailed information about the part of the body being scanned. A mildly **radioactive** drug will be injected into a vein in the back of your hand or arm and then you will need to rest for about an hour while it spreads throughout your body. The scan itself will take 30–60 minutes and, although you will need to lie still, you will be able to speak to the person operating the scanner. A **PET/CT** scan is often carried out to detect whether the cancer has spread to the bones.

Histopathology

Examination of a biopsy is recommended for all patients with NSCLC as it helps to determine the best treatment approach

Histopathology is the study of diseased cells and tissues using a microscope; a **biopsy** of the **tumour** allows a sample of cells to be closely examined. Examination of a **biopsy** is recommended for all patients as it is used to confirm a diagnosis of NSCLC, to identify the **histological subtype** of NSCLC, and to identify any abnormal proteins within the **tumour** cells that could help to determine the best treatment for you *(Planchard et al., 2018)*.

Techniques for obtaining a **biopsy** include:



- **Bronchoscopy:** A doctor or specially-trained nurse examines the insides of the airways and lungs using a tube called a **bronchoscope**. It is carried out under **local anaesthetic**. During a **bronchoscopy**, the doctor or nurse will take samples of cells (**biopsies**) from the airways or lungs.
- **CT-guided needle lung biopsy**: If a **biopsy** is difficult to obtain with a **bronchoscopy**, your doctor may choose to obtain a **biopsy** during a **CT** scan. In this procedure, you will have a **local anaesthetic** to numb the area. A thin needle is then inserted through your skin into your lung so that the doctor can remove a sample of cells from the **tumour**. This should only take a few minutes.
- **Endobronchial ultrasound-guided sampling (EBUS):** This technique is used to confirm whether the cancer has spread to nearby **lymph nodes**, after **radiological examinations** have suggested that this might be the case. A **bronchoscope**, containing a small **ultrasound** probe, is passed through the **trachea** to see whether any nearby **lymph nodes** are larger than

normal. The doctor can pass a needle along the **bronchoscope** to take **biopsies** from the **tumour** or the **lymph nodes**. This test can be uncomfortable but shouldn't be painful. It takes less than an hour and you should be able to go home the same day after it is finished.

- **Oesophageal ultrasound-guided sampling (EUS):** Similar to EBUS, this technique is used to confirm whether the cancer has spread to nearby **lymph nodes**, after **radiological examinations** have suggested that this might be the case. However, unlike EBUS, the **ultrasound** probe is inserted through the **oesophagus**.
- **Mediastinoscopy:** This procedure is more invasive than EBUS/EUS but is recommended as an extra test if EBUS/EUS does not confirm that the cancer has spread to nearby **lymph nodes** or if the **lymph nodes** requiring investigation cannot be reached by EBUS. A mediastinoscopy is carried out under **general anaesthetic** and requires a short stay in hospital. A small cut is made in the skin at the front of the base of your neck and a tube passed through the cut into your chest. A light and a camera attached to the tube allow the doctor to closely look at the middle of your chest – the mediastinum – for any abnormal **lymph nodes**, as these are the first areas that the cancer may spread to. Samples of tissue and **lymph nodes** can be taken for further examination.

Ask your doctor for details if you have any questions about these procedures

Cyto(patho)logy

Whereas histopathology is the laboratory examination of tissue or cells, cytology (or cytopathology) is the examination of cancerous cells spontaneously detached from the **tumour**. Common methods for obtaining samples for cytological examination include:

- **Bronchoscopy**: Bronchial washings (in which a mild salt solution is washed over the surface of the airways) and the collection of secretions can be carried out during a **bronchoscopy** to look for the presence of cancerous cells.
- **Thoracentesis/pleural drainage:** Pleural effusion is an abnormal collection of fluid between the thin layers of tissue (**pleura**) that line the lung and the wall of the chest cavity. This fluid can be taken from the pleural cavity by thoracentesis or pleural drainage and examined in the laboratory for the presence of cancerous cells.
- **Pericardiocentesis/pericardial drainage:** Pericardial effusion is an abnormal collection of fluid between the heart and the sac that surrounds the heart (**pericardium**). This fluid can be taken from the pericardial cavity by pericardiocentesis or pericardial drainage and examined in the laboratory for the presence of cancerous cells. These techniques are carried out in the hospital, usually with the aid of **ultrasound** to help position the needle. You will be given a **local anaesthetic** and monitored closely for any complications afterwards.

Because of the location of your lungs in your body, obtaining samples of cells/tissue can be difficult and it may be necessary to repeat some of these tests if results are found to be inconclusive.

How will my treatment be determined?

After a diagnosis is confirmed, your cancer specialist will look at a number of factors to help plan your treatment. This includes information about yourself and about the cancer.

Patient-related factors

- Your age.
- Your general health.
- Your medical history.
- Your smoking history.
- Results of blood tests and scans.

Cancer-related factors

Treatment also depends on the type of lung cancer that you have (histopathology or cytopathology results), where it is in the lung (its location) and whether it has spread to other parts of the body (imaging results).

Staging

It is important for your doctor to know the stage of the cancer so that he/she can determine the best treatment approach

Staging of the cancer is used to describe its size and position and whether it has spread from where it started. Cancer is staged using a number/letter system – described as Stages IA–IV. Generally, the lower the stage the better the **prognosis**. Staging considers:

- How big the cancer is (**tumour** size; T).
- Whether it has spread into the **lymph nodes** (N).
- Whether it has **metastasised** (spread) to other areas within the lungs or to other parts of the body (M).

Staging is usually carried out twice: after clinical and **radiological examinations**; and after surgery, in the case of surgically resected **tumours**.

The different stages of NSCLC are described in the table below. This may seem complicated but your doctor will be able to explain which parts of this table correspond to your cancer, and how the stage of your cancer impacts on treatment choice.

STAGE IA (T1-N0-M0)	• The **tumour** is no larger than 3 cm, is still inside the lung and has **not** spread to any of the nearby **lymph nodes**	**Early-stage** NSCLC
STAGE IB (T2a-N0-M0)	• The **tumour** is 3–4 cm in size, is still inside the lung and has **not** spread to any of the nearby **lymph nodes**	
STAGE IIA (T2b-N0-M0)	• The **tumour** is 4–5 cm in size, is still inside the lung and has **not** spread to any of the nearby **lymph nodes**	
STAGE IIB (T1/2-N1-M0 or T3-N0-M0)	• The **tumour** is no larger than 5 cm, has spread to nearby **lymph nodes** but is **not** in any other part of the body; or • The **tumour** is 5–7 cm in size or there is more than one **tumour** in the same **lobe**; it has **not** spread to nearby **lymph nodes** but may invade other parts of the lung, the airway or the surrounding areas just outside the lung, e.g. the **diaphragm**	
STAGE IIIA (T1/2-N2-M0 or T3-N1-M0 or T4-N0/1-M0)	• The **tumour** is no larger than 5 cm, has spread to further **lymph nodes** but is **not** in any other part of the body; or • The **tumour** is 5–7 cm in size or there is more than one tumour in the same **lobe**; it has spread to nearby **lymph nodes** and may invade other parts of the lung, the airway or the surrounding areas just outside the lung, e.g. the **diaphragm**; or • The **tumour** is larger than 7 cm and invades tissues and structures further away from the lung, such as the heart, windpipe or **oesophagus**, but it has not spread to other parts of the body; or there is more than one **tumour** in different **lobes** of the same lung. The cancer may or may not have spread to nearby **lymph nodes**	**Locally advanced** NSCLC
STAGE IIIB (T1/2-N3-M0 or T3-N2-M0 or T4-N2-M0)	• The **tumour** is no larger than 5 cm, has spread to more distant **lymph nodes** but is **not** in any other part of the body; or • The **tumour** is 5–7 cm in size or there is more than one **tumour** in the same **lobe**; it has spread to further **lymph nodes** and may invade other parts of the lung, the airway or the surrounding areas just outside the lung, e.g. the **diaphragm**; or • The **tumour** is larger than 7 cm and invades tissues and structures further away from the lung, such as the heart, windpipe or **oesophagus**, but it has **not** spread to other parts of the body; or there is more than one **tumour** in different **lobes** of the same lung. The cancer has spread to further **lymph nodes**	
STAGE IV (any T-any N-M1)	• The **tumour** is of any size and may or may not have spread to the **lymph nodes**. The cancer is in both lungs, has spread to another part of the body (e.g. the liver, **adrenal glands**, brain or bones) or it has caused a collection of fluid around the lung or heart that contains cancer cells	**Metastatic** NSCLC

AJCC/UICC system 8th edition – abridged version (Planchard et al., 2018)
AJCC, American Joint Committee on Cancer; NSCLC, non-small-cell lung cancer; UICC, Union for International Cancer Control

Type of NSCLC

Biopsy results

Your **biopsy** will be examined in the laboratory to determine:

- The **histological subtype** (**adenocarcinoma**, **SCC**or **large cell carcinoma**).
- **Grade**.
- **Tumour** biology.

Histological subtype

The **histological subtype** of the **tumour** can influence the type of treatment you will receive. For example,
non-squamous cancers may benefit from certain anti-cancer therapies that have been shown to be effective only in patients with this **histological subtype**.

Grade

Grade is based on how different **tumour** cells look from normal lung cells, and on how quickly they grow. The **grade** will be a value between one and three and reflects the aggressiveness of the **tumour** cells; the higher the **grade**, the more aggressive the **tumour**.

Biological testing of the tumour

Tissue specimens from **metastatic** NSCLC belonging to the non-squamous subtype should be tested for the presence of specific **mutations** in the **EGFR gene**. Even though such **mutations** are rare (approximately 10–20% in Caucasians with **adenocarcinoma**), the detection of an **EGFR gene mutation** has important prognostic and therapeutic implications in patients with **metastatic** NSCLC. **EGFR** testing is not recommended in patients with a diagnosis of **SCC**, except in never-, long-time ex- or light smokers (<15 pack years). Tissue should also be tested for the presence of a specific **mutation** (known as V600E) in the **BRAF gene**, as therapies are available to treat **tumours** with this **mutation** *(Planchard et al., 2018)*. Routine testing for rearrangement in the **ALK** and **ROS1 genes** is now standard of care and should be carried out, if possible, in parallel with **EGFR mutation** analysis. **ALK rearrangement** is more frequent in people who have never smoked, those with the **adenocarcinoma** subtype (5%) and in younger patients (aged <50 years old). Detecting **ALK rearrangements** has important therapeutic implications for patients with **metastatic** NSCLC due to the existence of drugs targeting **ALK** (e.g. **crizotinib**, **ceritinib** and **alectinib**) *(Planchard et al., 2018; Novello et al., 2016)*. Some **ALK** inhibitors, including **crizotinib**, also inhibit **ROS1**, therefore the presence of **ROS1 rearrangements** also guides treatment decisions in **metastatic** NSCLC *(Planchard et al., 2018)*.

Programmed death-ligand 1 (PD-L1): This is a cellular protein thought to be involved in helping the **tumour** to evade detection by the body's immune system. The amount of **PD-L1** present in a **tumour** may influence the decision to treat the cancer with anti-**PD-L1 immunotherapy**.

Who is involved in planning my treatment?

In most hospitals, a team of specialists will plan the treatment they feel is best for your individual situation. This **multidisciplinary team** of medical professionals may include:

- A surgeon.
- A medical **oncologist** (a doctor who specialises in the medical management of cancer).
- A radiation **oncologist**.
- A chest physician.
- A **nurse specialist**.
- A **radiologist** (or radiographer) who has been involved in the assessment of any **x-rays** and scans.
- A **pathologist** who has been involved in the analysis of your **tumour biopsy**.
- A molecular biologist who has been involved in the genetic analysis of your **tumour biopsy**.
- A psycho-oncologist to provide psychiatric assessment and counselling.

Other services that may be offered include: a dietician, a social worker, a community care nurse, a physiotherapist, a clinical psychologist and a **palliative care** service (who can assist with pain management). After consultation with the **multidisciplinary team**, your doctor, possibly with other members of the care team, will talk to you about the best treatment plan for your situation *(Planchard et al., 2018)*. They will explain the benefits and potential drawbacks of different treatments.

It is important that patients are fully involved in the treatment decision-making – when there are several treatments available, doctors should involve patients in making decisions about their care so that the patients can choose the care that meets their needs and reflects what is important to them. This is called 'shared decision-making'.

It is important that patients are fully involved in discussions and decisions about their treatment

Your doctor will be happy to answer any questions you have about your treatment. Three simple questions that may be helpful when talking with your doctor or any healthcare professional involved in your care are:

- What treatment options do I have?
- What are the possible benefits and side effects of these options?
- How likely am I to experience these benefits and side effects?

What are the treatment options for NSCLC?

Aims of treatment

In **early-stage** NSCLC, when the cancer is confined to the lung and therefore considered to be curable, the main treatment is surgical **resection** *(Postmus et al., 2017)*. For **locally advanced** NSCLC, **multimodal therapy** is usually adopted to help shrink or in some cases completely remove the cancer *(Eberhardt et al., 2015)*. For **metastatic** NSCLC, when the cancer has spread to other parts of the body, and cure is not an option, various **systemic anti-cancer treatments** may be used in an attempt to slow down **tumour** growth and improve symptoms and quality of life – this is called **supportive** or **palliative care** *(Planchard et al., 2018)*.

Overview of treatment types

Treatments for NSCLC include surgery, radiotherapy, chemotherapy and targeted therapies

The treatment you receive will depend on the stage and type of cancer, as well as your general health and treatment preferences, which will be discussed together with your doctor. You may have a combination of treatments. The main types of treatment are listed below:

- **Surgery** may be possible to remove NSCLC if it is diagnosed at an early stage. The type of operation that is offered will depend on the size and location of the cancer *(Postmus et al., 2017)*:
  - A **wedge** or **segment resection** is the removal of a very small amount of the lung; this is sometimes offered if the cancer is at a very early stage
  - A **lobectomy** is the removal of one of the **lobes** of the lung; it is the standard surgical treatment for NSCLC
  - A **pneumonectomy** is the total removal of one of the lungs; it is a more complex surgical **resection** than **lobectomy** or **wedge** (**segment**) **resection**.
- **Chemotherapy** works by disrupting the way that cancer cells grow and divide. However, these drugs can also affect normal cells. **Chemotherapy** can be given before or after surgery for NSCLC. Some people have **chemotherapy** at the same time as **radiotherapy** – this is called **chemoradiotherapy**. **Chemotherapy** may be given to try to cure the cancer or to prolong life and control symptoms (**palliative care**) *(Postmus et al., 2017; Planchard et al., 2018)*.
- **Targeted therapies** and **antiangiogenic therapies** are drugs that block specific signalling pathways in cancer cells that encourage them to grow *(Novello et al., 2016)*.

- **Immunotherapies** are treatments that block inhibitory pathways which restrict the body's immune response to cancer, thereby helping to reactivate the body's immune system to detect and fight the cancer *(Novello et al., 2016)*.
- **Radiotherapy** is a type of treatment that uses **ionising radiation**, which damages the **DNA** of cancerous cells, causing the cells to die. It may be used instead of surgery to try to cure **early-stage** NSCLC. **Radiotherapy** can be given after **chemotherapy** or **concurrently** (**chemoradiotherapy**). **Radiotherapy** is also used to control symptoms when the cancer is more advanced or has spread to other parts of the body. There are various different techniques for delivering **radiotherapy**, including **stereotactic ablative radiotherapy** (**SABR**) (when available), a type of external beam radiation therapy that delivers a high dose of radiation specifically to the **tumour** *(Postmus et al., 2017; Planchard et al., 2018)*.

Your doctor and **nurse specialist** can discuss all of the possible treatment options available to you to help you to make an informed decision about the best way forward for you.

The response to any treatment you receive will be assessed regularly to see how effective the treatment is and to check whether the benefits outweigh any side effects that you might experience. Evaluation of response is recommended after 6–12 weeks of **systemic anti-cancer treatment** for Stage IV NSCLC. This relies on repetition of the initial imaging tests that showed the cancer *(Novello et al., 2016; Planchard et al., 2018)*.

Treatment options for early (Stage I–II) NSCLC

Early-stage NSCLC that is confined to the lung may be curable with surgery

Surgery is the main treatment approach for **early-stage** NSCLC *(Postmus et al., 2017)*. This involves removing the cancer and some of the nearby **lymph nodes** in the chest. The number of **lymph nodes** removed is dependent on the type of surgery performed. Surgical **resection** of NSCLC is a major operation and you need to be in good general health to be able to cope with it. The type of operation will either be a **lobectomy** (preferred) or a **wedge** (**segment**) **resection** and may be carried out via open surgery or **video-assisted thoracic surgery** (**VATS**), depending on the preference of your surgeon. **VATS** is generally the preferred choice for Stage I **tumours** *(Postmus et al., 2017)*.

The **lymph nodes** removed during surgery will be examined under a microscope to check for cancer cells. Knowing if the cancer has spread to the **lymph nodes** also helps your doctors decide if you need further treatment with **adjuvant chemotherapy** or **radiotherapy** *(Postmus et al., 2017)*.

Adjuvant chemotherapy is typically given to patients with Stage II NSCLC and may be considered for some patients with Stage IB disease. Your general health and your postoperative recovery will be taken into account when deciding whether you should be offered **adjuvant chemotherapy**. A combination of two different drugs is preferred (one of them being **cisplatin**), and it is likely that you will be offered 3 or 4 cycles of treatment *(Postmus et al., 2017)*.

Adjuvant radiotherapy may be given after surgery in patients with Stage II NSCLC *(Postmus et al., 2017)*.

In patients with Stage I NSCLC who are unwilling or unable to undergo surgery, **SABR** may be offered. This treatment will be given to you as an outpatient over 3–8 visits. If your **tumour** is larger than 5 cm and/or is located at the centre of the lung, radical **radiotherapy** using more conventional daily or **accelerated schedules** is preferred *(Postmus et al., 2017)*.

Treatment of early (Stage I–II) NSCLC – summary *(Postmus et al., 2017)*

TREATMENT TYPE	PATIENTS	TREATMENT DETAILS	CONSIDERATIONS
Surgery	Stage I or II NSCLC	• Operation is either: – **Lobectomy**: The removal of one of the **lobes** of the lung (preferred option), or – **Wedge** or **segment resection**: Only a small amount of the lung is removed (sometimes used for very early NSCLC) • Carried out either by open surgery or by **VATS**	• Risks associated with major surgery • Recovery time (shorter with **VATS**) • Usually able to go home 3–7 days after surgery • Requires post-operative pain control
Adjuvant chemotherapy	Stage II NSCLC, following surgery Stage IB NSCLC following surgery, if **primary tumour** is >4 cm in size (Not recommended in Stage IA NSCLC)	• A combination of two different drugs usually given **intravenously** (one of which is **cisplatin**) • Typically, 3–4 cycles of treatment	• Need to recover from surgery before starting **chemotherapy** • Pre-existing medical conditions may affect whether you will be suitable for **chemotherapy**
SABR	Preferred for Stage I, if surgery not carried out	• More precise than **conventional radiotherapy**; very small areas can be targeted with a high dose • Shorter treatment time vs **conventional radiotherapy** (2-week course)	• **SABR** is associated with low toxicity in patients with **COPD** and in elderly patients • Surgery may be offered afterwards if **SABR** is not successful or if there are complications
Radical radiotherapy	**Tumours** >5 cm and/or centrally located Following incomplete surgery	• Conventional (4–7-week course of treatment of short, daily sessions Monday to Friday) or **accelerated schedule** (an increased number of treatments delivered over a shorter timeframe)	

COPD**, **chronic obstructive pulmonary disease**; NSCLC, non-small-cell lung cancer; **SABR**, **stereotactic ablative radiotherapy**; **VATS**, **video-assisted thoracic surgery

Treatment options for locally advanced (Stage III) NSCLC

Treatment for locally advanced disease is likely to involve different types of therapy

Locally advanced NSCLC represents a very diverse disease (see Stages IIIA and IIIB in the AJCC/UICC staging system table) and so it is not possible to recommend a 'one size fits all' approach to treatment. Some patients with Stage III NSCLC have a **tumour** that is considered **resectable**, i.e. your doctor/surgeon thinks that it can be completely removed by surgery either straight away or after a course of **chemotherapy** (with or without **radiotherapy**). On the other hand, some patients with Stage III NSCLC have a **tumour** that is considered **unresectable**, i.e. surgery is not possible due to the size/location of the **tumour** and involvement of **lymph nodes** in the middle of the chest. The best approach to treatment of Stage III NSCLC is therefore likely to be a combination of various treatment types (surgery, **chemotherapy** and/or **radiotherapy**), called **multimodal therapy** *(Postmus et al., 2017; Eberhardt et al., 2015)*.

In patients staged with potentially **resectable** Stage III NSCLC, treatment options are generally either **induction therapy** with **chemotherapy** or **chemoradiotherapy**, followed by surgery (preferred for those whose **tumour** is likely to be completely removed by **lobectomy**) or **chemoradiotherapy**.

In patients with **unresectable** Stage III NSCLC, the preferred treatment is **chemoradiotherapy**. Alternatively, **sequential chemotherapy** and then **radiotherapy** may be given to patients who are unable to tolerate **concurrent** treatment *(Postmus et al., 2017)*.

Chemotherapy is an integral part of the treatment of Stage III NSCLC. Generally, a **cisplatin**-based combination **regimen** (two different drugs) is offered. You will usually be offered 2–4 cycles, whether **chemotherapy** is given alone or as part of a course of **chemoradiotherapy**. In some patients who undergo surgery upfront for NSCLC that is thought to be Stage I or II, but found to be Stage III during surgery, then **adjuvant chemotherapy** will likely be administered after the surgery *(Postmus et al., 2017)*.

When **radiotherapy** is given **concurrently** with **chemotherapy** for Stage III NSCLC, it is given as conventional daily doses and treatment should not exceed 7 weeks. It may be given as an **accelerated schedule** as part of a pre-operative **chemoradiotherapy** course, but any potential advantages to the likely outcome of surgery will need to be weighed up against potential greater toxicity. When given **sequentially**, an **accelerated schedule** of **radiotherapy** may be given, i.e. higher doses over a shorter timeframe *(Postmus et al., 2017)*.

Following **first-line** treatment, the **immunotherapy** agent **durvalumab** may be offered to patients with **unresectable** disease that has not progressed following **platinum-based chemoradiotherapy**, if their **tumours** contain a certain level of **PD-L1** (determined by molecular testing using a **tumour biopsy**) *(Imfinzi SPC, 2018)*.

Treatment of locally advanced (Stage III) NSCLC – summary *(Postmus et al., 2017)*

TREATMENT TYPE	PATIENTS	TREATMENT DETAILS	CONSIDERATIONS
Surgery	**Resectable** Stage III NSCLC	• Preferred when a complete **resection** by **lobectomy** is expected, to spare as much lung tissue as possible • May require a **pneumonectomy** (removal of one lung) in some patients • May be offered after an initial course of **chemotherapy** (+/- **radiotherapy**) – called **induction therapy**	• Outcome depends on the extent of involvement of the **lymph nodes** at the centre of the chest – may not be known until after surgery • Lung function tests are important before deciding on surgery
Chemotherapy		• **Intravenous cisplatin**-based **regimen** is preferred (**cisplatin-etoposide** or **cisplatin-vinorelbine**) • Typically, 2–4 cycles of treatment are given	• A **carboplatin**-based combination may be chosen if you have other medical conditions that could affect how you tolerate **chemotherapy** • It is likely that you will experience more side effects if **chemotherapy** is given **concurrently** with **radiotherapy**
	Resectable Stage III NSCLC	• If your **tumour** is considered **resectable**, **chemotherapy** may be given before surgery as **induction therapy** (**chemotherapy** +/- **radiotherapy**) • If you have surgery upfront and it is found that the cancer had spread to **lymph nodes** in the chest, you may be offered **adjuvant chemotherapy**	
	Unresectable Stage III NSCLC	• Delivered **concurrently** with **radiotherapy** (preferred) or **sequentially** (before **radiotherapy**) if **concurrent** treatment cannot be tolerated	
Radiotherapy	**Resectable** Stage III NSCLC	• May be given post-operatively in patients who have had incomplete **resection** • When given pre-operatively **concurrently** with **chemotherapy**, may be conventional doses or as an **accelerated schedule**	
	Unresectable Stage III NSCLC	• May be given as conventional daily doses as part of a **chemoradiotherapy** schedule (up to 7 weeks), or **sequentially** (after **chemotherapy**) as an **accelerated schedule**	
Immunotherapy	**Unresectable** Stage III NSCLC	• **Durvalumab** may be offered if disease has not progressed after **chemoradiotherapy** (**PD-L1** on ≥1% of **tumour** cells)	

NSCLC, non-small-cell lung cancer; ***PD-L1, programmed death-ligand 1***

Treatment options for metastatic (Stage IV) NSCLC

Chemotherapy is the main treatment for metastatic NSCLC

Metastatic NSCLC is usually considered inoperable. Complete removal of the **tumour**(s) is very unlikely and therefore a chance of cure cannot be offered. However, surgical interventions can relieve symptoms caused by the disease spreading to other parts of the body. Similarly, **radiotherapy** may help control symptoms that arise due to the disease spreading to certain organs, including the brain and bones *(Planchard et al., 2018)*.

Systemic anticancer treatment is the main treatment for Stage IV NSCLC, the aims of which are to improve quality of life and to prolong survival. There are many different types of drugs available and the choice of which drugs are offered will largely depend on your general health and the type of **tumour** that you have *(Planchard et al., 2018)*.

Intravenous chemotherapy with a two-drug combination (**doublet chemotherapy**) is the main treatment for patients with **metastatic** NSCLC whose cancer does not contain specific modifications to the **EGFR** or **ALK genes** or high levels of the **PD-L1** protein (determined by molecular testing using a **tumour biopsy**). **Doublet chemotherapy** is likely to include a **platinum-based** compound plus either **gemcitabine**, **vinorelbine** or a **taxane**. Addition of **pemetrexed**, the **targeted therapy bevacizumab** or the **immunotherapy** agent **pembrolizumab** may also be considered for non-squamous NSCLC. In patients whose general health is poor, single-agent **chemotherapy** with **gemcitabine**, **vinorelbine** or **docetaxel** is another treatment option *(Planchard et al., 2018)*.

Patients whose **tumours** have **EGFR** or **BRAF mutations**, or **ALK** or **ROS1 rearrangements**, are best treated with oral **targeted therapies**. **Gefitinib**, **erlotinib**, **afatinib**, **osimertinib** or **erlotinib** in combination with **bevacizumab** are options for **EGFR**-mutated **tumours**. **Dabrafenib** in combination with **trametinib** is recommended for patients with **tumours** that have a **BRAF** V600E **mutation**. **Crizotinib**, **ceritinib** or **alectinib** are offered to patients who have an **ALK rearrangement**, and **crizotinib** is recommended for patients with a **ROS1 rearrangement** *(Planchard et al., 2018)*.

Patients whose **tumours** express relatively high levels of **PD-L1** protein (determined by molecular testing using a **tumour biopsy**) may receive **first-line immunotherapy** with **pembrolizumab** *(Planchard et al., 2018)*.

After 4–6 cycles of **doublet chemotherapy**, **maintenance treatment** with **pemetrexed** may be given to patients in good general health with non-squamous **tumours** to prolong the effect of **first-line chemotherapy** on **tumour** control. **Erlotinib** may be offered as **maintenance treatment** in patients whose **tumours** have **EGFR mutations** *(Planchard et al., 2018)*.

Further lines of treatment may be offered, depending on the **first-line** treatment received and on the general health of the patient. Treatment options include: **chemotherapy** (**pemetrexed** or **docetaxel**), **immunotherapy** (**nivolumab**, **pembrolizumab** or **atezolizumab**), **antiangiogenic therapy** (**nintedanib** or **ramucirumab**) plus **docetaxel**, and **targeted therapies** (**afatanib** or **erlotinib**). Patients whose **tumours** have **EGFR mutations** who have received **first-line** treatment with **erlotinib**, **gefitinib** or **afatinib**, and who have a confirmed abnormality called a **T790M mutation**, may be treated with **second-line osimertinib**. Patients with a confirmed **BRAF** V600E **mutation** who have received **first-line** treatment with **dabrafenib** and **trametinib** may receive **second-line platinum-based chemotherapy**. Patients whose **tumours** have **ALK rearrangements** who have received **first-line** treatment with **crizotinib** may be treated with **second-line ceritinib**, **alectinib**, **brigatinib** or **lorlatinib** if available. Patients with confirmed **ROS1 rearrangements** who have received **first-line treatment** with **crizotinib** might be offered **second-line platinum-based chemotherapy** *(Planchard et al., 2018)*.

continued overleaf

Treatment of metastatic (Stage IV) NSCLC – summary *(Planchard et al., 2018)*

TREATMENT TYPE	PATIENTS	TREATMENT DETAILS	CONSIDERATIONS
Chemotherapy	EGFR- and ALK-negative tumours • Good general condition, no other major medical conditions	First line: • Intravenous platinum-based regimen preferred (2-drug combination including cisplatin or carboplatin + gemcitabine, vinorelbine or a taxane) • Pemetrexed may be incorporated into the treatment regimen in non-squamous histology • 4–6 cycles (may be offered maintenance treatment with single agent pemetrexed after 4 cycles) Second line: • Pemetrexed (non-squamous type) or docetaxel	• Response to platinum-based therapy, toxicity and patient's general health after initial treatment needs to be considered when deciding upon maintenance treatment • Patients with a very poor general condition are not suitable for chemotherapy; best supportive care is the only treatment
	• Less fit patients/ elderly	First line: • Carboplatin-based regimen preferred; may be offered single-agent treatment with gemcitabine, vinorelbine or docetaxel	
Targeted therapy	EFGR mutation	First line: • Gefitinib, erlotinib, afatinib or osimertinib • Erlotinib + bevacizumab Second line: • Osimertinib	• As most targeted therapies are generally well tolerated, they may also be offered to patients with a moderate/poor general condition
	BRAF mutation	First line: • Dabrafenib + trametinib	
	ALK rearrangement	First line: • Crizotinib, ceritinib or alectinib Second line: • Ceritinib, alectinib, brigatinib or lorlatinib following first-line crizotinib	
	ROS1 rearrangement	First line: • Crizotinib	
	Targeted therapy in tumours without specific mutations	First line: • Intravenous bevacizumab may be added to a platinum-based regimen (non-squamous type) in patients in good general condition Second line: • Erlotinib, nintedanib + docetaxel (adenocarcinoma), ramucirumab + docetaxel, afatinib	

continued overleaf

TREATMENT TYPE	PATIENTS	TREATMENT DETAILS	CONSIDERATIONS
Immunotherapy	**EGFR**- and **ALK**-negative **tumours** • Good general condition, no other major medical conditions	**First line**: • **Pembrolizumab** (in patients with **tumours** strongly positive for **PD-L1**) • **Pembrolizumab** in combination with **pemetrexed** and **platinum-based chemotherapy** (non-squamous type) **Second line**: • **Nivolumab**, **pembrolizumab** or **atezolizumab** (irrespective of **PD-L1** expression)	
Surgery	Can be used for relief of symptoms caused by cancer spreading	Minimally-invasive procedures can be helpful, e.g. placement of a stent to alleviate obstruction of the airways	
Radiotherapy	Can be used for relief of symptoms caused by cancer spreading	• **Radiotherapy** can achieve symptom control for bone and brain **metastases** • It can also relieve symptoms caused by airway obstruction	

ALK**, **anaplastic lymphoma kinase**; **EGFR**, **epidermal growth factor receptor**; NSCLC, non-small-cell lung cancer; **PD-L1**, **programmed death-ligand 1**; **SCC**, **squamous cell carcinoma

Oligometastatic disease

When the cancer has spread beyond the site at which it started but is not yet widely **metastatic**, it is called **oligometastatic disease**. If you have **synchronous oligometastases** at diagnosis, it may be possible to achieve long-term disease-free survival following **chemotherapy** and radical local treatment, such as high-dose **radiotherapy** or surgery; inclusion in a suitable **clinical trial** may be advised by your doctor *(Planchard et al., 2018)*. Similarly, if you have a limited number of **metachronous oligometastases** that appear following treatment for your **primary tumour**, you may be offered treatment with high-dose **radiotherapy** or surgery *(Planchard et al., 2018)*.

Clinical trials

Your doctor may ask you whether you would like to take part in a **clinical trial**. This is a research study conducted with patients in order to *(ClinicalTrials.gov, 2017)*:

- Test new treatments
- Look at new combinations of existing treatments, or change the way they are given to make them more effective or reduce side effects
- Compare the effectiveness of drugs used to control symptoms
- Find out how cancer treatments work.

Clinical trials help to improve knowledge about cancer and develop new treatments, and there can be many benefits to taking part. You would be carefully monitored during and after the study, and the new treatment may offer benefits over existing therapies. It's important to bear in mind, however, that some new treatments are found not to be as good as existing treatments or to have side effects that outweigh the benefits *(ClinicalTrials.gov, 2017)*.

Clinical trials help to improve knowledge about diseases and develop new treatments – there can be many benefits to taking part

Several new drugs for the treatment of NSCLC are being studied in **clinical trials**, including **targeted therapies** and **immunotherapy** agents.

Lorlatinib is a **targeted therapy** that has recently been approved in Europe for the treatment of **ALK**-positive **metastatic** NSCLC following treatment with one or more **ALK** inhibitors *(EMA, 2019a)*. Another **targeted therapy**, **dacomitinib**, is newly approved for the **first-line** treatment of **locally advanced** or **metastatic** NSCLC with **EGFR**-activating **mutations** *(EMA, 2019b)*.

Clinical trials have also investigated different combinations of existing drugs; for example, while **atezolizumab** is currently used for the **second-line** treatment of NSCLC, it has recently shown promise as **first-line** treatment of **metastatic** non-squamous NSCLC in combination with **chemotherapy** *(Cappuzzo et al., 2018)* and **bevacizumab** plus **chemotherapy** *(Socinski et al., 2018a)* and in squamous NSCLC in combination with **chemotherapy** *(Socinski et al., 2018b)*. **Erlotinib** has also shown promise as **neoadjuvant** treatment in **locally advanced EGFR**-mutated NSCLC *(Zhong et al., 2018)*.

You have the right to accept or refuse participation in a **clinical trial** without any consequences for the quality of your treatment. If your doctor does not ask you about taking part in a **clinical trial** and you want to find out more about this option, you can ask your doctor if there is a trial for your type of cancer taking place nearby *(ClinicalTrials.gov, 2017)*.

Supplementary interventions

Patients may find that supplementary care helps them to cope with their diagnosis, treatment and the long-term effects of NSCLC

Over the course of disease, anti-cancer treatments should be supplemented with interventions that aim to prevent the complications of disease and treatment, and to maximise your quality of life. These interventions may include **supportive**, **palliative**, survivorship and end-of-life care, which should all be coordinated by a **multidisciplinary team** *(Jordan et al., 2018)*. Ask your doctor or nurse about which supplementary interventions are available; you and your family may receive support from several sources, such as a dietician, social worker, priest or occupational therapist.

Supportive care

Supportive care involves the management of cancer symptoms and the side effects of therapy. There is a range of therapies available that can help with the management of NSCLC. These include bone modifying agents (e.g. **zoledronic acid** and **denosumab**, used to reduce the occurrence of fractures commonly associated with the presence of bone **metastases**), **stents** (for relieving major airway obstructions that can cause **dyspnoea**), pain management and nutritional support *(Planchard et al., 2018)*. Generally, early **supportive care** is recommended in parallel with treatments for the cancer itself: it may improve your quality of life and mood and lessen the need for aggressive treatment *(Planchard et al., 2018)*.

Palliative care

Palliative care is a term used to describe care interventions in advanced disease, including the management of symptoms as well as support for coping with **prognosis**, making difficult decisions and preparation for end-of-life care. **Palliative care** in advanced lung cancer may include treatment for pain, airway obstructions and bedsores.

Survivorship care

Support for patients surviving cancer includes social support, education about the disease and rehabilitation. For example, psychological support can help you to cope with any worries or fears. Patients often find that social support is essential for coping with the cancer diagnosis, treatment and the emotional consequences. A survivor care plan can help you to recover wellbeing in your personal, professional and social life. For further information and advice on survivorship, see ESMO's patient guide on survivorship (http://www.esmo.org/Patients/Patient-Guides/Patient-Guide-on-Survivorship).

End-of-life care

End-of-life care for patients with incurable cancer primarily focusses on making the patient comfortable and providing adequate relief of physical and psychological symptoms, for example **palliative** sedation to induce unconsciousness can relieve severe pain, **dyspnoea**, delirium or convulsions *(Cherny, 2014)*. Discussions about end-of-life care can be very distressing, but support should always be available to you and your family at this time.

What are the possible side effects of treatment?

As with any medical treatment, you may experience side effects from your anti-cancer treatment. The most common side effects for each type of treatment are highlighted below, along with some information on how they can be managed. You may experience side effects other than those discussed here. It is important to talk to your doctor or **nurse specialist** about any potential side effects that you are concerned about.

Doctors classify side effects from any cancer therapy by assigning each event a 'grade', on a scale of 1–4, by increasing severity. In general, 'grade' 1 side effects are considered to be mild, 'grade' 2 moderate, 'grade' 3 severe and 'grade' 4 very severe. However, the precise criteria used to assign a 'grade' to a specific side effect varies depending on which side effect is being considered. The aim is always to identify and address any side effect before it becomes severe, so you should always report any worrying symptoms to your doctor as soon as possible.

It is important to talk to your doctor about any treatment-related side effects that you are concerned about

Fatigue is very common in patients undergoing cancer treatment, and can result from either the cancer itself or the treatments. Your doctor or nurse can provide you with strategies to limit the impact of **fatigue**, including getting enough sleep, eating healthily and staying active *(Cancer.Net, 2017)*. Loss of appetite and weight loss can also arise due to the cancer itself or the treatments. Significant weight loss, involving loss of both fat and muscle tissue, can lead to weakness, reduced mobility and loss of independence, as well as anxiety and depression *(Escamilla and Jarrett, 2016)*. Your doctor may refer you to a dietician, who can look at your nutritional needs and advise you on your diet and any supplements that you might need.

continued overleaf

Surgery

Side effects following cancer surgery vary depending on the location and type of the surgery and your general health *(Cancer.Net, 2018)*. Common side effects following lung **resection** are summarised in the table.

POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECT MAY BE MANAGED
Pain	Pain or discomfort following surgery is common and can usually be controlled using pain-relief medication. Always let your doctor or nurse know if you are in pain, so they can treat it as soon as possible *(Cancer.Net, 2018)*
Infection	You will be taught how to lower the risk of infection occurring. Signs of infection include redness, warmth, increased pain and weeping from around the wound. If you notice any of these signs, contact your nurse or doctor *(Cancer.Net, 2018)*
Prolonged **air leak**	**Air leak** is a natural occurrence after lung **resection** but its prolongation to over 7 days increases the risks of other complications. Your surgeon will take precautions to minimise the risk of prolonged **air leak** *(Ziarnik et al., 2015)*
Pneumonia	The risk of **pneumonia** can be decreased by following advice provided by your doctor, e.g. you should perform any recommended physiotherapy exercises (e.g. coughing), start walking/moving about as soon as possible after surgery and refrain from smoking. If **pneumonia** occurs, then it can usually be treated with an **antibiotic** *(Ziarnik et al., 2015)*

Common side effects of lung cancer surgery and how they can be managed

continued overleaf

Radiotherapy

For some patients, **radiotherapy** causes few or no side effects; for others, the side effects can be severe. Side effects occur because radiation therapy can damage healthy tissues near the treatment area. The side effects will depend upon the location of the treatment area, the radiation dose and your general health. Usually, side effects start to appear after 2 or 3 weeks of treatment, and resolve a few weeks following the final treatment *(Cancer.Net, 2016)*.

POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECT MAY BE MANAGED
Skin damage (e.g. dryness, itching, blistering or peeling)	These side effects usually go away a few weeks after treatment has finished. If skin damage becomes a serious problem, then your doctor may change your treatment plan *(Cancer.Net, 2016)*
Oesophagitis	After 2–3 weeks of **radiotherapy** to the chest, you may have difficulty swallowing, heartburn or indigestion. This is because **radiotherapy** can cause inflammation in the **oesophagus**. Your doctor or nurse will be able to advise you on how to cope with these symptoms and may prescribe medicines to help *(Macmillan, 2015a)*
Radiation pneumonitis (cough, fever and fullness of chest)	Patients receiving **radiotherapy** to the chest may develop a condition called **radiation pneumonitis**. This generally appears between 2 weeks and 6 months following radiotherapy but is usually temporary. Tell your doctor or nurse if you experience any of the signs of **radiation pneumonitis** *(Cancer.Net, 2016)*

*Common side effects of **radiotherapy** used to treat lung cancer and how they can be managed*

continued overleaf

Chemotherapy

Side effects from **chemotherapy** vary depending upon the drugs and the doses used – you may get some of those listed below but you are very unlikely to get all of them. Patients who receive a combination of different **chemotherapy** drugs are likely to experience more side effects than those who receive a single **chemotherapy** drug. The main areas of the body affected by **chemotherapy** are those where new cells are being quickly made and replaced (**bone marrow**, **hair follicles**, the **gastrointestinal system**, the lining of your mouth). Reductions in your levels of **neutrophils** (a type of white blood cell) can lead to **neutropenia**, which will make you more susceptible to infections. Some **chemotherapy** drugs can affect fertility – if you are worried about this, speak to your doctor before treatment starts. Most side effects of **chemotherapy** are temporary and can be controlled with drugs or lifestyle changes – your doctor or nurse will help you to manage them *(Macmillan, 2016)*.

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Carboplatin (Macmillan, 2015b)	• **Anaemia** • Constipation • **Fatigue** • **Hepatic** (liver) toxicity • Nausea • **Neutropenia** • **Renal** (kidney) toxicity • **Thrombocytopenia** • Vomiting	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **anaemia** or **thrombocytopenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Your doctor will be able to help you prevent or manage any nausea, vomiting or constipation. • You will have tests before and during treatment to check how well your kidneys and liver are functioning, and you will be asked to drink plenty of fluids to prevent your kidneys from becoming damaged.
Cisplatin (Macmillan, 2015c)	• **Anaemia** • **Anorexia** • Changes in kidney function • Decreased fertility • Diarrhoea • **Fatigue** • Increased risk of **thrombosis** • Nausea/vomiting • **Neutropenia** • **Peripheral neuropathy** • Taste changes • **Thrombocytopenia** • **Tinnitus**/changes in hearing	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **anaemia** or **thrombocytopenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Effects on the **gastrointestinal system** (nausea, vomiting, diarrhoea, taste changes) may result in loss of appetite (**anorexia**). Your doctor will be able to help you to prevent or manage these side effects. • Report any signs of **peripheral neuropathy** (tingling or numbness in your hands or feet) to your doctor, who will help you to manage this side effect. • You will have tests before and during treatment to check how well your kidneys are functioning. You will be asked to drink plenty of fluids to prevent your kidneys from becoming damaged. • Tell your doctor if you notice any changes in your hearing or experience **tinnitus**. Changes in hearing are usually temporary but can occasionally be permanent.

continued overleaf

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Docetaxel (Taxotere SPC, 2016)	• **Alopecia** • **Anaemia** • **Anorexia** • **Asthenia** • Diarrhoea • Nausea • **Neutropenia** • **Oedema** • **Peripheral neuropathy** • Skin reaction • **Stomatitis** • **Thrombocytopenia** • Vomiting	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **anaemia** or **thrombocytopenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. Report any fever to your doctor, as this may be a sign of infection. • Report any signs of **peripheral neuropathy** (tingling or numbness in your hands or feet) to your doctor, who will help you to manage this side effect. • Effects on the **gastrointestinal system** (nausea, vomiting, diarrhoea) and **stomatitis** may result in loss of appetite (**anorexia**) or feelings of weakness (**asthenia**). Your doctor will be able to help you to prevent or manage these side effects. • Let your doctor know if you experience any skin reactions or fluid retention/swelling (**oedema**) – they will help you to manage these side effects. • **Alopecia** can be upsetting for many patients; your doctor will provide you with information on how to cope with this side effect. Some hospitals can provide **cold caps** to reduce hair loss.
Etoposide (Vepesid SPC, 2017)	• **Alopecia** • **Anaemia** • **Anorexia** • **Asthenia** • Changes in liver function • Constipation • **Leukopenia** • Nausea • **Neutropenia** • **Thrombocytopenia** • Vomiting	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **anaemia**, **thrombocytopenia** or **leukopenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Effects on the **gastrointestinal system** (constipation, nausea, vomiting) may result in loss of appetite (**anorexia**) or feelings of **fatigue/asthenia**. Your doctor will be able to help you to prevent or manage these side effects. • You will have tests before and during treatment to check how well your liver is functioning. • **Alopecia** can be upsetting for many patients; your doctor will provide you with information on how to cope with this side effect. Some hospitals can provide **cold caps** to reduce hair loss.

continued overleaf

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
nab-Paclitaxel (Abraxane SPC, 2018)	• **Alopecia** • **Anaemia** • **Anorexia** • **Arthralgia** • **Asthenia** • Constipation • Diarrhoea • **Fatigue** • Fever • **Leukopenia** • **Lymphopenia** • **Myalgia** • Nausea • **Neutropenia** • **Peripheral neuropathy** • Rash • **Stomatitis** • **Thrombocytopenia** • Vomiting	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **anaemia**, **leukopenia**, **thrombocytopenia** or **lymphopenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. Report any fever to your doctor, as this may be a sign of infection. • Effects on the **gastrointestinal system** (nausea, vomiting, diarrhoea, constipation, **stomatitis**) may result in loss of appetite (**anorexia**) or feelings of **fatigue**/**asthenia**. Your doctor will be able to help you to prevent or manage these side effects. • Let your doctor know if you experience **arthralgia**, **myalgia** or rash and they will help you to manage these side effects. • Report any signs of **peripheral neuropathy** (tingling or numbness in your hands or feet) to your doctor, who will help you to manage this side effect. • **Alopecia** can be upsetting for many patients; your doctor will provide you with information on how to cope with this side effect. Some hospitals can provide **cold caps** to reduce hair loss.
Paclitaxel (Paclitaxel SPC, 2017)	• **Alopecia** • **Anaemia** • **Arthralgia** • Diarrhoea • Hypersensitivity reactions • **Leukopenia** • Low blood pressure • **Mucositis** • **Myalgia** • Nail disorders • Nausea • **Neutropenia** • **Peripheral neuropathy** • **Thrombocytopenia** • Vomiting	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **leukopenia**, **anaemia** or **thrombocytopenia** – your doctor may adjust your treatment according to test results and will advise you on how to prevent infections. Report any fever to your doctor, as this may be a sign of infection. Report any prolonged or unusual bleeding to your doctor as this can be a sign of **thrombocytopenia**. • Report any effects on the **gastrointestinal system** (nausea, vomiting, diarrhoea) to your doctor as they may be able to help you to prevent or manage these side effects. • To prevent and treat **stomatitis/mucositis**, you can maintain good oral hygiene using a steroid mouthwash and mild toothpaste. Steroid dental paste can be used to treat developing ulcerations. For more severe (Grade 2 and above) **stomatitis**, your doctor may suggest lowering the dose of treatment, or delaying therapy until the **stomatitis** resolves, but in most cases, symptoms will be mild and will subside once you have finished treatment. • Report any signs of **peripheral neuropathy** to your doctor, who will help you to manage this side effect. • Let your doctor know if you experience nail changes, **arthralgia** or **myalgia**, so that they can decide how to manage these. • **Alopecia** can be upsetting for many patients; your doctor will provide you with information on how to cope with this side effect. Some hospitals can provide **cold caps** to reduce hair loss.

continued overleaf

CHEMOTHERAPY DRUG	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Pemetrexed (Alimta SPC, 2018)	• **Anaemia** • **Anorexia** • **Fatigue** • **Leukopenia** • Nausea • **Neutropenia** • **Pharyngitis** • Rash • **Stomatitis**	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **anaemia**, or **leukopenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Effects on the **gastrointestinal system** (**stomatitis**, **pharyngitis**, nausea) may result in loss of appetite (**anorexia**). Your doctor will be able to help you to prevent or manage these side effects. • Let your doctor know if you develop a rash – they will help you to manage this side effect.
Vinorelbine (Vinorelbine SPC, 2018)	• **Alopecia** • **Anaemia** • Constipation • Nausea • **Neurological** disorders • **Neutropenia** • **Oesophagitis** • Skin reactions • **Stomatitis** • Vomiting	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia** or **anaemia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Report any signs of **neurological** disorders (e.g. loss of reflexes, weakness of the legs and feet) to your doctor, who will decide how to manage these side effects. • Your doctor will be able to help you to prevent or manage any effects on the **gastrointestinal system** (**stomatitis**, nausea, vomiting, constipation, **oesophagitis**). • Let your doctor know if you experience any burning or skin changes at the injection site, so that they can decide how to manage these. • **Alopecia** can be upsetting for many patients; your doctor will provide you with information on how to cope with this side effect. Some hospitals can provide **cold caps** to reduce hair loss.

***Important side effects with chemotherapy (used as single drugs) in the treatment of NSCLC**. The most recent Summary of Product Characteristics (SPCs) for individual drugs can be located at: http://www.ema.europa.eu/ema/.*

continued overleaf

Targeted therapies and antiangiogenic therapies

Common side effects in patients treated with **targeted therapies** or **antiangiogenic therapies** include effects on the **gastrointestinal system** (e.g. diarrhoea, vomiting, nausea), skin problems (e.g. rash, dry skin, nail changes, discolouration) and **hypertension** (high blood pressure). Many of the side effects from **targeted therapies** can be effectively prevented or managed effectively. Always tell your doctor or nurse as soon as possible if you notice any side effects from taking a **targeted therapy** or **antiangiogenic therapy**.

THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Afatinib (Giotrif SPC, 2018)	• Decreased appetite • Diarrhoea • **Epistaxis** • Nail disorders • Nausea • Skin reactions (rash, acne, dry skin, itchiness) • **Stomatitis** • Vomiting	• Effects on the **gastrointestinal system** (diarrhoea, nausea, vomiting, **stomatitis**) may result in loss of appetite (**anorexia**). Your doctor will be able to help you to prevent or manage these side effects. • Let your doctor know if you experience **epistaxis** (nose bleeds) – they will help you to manage this side effect. • Report any skin reactions or nail changes to your doctor – they will help you to manage these side effects.
Alectinib (Alecensa SPC, 2018)	• Constipation • **Myalgia** • Nausea • **Oedema**	• Report any nausea or constipation to your doctor, who will be able to help you to prevent or manage these side effects. • Let your doctor know if you develop any **oedema** (fluid retention) or **myalgia** (muscle pain) – they will help you to manage these side effects.
Bevacizumab (Avastin SPC, 2018)	• **Anorexia** • **Arthralgia** • Bleeding disorders • Constipation • Diarrhoea • **Dysarthria** • **Dysgeusia** • **Dyspnoea** • **Fatigue** • Headache • **Hypertension** • **Leukopenia** • Nausea • **Neutropenia** • **Peripheral neuropathy** • **Rhinitis** • Skin reactions • **Stomatitis** • **Thrombocytopenia** • Vomiting • Watery eyes • Wound healing complications	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **leukopenia** or **thrombocytopenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Report any signs of **peripheral neuropathy** (tingling or numbness in your hands or feet) to your doctor, who will help you to manage this side effect. • Any treatment will be delayed until wounds have healed satisfactorily. • Your blood pressure will be monitored throughout treatment and any **hypertension** will be managed appropriately. • Effects on the **gastrointestinal system** (**stomatitis**, constipation, diarrhoea, nausea, vomiting) and **dysgeusia** (taste changes) may result in loss of appetite (**anorexia**). Your doctor will be able to help you to prevent or manage these side effects. • Let your doctor know if you develop any skin reactions (e.g. rash, dry skin, discolouration) – they will help you to manage these side effects. • Report any other side effects, including changes in vision, **dyspnoea** (breathlessness), **dysarthria** (difficulty with speech), **arthralgia** (painful joints) or headache to your doctor, who will help you to manage these side effects.

continued overleaf

THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Ceritinib (Zykadia SPC, 2018)	• **Anaemia** • Changes in liver function • Constipation • Decreased appetite • Diarrhoea • **Dyspepsia**, acid reflux, **dysphagia** • **Fatigue** • Nausea • Rash • Vomiting	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **anaemia** – your doctor may adjust your treatment according to test results. • You will have tests before and during treatment to check how well your liver is functioning. • If you experience diarrhoea, nausea, vomiting, constipation, indigestion, heartburn or problems swallowing, your doctor will be able to help you to prevent or manage these side effects. • Report any rashes to your doctor – they will help you to manage this side effect.
Crizotinib (Xalkori SPC, 2018)	• **Anaemia** • **Bradycardia** • Changes in liver function • Constipation • Diarrhoea • Dizziness • **Dysgeusia** • **Fatigue** • Impaired vision • **Leukopenia** • Nausea • **Neutropenia** • **Oedema** • **Peripheral neuropathy** • Rash • Vomiting	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **anaemia** or **leukopenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Report any signs of **peripheral neuropathy** (tingling or numbness in your hands or feet) to your doctor, who will help you to manage this side effect. • You will have tests before and during treatment to check how well your liver is functioning. • If you experience diarrhoea, nausea, vomiting, constipation, or changes in your sense of taste (**dysgeusia**), your doctor will be able to help you to prevent or manage these side effects. • Let your doctor know if you develop any problems with your eyes, experience dizziness, **oedema** (fluid retention) or develop a rash – they will help you to manage these side effects.

continued overleaf

THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Dabrafenib[b] (Tafinlar SPC, 2018)	• Abdominal pain • **Arthralgia** • **Asthenia** • Bleeding • Changes in liver function • Chills • Constipation • Cough • Decreased appetite • Diarrhoea • Dizziness • Dry skin • **Fatigue** • Fever • Flu-like symptoms • Headache • **Hypertension** • Muscle spasms • **Myalgia** • **Nasopharyngitis** • Nausea • **Oedema** • Pain in extremities • **Pruritus** • Rash • Vomiting	• Effects on the **gastrointestinal system** (diarrhoea, constipation, abdominal pain, nausea, vomiting) may result in loss of appetite (**anorexia**) and **asthenia** (weakness). Your doctor will be able to help you to prevent or manage these side effects. • You will have tests before and during treatment to check how well your liver is functioning. • Your blood pressure will be monitored throughout treatment and any **hypertension** will be managed appropriately. • You should tell your doctor immediately if you notice any signs of increased bleeding (e.g. nose bleeds) as your medication may need to be adjusted. • Let your doctor know if you develop any skin reactions (e.g. rash, dry skin, itchiness) – they will help you to manage these side effects. • Tell your doctor if you experience flu-like symptoms, including **fatigue**, **nasopharyngitis**, chills or fever. • Report any other side effects, including cough, muscle spasms, **arthralgia** (painful joints), **myalgia** (muscle pain), swelling, headache or dizziness to your doctor, who will help you to manage these side effects.
Erlotinib (Tarceva SPC, 2018)	• **Anorexia** • **Conjunctivitis** • Cough • Diarrhoea • Dry eyes • **Dyspnoea** • **Fatigue** • Increased risk of infection • Nausea • Rash • **Stomatitis** • Vomiting	• Your doctor will advise you on how to prevent infections. • Effects on the **gastrointestinal system** (diarrhoea, nausea, vomiting, **stomatitis**) may result in loss of appetite (**anorexia**). Your doctor will be able to help you to prevent or manage these side effects. • Let your doctor know if you develop any problems with your eyes (e.g. dry eyes, **conjunctivitis**), experience increased **dyspnoea** (breathlessness) or cough, or develop a rash – they will help you to manage these side effects.

continued overleaf

THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Gefitinib (Iressa SPC, 2018)	• **Anorexia** • **Asthenia** • Changes in liver function • Diarrhoea • Skin reactions	• Diarrhoea may result in loss of appetite (**anorexia**) and **asthenia** (weakness). Your doctor will be able to help you to prevent or manage these side effects. • You will have tests before and during treatment to check how well your liver is functioning. • Let your doctor know if you develop any skin reactions (e.g. rash, acne, dry skin, itchiness) – they will help you to manage these side effects.
Nintedanib[a] (Vargatef SPC, 2018)	• Changes in liver function • Diarrhoea • **Mucositis** • Nausea • **Neutropenia** • **Peripheral neuropathy** • Rash • **Stomatitis** • Vomiting	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Report any signs of **peripheral neuropathy** (tingling or numbness in your hands or feet) to your doctor, who will help you to manage this side effect. • If you experience diarrhoea, nausea, vomiting, a sore mouth or lips, your doctor will be able to help you to prevent or manage these side effects. • You will have tests before and during treatment to check how well your liver is functioning. • Let your doctor know if you develop any rash – they will help you to manage this side effect.
Osimertinib (Tagrisso SPC, 2018)	• Diarrhoea • **Leukopenia** • Nail disorders • **Neutropenia** • Skin reactions (rash, dry skin, itchiness) • **Stomatitis** • **Thrombocytopenia**	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **leukopenia** or **thrombocytopenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • If you experience diarrhoea or a sore mouth or lips, your doctor will be able to help you to prevent or manage these side effects. • Report any skin reactions or nail changes to your doctor – they will help you to manage these side effects.
Ramucirumab[a] (Cyramza SPC, 2018)	• **Epistaxis** • **Fatigue/asthenia** • **Hypertension** • **Neutropenia** • **Oedema** • **Stomatitis** • **Thrombocytopenia**	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia** or **thrombocytopenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • Your blood pressure will be monitored throughout treatment and any **hypertension** will be managed appropriately. • Let your doctor know if you experience a sore mouth or lips, or **oedema** (fluid retention), your doctor will be able to help you to prevent or manage these side effects.

continued overleaf

THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Trametinib[c] (Mekinist SPC, 2018)	• Abdominal pain • **Arthralgia** • **Asthenia** • Bleeding • Changes in liver function • Chills • Constipation • Cough • Decreased appetite • Diarrhoea • Dizziness • Dry skin • **Fatigue** • Fever • Flu-like symptoms • Headache • **Hypertension** • Muscle spasms • **Myalgia** • **Nasopharyngitis** • Nausea • **Oedema** • Pain in extremities • **Pruritus** • Rash • Vomiting	• Effects on the **gastrointestinal system** (diarrhoea, constipation, abdominal pain, nausea, vomiting) may result in loss of appetite (**anorexia**) and **asthenia** (weakness). Your doctor will be able to help you to prevent or manage these side effects. • You will have tests before and during treatment to check how well your liver is functioning. • Your blood pressure will be monitored throughout treatment and any **hypertension** will be managed appropriately. • You should tell your doctor immediately if you notice any signs of increased bleeding (e.g. nose bleeds) as your medication may need to be adjusted. • Let your doctor know if you develop any skin reactions (e.g. rash, dry skin, itchiness) – they will help you to manage these side effects. • Tell your doctor if you experience flu-like symptoms, including **fatigue**, **nasopharyngitis**, chills or fever. • Report any other side effects, including cough, muscle spasms, **arthralgia** (painful joints), **myalgia** (muscle pain), swelling, headache or dizziness to your doctor, who will help you to manage these side effects.

Important side effects with targeted therapy and antiangiogenic therapy in the treatment of NSCLC. *The most recent Summary of Product Characteristics (SPCs) for individual drugs can be located at: http://www.ema.europa.eu/ema/.*

[a]In combination with **docetaxel chemotherapy**; [b]In combination with **trametinib**; [c]In combination with **dabrafenib**.

continued overleaf

Immunotherapies

Common side effects in patients treated with **immunotherapies** include effects on the skin (e.g. rash, **pruritus**) and **gastrointestinal system** (e.g. diarrhoea, nausea). Many of the side effects from **immunotherapies** can be effectively prevented or managed. Always tell your doctor or nurse as soon as possible if you notice any side effects from taking an **immunotherapy**.

For further information and advice on **immunotherapy** side effects, see ESMO's patient guide on **immunotherapy**-related side effects and their management (https://www.esmo.org/Patients/Patient-Guides/Patient-Guide-on-Immunotherapy-Side-Effects).

THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Atezolizumab (Tecentriq SPC, 2018)	• **Arthralgia** • **Asthenia** • Back pain • Cough • Decreased appetite • Diarrhoea • **Dyspnoea** • **Fatigue** • Fever • Nausea • **Pruritus** • Rash • Urinary tract infection • Vomiting	• Effects on the **gastrointestinal system** (nausea, vomiting, diarrhoea, taste changes) may result in loss of appetite and **asthenia**. Your doctor will be able to help you to prevent or manage these side effects. • Let your doctor know if you experience increased **dyspnoea** or cough, joint pain, itchiness or develop a rash – they will help you to manage these side effects.
Durvalumab (Imfinzi SPC, 2018)	• Abdominal pain • Cough • Diarrhoea • Fever • **Hypothyroidism** • **Pneumonia** • **Pruritus** • Rash • Upper respiratory tract infection	• Let your doctor know if you experience respiratory symptoms. • Your thyroid function will be monitored before and during treatment. • Your doctor will be able to help you to prevent or manage any diarrhoea or nausea. • Let your doctor know if you experience any skin rash or itchiness – they will be able to help you to prevent or manage these side effects.

continued overleaf

THERAPY	POSSIBLE SIDE EFFECT	HOW THE SIDE EFFECTS MAY BE MANAGED
Nivolumab (Opdivo SPC, 2018)	• Altered levels of minerals and salts (**hypercalcaemia, hyperkalaemia, hypokalaemia, hypomagnesaemia, hyponatraemia**) • **Anaemia** • Changes in liver function • Diarrhoea • **Fatigue** • **Leukopenia** • **Lymphopenia** • Nausea • **Neutropenia** • **Pruritus** • Rash • **Thrombocytopenia**	• Your blood cell counts will be monitored frequently throughout your treatment in order to detect any **neutropenia**, **lymphopenia**, **leukopenia**, **anaemia** or **thrombocytopenia** – your doctor may adjust your treatment according to test results, and will advise you on how to prevent infections. • You will have tests before and during treatment to check how well your liver is functioning. • Your doctor will be able to help you to prevent or manage any diarrhoea or nausea. • Your body's levels of minerals and salts will be measured during your treatment – your treatment may be adapted according to any changes. • Let your doctor know if you experience any skin rash or itchiness – they will be able to help you to prevent or manage these side effects.
Pembrolizumab (Keytruda SPC, 2018)	• **Arthralgia** • Diarrhoea • **Fatigue** • Nausea • **Pruritus** • Rash	• Your doctor will be able to help you to prevent or manage any diarrhoea or nausea. • Let your doctor know if you experience any skin rash or itchiness or joint pain – they will be able to help you to prevent or manage these side effects.

Important side effects with immunotherapy in the treatment of NSCLC. *The most recent Summary of Product Characteristics (SPCs) for individual drugs can be located at: http://www.ema.europa.eu/ema/.*

continued overleaf

What happens after my treatment has finished?

Follow-up appointments

You will be able to discuss any concerns you have at your follow-up appointments

After your treatment has finished, your doctor will arrange follow-up appointments. You will have regular chest **x-rays** and/or **CT** scans to check that there are no further **tumours**. Your doctor will also evaluate any treatment complications or side effects related to surgery, **radiotherapy** and/or **systemic anti-cancer treatment**. The frequency of these appointments will be tailored to your situation, and will depend on the stage of the cancer when you were initially diagnosed and the treatment that you have had *(Postmus et al., 2017; Planchard et al., 2018)*.

Recommendations

- After surgery for Stage I-III NSCLC, you should be seen every 6 months for the first 2 years and then yearly after that *(Postmus et al., 2017)*.
- You may have a **CT** scan every 6 months, particularly if you are suitable for salvage treatment should there be any complications *(Postmus et al., 2017)*.
- After treatment for **metastatic** disease, depending on your suitability for further treatment, your doctor will see you every 6–12 weeks so that **second-line** therapy can be started promptly, if needed *(Planchard et al., 2018)*.
- If you have had **multimodal therapy** for Stage III disease you are likely to have brain scans to monitor for the development of brain **metastases**, for which you may be offered treatment *(Eberhardt et al., 2015)*.

What if I need more treatment?

Cancer that comes back is called a **recurrence**. The treatment that you will be offered depends on the extent of the **recurrence**. When the **tumour** comes back as a **recurrence** at a single site, you may be offered treatment such as surgical removal or **radiotherapy**. However, this approach is limited to a very small group of patients. Recurrent **tumours** are normally regarded as **metastatic** cancers and you can usually have further **chemotherapy** with different drugs, and some patients may be suitable for treatment with **targeted therapies** or **immunotherapy** (see section *'Treatment options for metastatic (Stage IV) NSCLC'* for more information).

In some cases, a repeated **biopsy** of the **tumour** may be carried out as it may result in a change to the treatment decision. This may be particularly true if you have been cancer-free for some time after surgical **resection**. Where available, patients who were previously treated for NSCLC with an **EGFR**-activating **mutation** may undergo a **liquid biopsy** to detect any **T790M mutation** (also called plasma **EGFR** mutational analysis). This will involve providing a small blood sample for analysis. Re-**biopsy** may be useful to differentiate between disease **recurrence** and a new **primary lung tumour** (if the **recurrence** is detected in the lung) to ascertain the type of **tumour** or to repeat the **EGFR mutation** test if a non-squamous cancer is detected *(Planchard et al., 2018)*.

Looking after your health

After you have had treatment for NSCLC, you may feel very tired and emotional. It is important to take good care of yourself and get the support that you need.

- **Stop smoking:** If you are a smoker, it is important to stop smoking as soon as you can as it may reduce the risk of disease **recurrence** *(Postmus et al., 2017; Planchard et al., 2018)*. Your doctor and nurse can offer help with stopping smoking.
- **Take plenty of rest when you need it:** Give your body time to recover and make sure you rest as much as you can. Complementary therapies, such as aromatherapy, may help you relax and cope better with side effects. Your hospital may offer complementary therapy; ask your doctor for details.
- **Eat well and keep active:** Eating a healthy diet and keeping active can help improve your fitness. It is important to start slowly, with gentle walking, and build up as you start to feel better.

The following eight recommendations form a good foundation for a healthy lifestyle after cancer *(Wolin et al., 2013)*:

- Don't smoke.
- Avoid second-hand smoke.
- Exercise regularly.
- Avoid weight gain.
- Eat a healthy diet.
- Drink alcohol in moderation (if at all).
- Stay connected with friends, family and other cancer survivors.
- Attend regular check-ups and screening tests.

A healthy, active lifestyle will help you to recover physically and mentally

Regular exercise is an important part of a healthy lifestyle, helping you to keep physically fit and avoid weight gain. Studies have shown that an exercise training programme can improve **fatigue** and well-being in patients with **unresectable** lung cancer *(Wiskemann et al., 2018)*. It is very important that you listen carefully to the recommendations of your doctor or nurse, and talk to them about any difficulties you have with exercise.

Emotional support

It is common to be overwhelmed by your feelings when you have been diagnosed with cancer and when you have been through treatment. If you feel anxious or depressed, talk to your doctor or nurse – they can refer you to a specialist counsellor or psychologist who has experience of dealing with emotional problems of people dealing with cancer. It may also help to join a support group so that you can talk to other people who understand exactly what you are going through.

For further information and advice regarding how to regain your life as far as possible after treatment for cancer, see ESMO's patient guide on survivorship (http://www.esmo.org/Patients/Patient-Guides/Patient-Guide-on-Survivorship).

Support groups

In Europe, there are some lung cancer patient advocacy groups, which help patients and their families to navigate the lung cancer landscape. They can be local, national or international, and they work to ensure patients receive appropriate and timely care and education. These groups can provide you with the tools you may need to help you better understand your disease, and to learn how to cope with it, living the best quality of life that you can.

You can access information from the following organisations:

- **Global Lung Cancer Coalition (GLCC):** www.lungcancercoalition.org
- **Lung Cancer Europe (LuCE):** www.lungcancereurope.eu
- **Women Against Lung Cancer in Europe (WALCE) educational booklets:** www.womenagainstlungcancer.eu/?lang=en

References

Bailey-Wilson JE, Amos CI, Pinney SM, *et al.* A major lung cancer susceptibility locus maps to chromosome 6q23-25. Am J Hum Genet 2004;75(3):460–474.

Cancer.Net. 2016. Side effects of radiation therapy. Available from: http://www.cancer.net/navigating-cancer-care/how-cancer-treated/radiation-therapy/side-effects-radiation-therapy. Accessed 20th November 2018.

Cancer.Net. 2017. Fatigue. Available from: http://www.cancer.net/navigating-cancer-care/side-effects/fatigue. Accessed 20th November 2018.

Cancer.Net. 2018. Side effects of surgery. Available from: http://www.cancer.net/navigating-cancer-care/how-cancer-treated/surgery/side-effects-surgery. Accessed 20th November 2018.

Cappuzzo F, McCleod M, Hussein M, *et al.* IMpower130: Progression-free survival (PFS) and safety analysis from a randomised phase III study of carboplatin + nab-paclitaxel (CnP) with or without atezolizumab (atezo) as first-line (1L) therapy in advanced non-squamous NSCLC. Ann Oncol 2018;29(suppl 8):abstr LBA53.

Cherny NI; ESMO Guidelines Working Group. ESMO Clinical Practice Guidelines for the management of refractory symptoms at the end of life and the use of palliative sedation. Ann Oncol 2014;25(Suppl 3):iii143–iii152.

ClinicalTrials.gov. 2017. Learn about clinical studies. Available from: https://clinicaltrials.gov/ct2/about-studies/learn. Accessed 20th November 2018.

De Koning H, Van Der Aalst C, Ten Haaf K, *et al.* Effects of volume CT lung cancer screening: Mortality results of the NELSON randomized-controlled population based trial. 2018 World Conference on Lung Cancer. Abstract PL02.05.

Eberhardt WEE, De Ruysscher D, Weder W, *et al.* 2nd ESMO Consensus Conference in Lung Cancer: locally advanced stage III non-small-cell lung cancer. Ann Oncol 2015;26:1573–1588.

Escamilla DM and Jarrett P. The impact of weight loss on patients with cancer. Nurs Times 2016;112(11):20–22.

European Medicines Agency (EMA). 2019a. Summary of opinion (initial authorisation): Lorviqua (lorlatinib). Available from: https://www.ema.europa.eu/en/medicines/human/summaries-opinion/lorviqua. Accessed 11th March 2019.

European Medicines Agency (EMA). 2019b. Summary of opinion (initial authorisation): Vizimpro (dacomitinib). Available from: https://www.ema.europa.eu/en/medicines/human/summaries-opinion/vizimpro. Accessed 11th March 2019.

Ferlay J, Ervik M, Lam F, *et al.* Global cancer observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer 2018. Available from: https://gco.iarc.fr/today. Accessed 20th November 2018.

Jordan K, Aapro M, Kaasa S, *et al.* European Society for Medical Oncology (ESMO) position paper on supportive and palliative care. Ann Oncol 2018;29(1):36–43.

Macmillan. 2016. Possible side effects of chemotherapy. Available from: http://www.macmillan.org.uk/information-and-support/lung-cancer/non-small-cell-lung-cancer/treating/chemotherapy/side-effects-of-chemotherapy/possible-side-effects.html. Accessed 20th November 2018.

Macmillan. 2015a. Possible side effects of radiotherapy. Available from: http://www.macmillan.org.uk/information-and-support/lung-cancer/non-small-cell-lung-cancer/treating/radiotherapy/radiotherapy-explained/possible-side-effects.html#236381. Accessed 20th November 2018.

Macmillan. 2015b. Carboplatin. Available from: https://www.macmillan.org.uk/cancerinformation/cancertreatment/treatmenttypes/chemotherapy/individualdrugs/carboplatin.aspx. Accessed 20th November 2018.

Macmillan. 2015c. Cisplatin. Available from: https://www.macmillan.org.uk/cancerinformation/cancertreatment/treatmenttypes/chemotherapy/individualdrugs/cisplatin.aspx. Accessed 20th November 2018.

Malvezzi M, Carioli G, Bertuccio P, *et al*. European cancer mortality predictions for the year 2016 with focus on leukaemias. Ann Oncol 2016;27(4):725–731.

Novello S, Barlesi F, Califano R, *et al*. Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2016;27(Suppl 5):v1–v27.

Planchard D, Popat S, Kerr K, *et al*. Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2018;29(Suppl 5):iv192–iv237.

Postmus PE, Kerr KM, Oudkerk M, *et al*. Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017;28(Suppl 4):iv1–iv21.

Socinski MA, Jotte RM, Cappuzzo F, *et al*. Atezolizumab for first-line treatment of metastatic nonsquamous NSCLC. N Engl J Med 2018a;378(24):2288–2301.

Socinski MA, Rittmeyer A, Shapovalov D, *et al*. IMpower131: Progression-free survival (PFS) and overall survival (OS) analysis of a randomised phase III study of atezolizumab + carboplatin + paclitaxel or nab-paclitaxel vs carboplatin + nab-paclitaxel in 1L advanced squamous NSCLC. Ann Oncol 2018b;29(suppl 8):abstr LBA65.

Torre LA, Bray F, Siegel RL, *et al*. Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87–108.

Wiskemann J, Titz C, Schmidt M, *et al*. Effects of physical exercise in non-operable lung cancer patients undergoing palliative treatment. Ann Oncol 2018;29(Suppl 8):Abstr 1480P.

Wolin KY, Dart H, Colditz GA. Eight ways to stay healthy after cancer: an evidence-based message. Cancer Causes Control 2013;24(5):827–837.

Zhong W-Z, Wu Y-L, Chen K-N, *et al*. CTONG 1103: Erlotinib versus gemcitabine plus cisplatin as neo-adjuvant treatment for stage IIIA-N2 EGFR-mutation non-small cell lung cancer (EMERGING): A randomised study. Ann Oncol 2018;29(Suppl 8):Abstr LBA48.

Ziarnik E, Grogan EL. Post-lobectomy early complications. Thorac Surg Clin 2015;25(3):355–364.

GLOSSARY

ACCELERATED SCHEDULE
A higher dose of radiation is given at each treatment and there are fewer total treatments than in a **conventional radiotherapy** schedule. The total amount of radiation given is about the same in each schedule

ADENOCARCINOMA
The most common type of lung cancer; it develops from mucus-producing cells that line the airways

ADRENAL GLANDS
Glands in the body that produce hormones, such as adrenaline and steroids. They are located above the kidneys

ADJUVANT (TREATMENT)
Additional treatment given after the primary treatment to reduce the chance of the cancer coming back; usually refers to **radiotherapy** and/or **chemotherapy** after surgery

AFATINIB
A type of **targeted therapy** called a **tyrosine kinase inhibitor**, which works by blocking signals within cancer cells and stopping the action of **epidermal growth factor receptor**, causing cancer cells to die. It is administered as a once daily tablet

AIR LEAK
When air escapes from the airways (**bronchioles**, **alveoli**) into the parts of the lung where air is not usually present

ALECTINIB
A type of **targeted therapy** called a **tyrosine kinase inhibitor**, which works by blocking a protein called **anaplastic lymphoma kinase**. It only works in cancer cells with an abnormal version of this protein. It is administered twice-daily as oral capsules

ANAPLASTIC LYMPHOMA KINASE REARRANGEMENTS (ALK)
Anaplastic lymphoma kinase is a cell surface protein. Rearrangement of the **ALK gene** is an abnormality found in some cancer cells, including NSCLC

ALOPECIA
Hair loss

ALVEOLI
Tiny air sacs within the lungs that allow oxygen and carbon dioxide to move between the lungs and bloodstream

ANAEMIA
A condition characterised by the shortage of haemoglobin (a protein in red blood cells that carries oxygen throughout the body)

ANOREXIA
A lack or loss of appetite

ANTIANGIOGENIC THERAPY
A type of therapy that interferes in the growth and survival of new **blood vessels** (angiogenesis), which plays a critical role in the growth and spread of cancer

ANTIBIOTIC
A type of drug used to treat and prevent bacterial infections

ARSENIC
A naturally occurring substance that has been widely used in some industries (copper or lead smelting; agriculture/pesticides), but has been linked to cancer, including lung cancer

ARTHRALGIA
Pain in a joint(s)

ASBESTOS
A natural, fibrous material that was previously widely used as a building material. Its use is now banned throughout Europe as it is linked to lung diseases, including cancer

ASTHENIA
Abnormal feeling of weakness or lack of energy

ATEZOLIZUMAB
A type of **immunotherapy** that blocks a protein called **PD-L1** on the surface of certain immune cells called T-cells; this activates the T-cells to find and kill cancer cells. It is administered through a drip into a vein in your arm or chest

BEVACIZUMAB
A type of **targeted therapy** used to treat some cancers, including advanced NSCLC. It is a **monoclonal antibody** that targets **vascular endothelial growth factor** and prevents the cancer cells from developing their own blood supply, thus helping to slow down **tumour** growth

BIOPSY
A medical procedure in which a small sample of cells or tissue is taken for examination under a microscope

BLOOD VESSELS
The structures (tubes) carrying blood through the tissues and organs of the body – they include veins, arteries and capillaries

GLOSSARY

BONE MARROW
A spongy tissue found inside some bones (e.g. hip and thigh bones). It contains stem cells, which are cells that can develop into the red blood cells, white blood cells or **platelets**

BRADYCARDIA
Abnormally slow heart rate

BRAF
A **gene** that makes a protein involved in cell signalling and growth. **BRAF** may be mutated in cancer cells

BRIGATINIB
A type of **targeted therapy** that works by inhibiting a protein called **anaplastic lymphoma kinase**. It is administered as a once-daily tablet to patients who have previously received **crizotinib**

BRONCHI
The right bronchus and the left bronchus (the **bronchi**) are the two main airways that take air into the lungs

BRONCHIOLES
The **bronchi** divide into smaller bronchioles, which then lead to the **alveoli**

BRONCHOSCOPE
A thin, fibre-optic cable that is inserted into the airways (usually through the nose or mouth)

BRONCHOSCOPY
A clinical investigation where your doctor examines your airways using a **bronchoscope**

CARBOPLATIN
A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

CERITINIB
A type of **targeted therapy** that works by inhibiting a protein called **anaplastic lymphoma kinase**. It is administered as a once-daily capsule to patients who have previously received **crizotinib**

CHEMORADIOTHERAPY
Chemotherapy and **radiotherapy** given together

CHEMOTHERAPY
A type of cancer treatment using medicine that kills the cancer cells by damaging them, so that they cannot reproduce and spread

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)
A type of lung disease characterised by long-term poor airflow. The main symptoms include shortness of breath and cough

CISPLATIN
A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

CLINICAL TRIAL
A study that evaulates the effects of treatment

COLD CAP
A cap that cools the scalp before, during and after treatment to reduce the effects of the treatment on **hair follicles**

COMORBIDITIES
Additional diseases or disorders experienced by the patient at the same time

COMPUTED TOMOGRAPHY (CT)
A scan using **x-rays** and a computer to create detailed images of the inside of your body

CONCURRENT
Different types of treatment (e.g. **chemotherapy** and **radiotherapy**) given at the same time

CONJUNCTIVITIS
Inflammation of the membrane that covers the eyeball and lines the eyelid

CONVENTIONAL RADIOTHERAPY
Refers to **radiotherapy** that is given to the **tumour** as a fraction of the complete dose over several sessions – treatment usually consists of a small daily dose over several weeks

CRIZOTINIB
A type of **targeted therapy** called a **tyrosine kinase inhibitor**, which works by blocking a protein called **anaplastic lymphoma kinase**. It only works in cancer cells with an abnormal version of this protein. It is administered as a twice-daily capsule

DABRAFENIB
A type of **targeted therapy**, which works by blocking signals within cancer cells and stopping the action of proteins made by the mutated **BRAF gene**. It is administered as a twice daily tablet

GLOSSARY

DACOMITINIB
A type of **targeted therapy** called a **tyrosine kinase inhibitor**, which works by blocking signals within cancer cells and stopping the action of **epidermal growth factor receptor**, causing cancer cells to die. It is administered as a once-daily tablet

DENOSUMAB
A drug used to treat osteoporosis and prevent broken bones and other bone problems caused by bone **metastases**

DIAPHRAGM
The muscle that separates the chest cavity from the abdomen; the **diaphragm** contracts and relaxes as we breathe in and out

DNA
Deoxyribose nucleic acid, the chemical that carries genetic information in the cells of your body

DOCETAXEL
A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

DOUBLET CHEMOTHERAPY
A combination of two different types of **chemotherapy** administered at the same time

DURVALUMAB
A type of **immunotherapy** that blocks a protein called **PD-L1** on the surface of certain immune cells called T-cells; this activates the T-cells to find and kill cancer cells. It is administered through a drip into a vein in your arm or chest

DYSARTHRIA
Difficult or unclear articulation of speech (e.g. slurred, nasal-sounding, hoarse or excessively loud or quiet)

DYSGEUSIA
A change in the sense of taste

DYSPEPSIA
The medical term for indigestion

DYSPHAGIA
The medical term for difficulties with swallowing

DYSPNOEA
Shortness of breath

EARLY-STAGE (CANCER)
Cancer that has not spread to the **lymph nodes** or other parts of the body

EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR)
A protein involved in cell growth and division. It is found in abnormally high amounts on the surface of many types of cancer cells

EPISTAXIS
The medical term for a nose bleed

ERLOTINIB
A type of **targeted therapy** called a **tyrosine kinase inhibitor**, which works by blocking signals within cancer cells and stopping the action of **epidermal growth factor receptor**, causing cancer cells to die. It is administered as a once-daily tablet

ETOPOSIDE
A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest, or as an oral tablet or capsule

FATIGUE
Overwhelming tiredness

FIRST-LINE TREATMENT
The initial treatment given to a patient

GASTROINTESTINAL SYSTEM
The system of organs responsible for getting food into and out of the body and for making use of food to keep the body healthy – includes the **oesophagus**, stomach and intestines

GEFITINIB
A type of **targeted therapy** called a **tyrosine kinase inhibitor**, which works by blocking signals within cancer cells and stopping the action of **epidermal growth factor receptor**, causing cancer cells to die. It is administered as a once-daily tablet

GEMCITABINE
A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

GENES
Pieces of **DNA** responsible for making substances that the body needs to function

GENERAL ANAESTHETIC
A medication that causes a reversible loss of consciousness

GLOSSARY

GRADE
Cancer **grade** is based on how different **tumour** cells look from normal cells under a microscope, and on how quickly they grow. The **grade** will be a value between one and three and reflects the aggressiveness of **tumour** cells; the higher the **grade**, the more aggressive the **tumour**

HAIR FOLLICLE
A small sac in the skin from which hair grows from

HEPATIC
Relating to the liver

HISTOLOGICAL SUBTYPE
Cancer type based on the type of tissue in which the cancer started

HYPERCALCAEMIA
An abnormally high level of calcium in the blood

HYPERKALAEMIA
An abnormally high level of potassium in the blood

HYPERTENSION
Abnormally high blood pressure

HYPOKALAEMIA
An abnormally low level of potassium in the blood

HYPOMAGNESAEMIA
An abnormally low level of magnesium in the blood

HYPONATRAEMIA
An abnormally low level of sodium in the blood

HYPOTHYROIDISM
Abnormally low levels of thyroid hormones

IMMUNOTHERAPY
A type of cancer treatment that stimulates the body's immune system to fight the cancer

INDUCTION THERAPY
Initial treatment with **chemotherapy** and/or **radiotherapy** to shrink the **tumour** before a second planned treatment (for example, surgery)

INTRAVENOUS
Administered into a vein

IONISING RADIATION
Any type of particle or electromagnetic wave that carries enough energy to ionise or remove electrons from an atom (e.g. **x-rays**)

LARGE CELL (UNDIFFERENTIATED) CARCINOMA
A type of NSCLC that does not look like **adenocarcinoma** or **squamous cell carcinoma** under the microscope

LEUKOPENIA
A decrease in the number of leukocytes (a type of white blood cell) in the blood, which places individuals at increased risk of infection

LIQUID BIOPSY
Tests performed in blood samples or other body fluids to detect the presence of substances that have originated in a **tumour**, and therefore, indicate the presence of a cancer

LOBE
A (usually rounded) part of an organ that appears to be separate in some way from the rest of that organ

LOBECTOMY
A type of lung cancer surgery in which one **lobe** of a lung is removed (the right lung has three **lobes**, and the left lung has two **lobes**)

LOCAL ANAESTHETIC
A medication that causes reversible absence of pain sensation around the site of administration

LOCALLY ADVANCED
Cancer that has spread from where it started to nearby tissue or **lymph nodes**

LORLATINIB
A type of **targeted therapy**, which works by inhibiting a protein called **anaplastic lymphoma kinase**. It is administered as a once-daily tablet

LYMPH
The fluid that circulates throughout the **lymphatic system**; it contains infection-fighting white blood cells

LYMPH NODES
Small structures throughout the **lymphatic system** that work as filters for harmful substances, such as cancer cells or bacteria

LYMPHATIC SYSTEM
A network of tissues and organs that help rid the body of toxins, waste and other unwanted materials. The primary function of the **lymphatic system** is to transport **lymph**, a fluid containing infection-fighting white blood cells, throughout the body

GLOSSARY

LYMPHOPENIA
An abnormally low level of lymphocytes (a type of white blood cell) in the blood, which places individuals at increased risk of infection

MAGNETIC RESONANCE IMAGING (MRI)
A type of scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body

MAINTENANCE TREATMENT
Treatment given after the initial cycles of **chemotherapy** with the aim of keeping the cancer under control

METACHRONOUS OLIGOMETASTASES
Oligometastases that appear following treatment for a **primary tumour**

METASTATIC
A cancer that has spread from its (**primary**) site of origin to different parts of the body

METASTASIS (METASTASES)
A cancerous **tumour** or growth that has originated from a **primary tumour**/growth in another part of the body (plural = **metastases**)

MONOCLONAL ANTIBODY
A type of **targeted therapy**. **Monoclonal antibodies** recognise and attach to specific proteins produced by cells. Each **monoclonal antibody** recognises one particular protein. They work in different ways depending on the protein they are targeting

MUCOSITIS
Inflammation and ulceration of the membranes lining the **gastrointestinal system**

MULTIDISCIPLINARY TEAM
A group of health care workers who are members of different disciplines (e.g. **oncologist**, **nurse specialist**, physiotherapist, **radiologist**) and provide specific services to the patient. The activities of the team are brought together using a care plan

MULTIMODAL THERAPY
A treatment approach that includes two or more treatment types – usually some combination of surgery, **chemotherapy** and **radiotherapy**

MUTATION
A permanent alteration in the **DNA** sequence that makes up a **gene**, such that the sequence differs from what is found in most people

MYALGIA
Pain in a muscle(s)

***NAB*-PACLITAXEL**
A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest. ***Nab*-Paclitaxel** is a protein-bound form of **paclitaxel**

NASOPHARYNGITIS
Swelling and inflammation of the nasal passages and the back of the throat

NEOADJUVANT (TREATMENT)
Treatment given as a first step to shrink a **tumour** before the main treatment is given

NEUROLOGICAL
Relating to the nerves and the nervous system

NEUTROPENIA
An abnormally low level of **neutrophils** in the blood, which increases risk of infection

NEUTROPHIL
A type of white blood cell that plays an important role in fighting off infection

NINTEDANIB
A type of **targeted therapy** that blocks proteins called protein kinases, which are present in cancer cells and involved in cancer cell growth. It is administered as a twice-daily capsule

NIVOLUMAB
A type of **immunotherapy** that blocks a protein called PD-1 on the surface of certain immune cells called T-cells; this activates the T-cells to find and kill cancer cells. It is administered through a drip into a vein in your arm or chest

NURSE SPECIALIST
A nurse specialised in the care of patients with a certain condition (e.g. cancer)

OEDEMA
A build-up of fluid in the body which causes the affected tissue to become swollen

OESOPHAGITIS
Inflammation of the **oesophagus**

OESOPHAGUS
The food pipe; the tube that connects your throat with your stomach

GLOSSARY

OLIGOMETASTATIC DISEASE (OLIGOMETASTASES)
Cancer that has spread from its original site to a limited number of other sites/organs; disease progression may occur at these sites but without spread to additional organs (**oligometastases** can be described as either **synchronous** or **metachronous**)

ONCOLOGIST
A doctor who specialises in the medical management of cancer

OSIMERTINIB
A type of **targeted therapy** called a **tyrosine kinase inhibitor**, which works by blocking signals within cancer cells and stopping the action of **epidermal growth factor receptor**, causing cancer cells to die. It is administered as a once-daily tablet to patients who have previously been treated with another **tyrosine kinase inhibitor**

PACLITAXEL
A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

PALLIATIVE CARE
The care of patients with advanced, progressive illness. It focuses on providing relief from pain, symptoms and physical and emotional stress, without dealing with the cause of the condition

PASSIVE SMOKING
The inhalation of smoke by a person who is not actively smoking themselves

PATHOLOGIST
Doctor who diagnoses disease by examining cell and tissue samples

PEMBROLIZUMAB
A type of **immunotherapy** that blocks a protein called PD-1 on the surface of certain immune cells called T-cells; this activates the T-cells to find and kill cancer cells. It is administered through a drip into a vein in your arm or chest

PEMETREXED
A type of **chemotherapy** drug used to treat NSCLC, which is given **intravenously** (directly into your bloodstream through a vein in your arm or chest)

PERICARDIUM
The membrane that encloses the heart

PERIPHERAL NEUROPATHY
Damage to the nerves in the extremities of the body. Symptoms may include pain, sensitivity, numbness or weakness in the hands, feet or lower legs

PHARYNGITIS
Inflammation of the pharynx, which is in the back of the throat

PLATELETS
Tiny blood cells that help your body form clots to stop bleeding

PLATINUM-BASED
A class of **chemotherapy** that includes **cisplatin** and **carboplatin**

PLEURA
One of the two membranes around the lungs. These two membranes are called the visceral and parietal pleurae

PNEUMONECTOMY
The surgical removal of a lung or part of a lung

PNEUMONIA
Inflammation of the lung, usually caused by an infection

POSITRON EMISSION TOMOGRAPHY (PET)
An imaging test that uses a dye with **radioactive** tracers, which is injected into a vein in your arm

PRIMARY LUNG CANCER
A cancer that first started in the lungs

PRIMARY TUMOUR
The **tumour** where the cancer first started to grow

PROGNOSIS
The likely outcome of a medical condition

PROGRAMMED DEATH LIGAND-1 (PD-L1)
A cellular protein thought to be involved in helping the **tumour** to evade detection by the body's immune system

PRURITUS
Severe itching of the skin

RADIATION PNEUMONITIS
Symptoms of cough, fever and fullness of the chest that usually appear between 2 weeks and 6 months following **radiotherapy** but are usually temporary

RADIOACTIVE
A material that is unstable and spontaneously emits energy (radiation)

RADIOLOGICAL EXAMINATION
A test that uses **x-rays** or other medical imaging techniques to visualise the body and organs for the detection of signs of cancer or other abnormalities

GLOSSARY

RADIOLOGIST
A doctor specialised in diagnosing and treating disease and injury through the use of medical imaging techniques such as **x-rays**, **computed tomography**, **magnetic resonance imaging**, **positron emission tomography** and **ultrasound**

RADIOTHERAPY
Treatment involving the use of high-energy radiation, which is commonly used to treat cancer

RAMUCIRUMAB
A type of **targeted therapy** that blocks the action of **vascular endothelial growth factor**, and prevents the cancer cells from developing their own blood supply, thus helping to slow down **tumour** growth. It is administered through a drip into a vein in your arm or chest in combination with another type of **chemotherapy**

RECURRENCE
Return of a cancer

REGIMEN
Treatment plan

REGIONAL LYMPH NODES
Lymph nodes close to the **tumour**

RELAPSE
Return of a cancer or deterioration in a person's state of health

RENAL
Relating to the kidneys

RESECTABLE
Able to be removed (resected) by surgery

RESECTION
Surgery to remove tissue

RHINITIS
Inflammation of the lining inside the nose

RISK FACTOR
Something that increases the chance of developing a disease

ROS1 REARRANGEMENT
ROS1 is a cell surface protein. Rearrangement of the **ROS1 gene** is an abnormality found in some cancer cells, including NSCLC

SECOND-LINE TREATMENT
The second treatment given to a patient once the initial (**first-line**) therapy has not worked or has been stopped because of the occurrence of side effects or other concerns

SEGMENT (OR WEDGE) RESECTION
Surgical removal of the segment of the lung where the **tumour** is located

SEQUENTIALLY
Treatment given one after the other

SQUAMOUS CELL CARCINOMA (SCC)
A type of NSCLC; usually occurs in the central part of the lung or in one of the **bronchi**

STENT
A small tube that is used to keep an airway or artery open

STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR)
A specialised type of **radiotherapy** that is given to the **tumour** from many different directions using detailed scans to ensure precise targeting so that higher doses can be given over a shorter time

STOMATITIS
Inflammation of the inside of the mouth

SUPPORTIVE CARE
Care that provides relief from pain, symptoms and physical and emotional stress, without treating the cancer itself

SYNCHRONOUS OLIGOMETASTASES
Oligometastases diagnosed within a few months of a **primary tumour**

SYSTEMIC ANTICANCER TREATMENT
Drugs that spread throughout the body to treat cancer cells wherever they may be. They include **chemotherapy**, hormonal therapy, **targeted therapy** and **immunotherapy**

T790M MUTATION
A **mutation** of the **epidermal growth factor receptor** (also known as Threonine 790 Methionine [Thr790Met] **mutation**)

TARGETED THERAPY
A newer type of cancer treatment that uses drugs or other substances to precisely identify and attack cancer cells, usually while doing little damage to normal cells

TAXANE
A class of **chemotherapy** that includes **paclitaxel** and **docetaxel**

GLOSSARY

THIRD-LINE TREATMENT
A third line of treatment given to a patient once the previous two lines (**first-line** and **second-line**) of therapy have not worked or have been stopped because of the occurrence of side effects or other concerns

THROMBOCYTOPENIA
A deficiency of **platelets** in the blood. This causes bleeding into the tissues, bruising, and slow blood clotting after injury

THROMBOSIS
The formation of a blood clot inside a blood vessel, obstructing the flow of blood through the blood system

TINNITUS
The hearing of a sound (such as ringing, whining or buzzing) when no external sound is present

TRACHEA
The windpipe – the wide, hollow tube that connects the larynx (or voice box) to the **bronchi** of the lungs

TRAMETINIB
A type of **targeted therapy**, which works by blocking signals within cancer cells and stopping the action of proteins called MEK1 and MEK2. It is administered as a once daily tablet

TUMOUR
A lump or growth of abnormal cells. **Tumours** may be benign (not cancerous) or malignant (cancerous). In this guide, the term '**tumour**' refers to a cancerous growth, unless otherwise stated

TYROSINE KINASE INHIBITOR (TKI)
A type of **targeted therapy** that inhibits tyrosine kinases, which are substances that send growth signals to cells

ULTRASOUND
A type of medical scan where sound waves are converted into images by a computer

UNRESECTABLE
Unable to be removed (resected) by surgery

URANIUM
A naturally **radioactive** element

VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF)
A protein produced by cells that stimulates the growth of new **blood vessels**

VIDEO-ASSISTED THORACIC SURGERY (VATS)
A surgical procedure that allows doctors to see inside the chest and lungs. It is a form of 'keyhole' surgery

VINORELBINE
A type of **chemotherapy** that is administered through a drip into a vein in your arm or chest

WEDGE (OR SEGMENT) RESECTION
Surgical removal of the segment of the lung where the **tumour** is located

X-RAY
An imaging test, using a type of radiation that can pass through the body, that allows your doctor to see inside your body

ZOLEDRONIC ACID
A type of bisphosphonate used to treat cancers that have spread to the bone

This guide has been prepared to help you, your friends and your family better understand the nature of non-small-cell lung cancer (NSCLC) and the treatments that are available. The medical information described in this document is based on the clinical practice guidelines of the European Society for Medical Oncology (ESMO) for the management of early-stage, locally advanced or metastatic NSCLC. We recommend that you ask your doctor about the tests and types of treatments available in your country for your type and stage of NSCLC.

This guide has been written by Kstorfin Medical Communications Ltd on behalf of ESMO.

European Society for Medical Oncology (ESMO)
Via Ginevra 4
6900 Lugano
Switzerland

Tel: +41 (0)91 973 19 99
Fax: +41 (0)91 973 19 02
E-mail: clinicalguidelines@esmo.org

GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

We can help you understand non-small-cell lung cancer and the available treatment options.

The ESMO Guides for Patients are designed to assist patients, their relatives and caregivers to understand the nature of different types of cancer and evaluate the best available treatment choices. The medical information described in the Guides for Patients is based on the ESMO Clinical Practice Guidelines, which are designed to guide medical oncologists in the diagnosis, follow-up and treatment in different cancer types.

For more information, please visit **www.esmo.org**