

# Cancer Association of South Africa (CANSA)



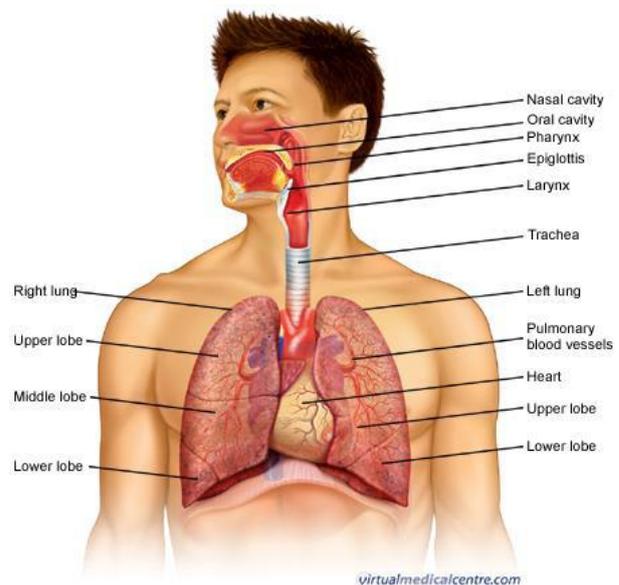
Research • Educate • Support

## Fact Sheet on Lung Cancer

### Introduction

The chest contains two lungs, one lung on the right side of the chest, and the other on the left side of the chest. Each lung is made up of sections called lobes – the right lung consists of three lobes and the left lung consists of two lobes. The lung is soft and protected by the ribcage. The purposes of the lungs are to absorb oxygen (O<sub>2</sub>), into the bloodstream for distribution throughout the body and to remove carbon dioxide (CO<sub>2</sub>), a waste product, from the body.

[Picture Credit – Anatomy of the Lungs]



### Lung Cancer

Lung cancer is a disease characterised by uncontrolled cell growth in tissues of the lung. If left untreated, this growth can spread beyond the lung in a process called metastasis into nearby tissue and, eventually, into other parts of the body. Most cancers that start in lung, known as primary lung cancers, are carcinomas that arise from epithelial cells.

### Incidence of Lung Cancer in South Africa

According to the outdated National Cancer Registry (2014), known for under reporting, the following number of lung cancer cases was histologically diagnosed in South Africa during 2014:

Group - Males 2014	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	1 791	1:80	4,87%
Asian males	93	1:54	9,98%
Black males	695	1:137	6,27%
Coloured males	346	1:41	8,23%
White males	657	1:47	3,19%

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Group - Females 2014	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	936	1:195	2,48%
Asian females	36	1:167	3,01%
Black females	274	1:466	1,70%
Coloured females	209	1:80	5,10%
White females	418	1:85	2,54%

The frequency of histologically diagnosed cases of lung cancer in South Africa for 2014 was as follows (National Cancer Registry, 2014):

Group - Males 2014	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	7	3	34	180	531	574	352	75
Asian males	0	0	1	12	18	39	16	1
Black males	4	2	10	77	249	194	105	16
Coloured males	0	1	11	48	114	97	58	9
White males	3	0	10	38	141	236	165	47

Group - Females 2014	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	2	3	20	74	215	329	211	70
Asian females	0	1	1	5	6	15	7	1
Black females	1	2	7	34	76	85	40	17
Coloured females	0	0	7	16	60	68	42	12
White females	1	0	5	19	70	151	122	40

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

According to **Bruni, et al.**, (2019), the burden of cervical cancer for South Africa for 2018 is estimated as:

- Annual number of lung cancer cases 8 239
- Annual number of lung cancer deaths 7 770

Lung Cancer is also estimated to be the number one cause of all cancer deaths.

### Types of Lung Cancer

There are two main types of lung cancer, non-small cell lung cancer and small cell lung cancer. These names refer to how the cancers look under a microscope to a pathologist (a person specifically qualified to make a diagnosis by looking at items under a microscope. Most lung cancers are non-small cell. There are also some subtypes of non-small cell lung cancer.

### Causes of Lung Cancer

The main cause of lung cancer (internationally) is smoking of tobacco products. Lung cancer has always been – and still is – more common among men. As more women have started smoking, the number of women developing lung cancer has been on the increase.

People who do not smoke can also develop lung cancer. Approximately 10–15% of people who get lung cancer have never smoked.

Other risk factors include the effects of past cancer treatment and exposure to asbestos, radon gas and – in very rare cases – substances such as uranium, chromium and nickel. Lung cancer is not infectious and can't be passed on to other people.

Smoking - The more one smokes, the greater the risk of developing lung cancer. It is also more likely to develop in people who start smoking at a young age. If someone stops smoking, their risk of developing lung cancer reduces over time. After about 15 years, the chance of developing the disease is similar to that of a non-smoker.

In a recent study by Alexandrov, *et al.*, (2016) their analysis shows a direct link between the number of cigarettes smoked in a lifetime and the number of mutations in tumour DNA.

The researchers found that, on average, smoking a packet of cigarettes a day led to:

- 150 mutations in each lung cell every year
- 97 in the larynx or voice box
- 23 in the mouth
- 18 in the bladder
- six in the liver

According to the researchers, the more mutations there are, the higher the chance that these will occur in the key genes that are called cancer genes, which convert a normal cell into a cancer cell.

Passive smoking- breathing in other people's cigarette smoke (passive smoking) increases the risk of lung disease and cancer

Pipes and cigars - although many believe that pipe and cigar smokers have a lower risk of lung cancer than cigarette smokers, there remains a risk of cancer.

Cannabis - Cannabis smoke contains a similar profile of carcinogenic (cancer causing) chemicals as tobacco smoke and is usually inhaled more deeply. Although cannabis smoke is known to contain similar harmful and carcinogenic substances to tobacco smoke, relatively little is understood regarding the respiratory health effects from cannabis smoking (Gates, *et al.*).

Radon gas – radon is a colourless, odourless radioactive gas that forms from the decay of radioactive elements such as uranium. Radon gas given off by soil and rock can enter homes and buildings through cracks in floors and walls, pipes, wires and pumps. Radon concentrations are usually highest in basements or in underground mining environments. Radon is the number one cause of lung cancer among non-smokers, according to estimates from the Environmental Protection Agency (EPA). Overall, radon is the second leading cause of lung cancer

Age - like most types of cancer, lung cancer is more common in older people. About 80% of lung cancers are diagnosed in people over 60. Lung cancer rarely affects people under 40

Genetic risk - some people with a close relative who has had lung cancer may be at an increased risk of it themselves, although the increase in risk is very small. The risk is slightly greater if a relative is a

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non-smoker and developed lung cancer at an early age, or if more than one relative on the same side of the family developed lung cancer

Asbestos - people who have been in contact with asbestos have a higher risk of developing lung cancer, especially smokers. Asbestos and tobacco smoke act together to increase the risk..

Industrial exposure - several industrial carcinogens, for example, arsenic and polycyclic hydrocarbons as well as some occupations including non-ferrous metal production and painting, have been linked to lung cancer

Exposure to Diesel Exhaust Fumes - diesel exhaust was classified as a cause of lung cancer by the International Agency for Research on Cancer (IARC) in June 2012, following a review of evidence mainly from highly-exposed workers. IARC cited a study of diesel exhaust exposure in miners, which showed risk of lung cancer was increased approximately three times in those most heavily exposed

Occupational exposure to silica - silica exposure can result in silicosis with an increased risk for lung cancer, but without silicosis there is no increased risk. The body of evidence supports an increased risk of lung cancer with exposure to asbestos in non-smokers and that risks are especially high in those who smoke, who also have past exposure to asbestos

Family History - a family history of lung cancer in a first-degree relative is associated with a two-fold (double) increased risk, independent of smoking. If both cancers are diagnosed before the age of 60, the risk ratio is almost five-fold. The association between family history and risk may be stronger in black individuals than white

### **Screening for Lung Cancer**

There is currently no specific screening test for lung cancer.

### **Signs and Symptoms of Lung Cancer**

Lung cancer typically doesn't cause signs and symptoms in its earliest stages. Signs and symptoms of lung cancer typically occur only when the disease is advanced. Signs and symptoms of lung cancer may include:

- a new cough that doesn't go away
- changes in a chronic cough or 'smoker's cough'
- a cough that gets worse or does not go away
- coughing up blood, even a small amount
- shortness of breath or wheezing
- constant chest pain – especially when coughing
- frequent chest infections, such as pneumonia, or an infection that does not go away
- wheezing
- hoarseness
- swelling of the neck and face
- fatigue (feeling very tired all the time)

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- loss of appetite
- losing weight without trying

### **Diagnosis of Lung Cancer**

The following may be used to diagnose cancer of the lung:

Medical history - to find out if lung cancer may be present, the doctor evaluates a person's medical history, smoking history, his/her exposure to environmental and occupational substances, and family history of cancer.

Physical examination - the doctor also performs a physical exam and may order a test to take an image of the chest or other tests. Seeing a spot on an image is usually how a doctor first suspects that lung cancer may be present.

Sputum cytology - if lung cancer is suspected, the doctor may order a test called 'sputum cytology'. This is a simple test where a doctor examines a sample of mucous cells coughed up from the lungs under a microscope to see if cancer is present.

Bronchoscopy – a procedure to observe the bronchi of the lungs. During a bronchoscopy the doctor can collect cells or small samples of tissues from the airways and lungs.

Imaging tests - doctors may use imaging methods such as a spiral Computerised Tomography (CT) scan or a Positron Emission Tomography (PET) scan to look for signs of cancer. A CT scan is a series of detailed pictures of areas inside the body. A PET scan is a computerised image of the metabolic activity of body tissues.

### **Staging of Lung Cancer**

Staging is the process of finding out how far a cancer has spread. This is important because treatment options and outlook for recovery and survival depend on the cancer's stage.

Staging of lung cancer can be done by means of:

- The *TNM system* for staging contains 3 key pieces of information:
  - **T** describes the size of the primary tumour, measured in centimetres (cm), and whether the cancer has spread to organs next to the tumour
  - **N** describes the extent of spread to nearby (regional) lymph nodes
  - **M** indicates whether the cancer has metastasised (spread) to other organs of the body

### **Where Lung Cancer May Spread to in the Body**

In the event of lung cancer spreading to other parts of the body, it may spread as indicated in the **bold section** below:

<b>Cancer Type:</b>	<b>Main Sites of Metastasis (Spread)</b>
Bladder	Bone, liver, lung
Breast	Bone, brain, liver, lung
Colon	Liver, lung
Colorectal	Liver, lung, peritoneum (lining of abdomen)
Kidney	Adrenal gland, bone, brain, liver, lung
<b>Lung</b>	<b>Adrenal gland, bone, brain, liver, other lung</b>
Melanoma	Bone, brain, liver, lung, skin, muscle
Ovary	Liver, lung, peritoneum (lining of abdomen)
Pancreas	Liver lung, peritoneum (lining of abdomen)
Prostate	Adrenal gland, bone, liver, lung
Stomach	Liver, lung, peritoneum (lining of abdomen), ovaries
Thyroid	Bone, liver, lung
Uterus	Boner, liver, lung, peritoneum (lining of abdomen), vagina
Non-melanoma skin cancer	Very rare: lymph nodes, lung, bone (if in head/neck region)

### **Treatment of Lung Cancer**

The type of treatment a patient may receive for lung cancer depends on several factors, including:

- the type of lung cancer (non-small cell or small cell)
- the size and position of the cancer
- how far advanced the cancer is (the stage)
- patient's overall health

Treatment options may include:

Surgery – surgical removal of cancerous tissue.

Radiation therapy - radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells or keep them from growing. There are two types of radiation therapy. External radiation therapy uses a machine outside the body to send radiation toward the cancer. Internal radiation therapy uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer.

Radiosurgery - is a method of delivering radiation directly to the tumour with little damage to healthy tissue. It does not involve surgery and may be used to treat certain tumours in patients who cannot have surgery.

Chemotherapy - chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.

Targeted therapy - targeted therapy is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells without harming normal cells.

Immunotherapy – use is made of medicines to stimulate the immune system of the body to fight the cancer.

Watchful waiting - watchful waiting is closely monitoring a patient's condition without giving any treatment until symptoms appear or change.

**Chun, S.G., Liao, Z., Jeter, M.D., Chang, J.Y., Lin, S.H., Komaki, R.U., Guerrero, T.M., Mayo, R.C., Korah, B.M., Koshy, S.M., Heymach, J.V., Koong, A.C. & Skinner, H.D. 2020.**

**BACKGROUND:** Metformin reduces glucose uptake in physiologic tissues and has been shown to affect non-small cell lung cancer (NSCLC) metabolism. We hypothesized that positron emission tomography (PET) scans could detect the impact of metformin on glucose uptake in NSCLC and we sought to redundant test this hypothesis in a prospective clinical trial.

**MATERIALS AND METHODS:** A single-blinded phase II clinical trial was performed with subjects randomized 6:1 to 3 to 4 weeks of metformin versus placebo for inoperable early-stage NSCLC. PET scans were performed at baseline, mid-treatment (after 2 wk study medication), and 6 months postradiation. The primary endpoint of the trial was tumor metabolic response to metformin by PERCIST before definitive radiation. Stereotactic body radiotherapy to 50 Gy in 4 fractions was used for peripheral tumors and 70 Gy in 10 fractions for central tumors.

**RESULTS:** There were 14 subjects randomized to the metformin and 1 to placebo. Histologies were 60% adenocarcinoma, 33.3% squamous cell carcinoma, and 6.7% poorly differentiated carcinoma. At mid-treatment PET scan, 57% of subjects randomized to metformin met PERCIST criteria for metabolic response, of which 75% had progressive metabolic disease and 25% had partial metabolic response, whereas the placebo subject had stable metabolic disease. At 6 months, the metformin arm had 69% complete metabolic response, 23% partial metabolic response and 1 progressive metabolic disease, and the subject treated with placebo had a complete metabolic response. There were no CTCAE grade  $\geq 3$  toxicities.

**CONCLUSIONS:** Despite low accrual, majority of subjects treated with metformin had metabolic responses by PERCIST criteria on PET imaging. Contrary to the effect of metformin on most physiologic tissues, most tumors had increased metabolic activity in response to metformin.

**Hanna, N.H., Schneider, B.J., Temin, S., Baker, S. (Jr), Brahmer, Jm, Ellis, P.M., Gaspar, L.E., Haddad, R.Y., Hesketh, P.J., Jain, D., Jaiyesimi, I., Johnson, D.H., Leighl, N.B., Phillips, T., Riely, G.J., Robinson, A.G., Rosell, R., Schiller, J.H., Singh, N., Spigel, D.R., Stabler, J.O., Tashbar, J. & Masters, G. 2020.**

**PURPOSE:** The aim of this work is to provide evidence-based recommendations updating the 2017 ASCO guideline on systemic therapy for patients with stage IV non-small-cell lung cancer (NSCLC) without driver alterations. A guideline update for patients with stage IV NSCLC with driver alterations will be published separately.

**METHODS:** The American Society of Clinical Oncology and Ontario Health (Cancer Care Ontario) NSCLC Expert Panel made updated recommendations based on a systematic review of randomized controlled trials from December 2015 to 2019.

**RESULTS:** This guideline update reflects changes in evidence since the previous guideline update. Five randomized controlled trials provide the evidence base. Additional literature suggested by the Expert Panel is discussed.

**RECOMMENDATIONS:** Recommendations apply to patients without driver alterations in epidermal growth factor receptor or ALK. For patients with high programmed death ligand 1 (PD-L1) expression (tumor proportion score [TPS]  $\geq 50\%$ ) and non-squamous cell carcinoma (non-SCC), the Expert Panel recommends single-agent pembrolizumab. Additional treatment options include pembrolizumab/carboplatin/pemetrexed, atezolizumab/carboplatin/paclitaxel/bevacizumab, or atezolizumab/carboplatin/nab-paclitaxel. For most patients with non-SCC and either negative (0%)

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or low positive (1% to 49%) PD-L1, the Expert Panel recommends pembrolizumab/carboplatin/pemetrexed. Additional options are atezolizumab/carboplatin/nab-paclitaxel, atezolizumab/carboplatin/paclitaxel/bevacizumab, platinum-based two-drug combination chemotherapy, or non-platinum-based two-drug therapy. Single-agent pembrolizumab is an option for low positive PD-L1. For patients with high PD-L1 expression (TPS  $\geq$  50%) and SCC, the Expert Panel recommends single-agent pembrolizumab. An additional treatment option is pembrolizumab/carboplatin/(paclitaxel or nab-paclitaxel). For most patients with SCC and either negative (0%) or low positive PD-L1 (TPS 1% to 49%), the Expert Panel recommends pembrolizumab/carboplatin/(paclitaxel or nab-paclitaxel) or chemotherapy. Single-agent pembrolizumab is an option in select cases of low positive PD-L1. Recommendations are conditional on the basis of histology, PD-L1 status, and/or the presence or absence of contraindications. Additional information is available at [www.asco.org/lung-cancer-guidelines](http://www.asco.org/lung-cancer-guidelines).

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**BACKGROUND:** Chemotherapy-induced damage of hematopoietic stem and progenitor cells (HSPC) causes multi-lineage myelosuppression. Trilaciclib is an intravenous CDK4/6 inhibitor in development to proactively preserve HSPC and immune system function during chemotherapy (myelopreservation). Preclinically, trilaciclib transiently maintains HSPC in G1 arrest and protects them from chemotherapy damage, leading to faster hematopoietic recovery and enhanced antitumor immunity.

**PATIENTS AND METHODS:** This was a phase Ib (open-label, dose-finding) and phase II (randomized, double-blind placebo-controlled) study of the safety, efficacy and PK of trilaciclib in combination with etoposide/carboplatin (E/P) therapy for treatment-naive extensive-stage small-cell lung cancer patients. Patients received trilaciclib or placebo before E/P on days 1-3 of each cycle. Select end points were prespecified to assess the effect of trilaciclib on myelosuppression and antitumor efficacy.

**RESULTS:** A total of 122 patients were enrolled, with 19 patients in part 1 and 75 patients in part 2 receiving study drug. Improvements were seen with trilaciclib in neutrophil, RBC (red blood cell) and lymphocyte measures. Safety on trilaciclib+E/P was improved with fewer  $\geq$ G3 adverse events (AEs) in trilaciclib (50%) versus placebo (83.8%), primarily due to less hematological toxicity. No trilaciclib-related  $\geq$ G3 AEs occurred. Antitumor efficacy assessment for trilaciclib versus placebo, respectively, showed: ORR (66.7% versus 56.8%,  $P = 0.3831$ ); median PFS [6.2 versus 5.0 m; hazard ratio (HR) 0.71;  $P = 0.1695$ ]; and OS (10.9 versus 10.6 m; HR 0.87;  $P = 0.6107$ ).

**CONCLUSION:** Trilaciclib demonstrated an improvement in the patient's tolerability of chemotherapy as shown by myelopreservation across multiple hematopoietic lineages resulting in fewer supportive care interventions and dose reductions, improved safety profile, and no detriment to antitumor efficacy. These data demonstrate strong proof-of-concept for trilaciclib's myelopreservation benefits.

**CLINICAL TRIAL NUMBER:** [NCT02499770](https://clinicaltrials.gov/ct2/show/study/NCT02499770).

## **Lowering the Risk for Lung Cancer**

Reducing the risk for lung cancer can be achieved by not smoking. Other means include:

Smoking cessation - smoking is responsible for the majority of lung cancers. Quitting all forms of smoking at any time can lower the risk of developing lung cancer, and appears to be beneficial after a diagnosis of lung cancer as well.

Preventing exposure to Radon - exposure to radon in the home is the second leading cause of lung cancer overall, and the number one cause in non-smokers. Radon is an invisible radioactive gas that results from the normal decay of radium in the soil.

Not being exposed to secondhand smoke - exposure to second hand smoke increases the risk of lung cancer in non-smokers two to three fold.

Asbestos - workplace exposure to asbestos increases the risk of lung cancer, and combined with smoking the risk is exponential. Employers should have safety recommendations for those exposed.

## **About Clinical Trials**

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: [www.sanctr.gov.za/](http://www.sanctr.gov.za/)

## **Medical Disclaimer**

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

Whilst the Cancer Association of South Africa (CANSA) has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action

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#### Anatomy of Lungs

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