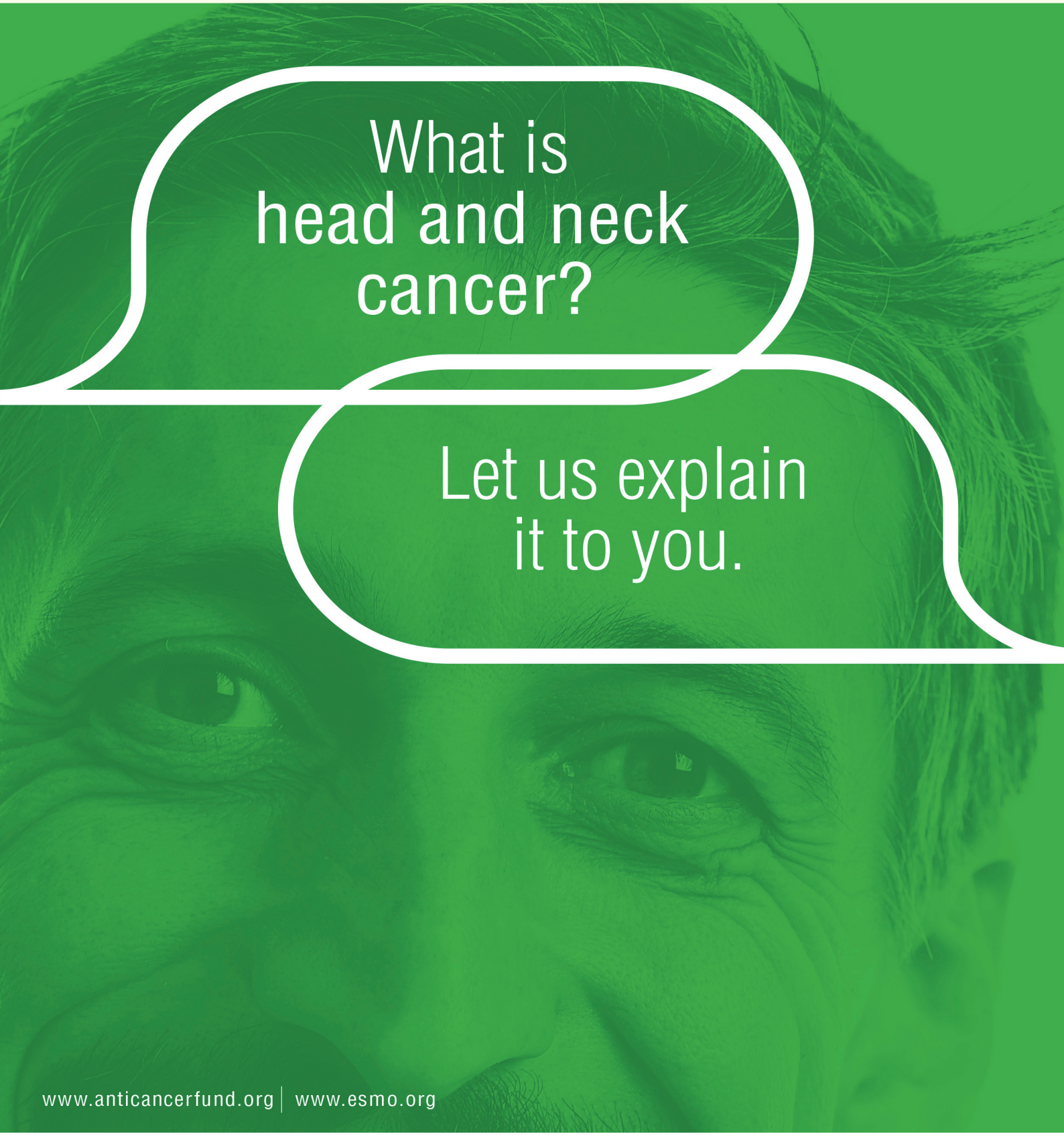
Head and Neck Cancer



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ESMO/ACF Patient Guide Series
based on the ESMO Clinical Practice Guidelines

CANCERS OF THE HEAD AND NECK: A GUIDE FOR PATIENTS

PATIENT INFORMATION BASED ON ESMO CLINICAL PRACTICE GUIDELINES

This guide for patients has been prepared by the Anticancer Fund as a service to patients, to help patients and their relatives better understand the nature of squamous cell carcinomas* of the head and neck and appreciate the best treatment choices available according to the subtype of squamous cell carcinoma* of the head and neck. We recommend that patients ask their doctors about what tests or types of treatments are needed for their type and stage of disease. 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 squamous cell carcinoma* of head and neck. This guide for patients has been produced in collaboration with ESMO and is disseminated with the permission of ESMO. It has been written by a medical doctor and reviewed by two oncologists from ESMO including the leading author of the clinical practice guidelines for professionals. It is also reviewed by three nurses of EONS. It has also been reviewed by patient representatives from ESMO's Cancer Patient Working Group.

More information about the Anticancer Fund: www.anticancerfund.org

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For words marked with an asterisk, a definition is provided at the end of the document.

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FACTSHEET ABOUT HEAD AND NECK CANCERS

Definition of head and neck cancers

- Head and neck cancers are a group of cancers that form in the tissues of the upper aerodigestive tract (lips, tongue, mouth, throat and larynx or voice box) or the sinuses and nasal cavity.
- Most head and neck cancers originate from the squamous cells making the lining of these tracts and cavities and are therefore called squamous cell carcinomas*. These cancers are the topic of the current guide.

Diagnosis

- Cancer in head and neck can be suspected in the presence of symptoms such as a lump in the neck, sore tongue, bleeding area, white or red patches in the mouth, sore throat, painful swallowing, persistent hoarseness, blocked nose on one side and/or bloody discharge from the nose, especially if they persist for more than 3 weeks.
- The direct observation and palpation of the suspicious lesions will be complemented by observation of mouth, nose, throat and upper airways with a flexible, lightened tube called endoscope.
- Medical imaging is used to know the shape and size of the tumour, and can also be used to verify whether the cancer has not disseminated to other parts of the body.
- A diagnosis of cancer can only be confirmed by the analysis of the tumour tissue (biopsy*) under a microscope.

Treatment according to the extension of the disease (classified into different stages)

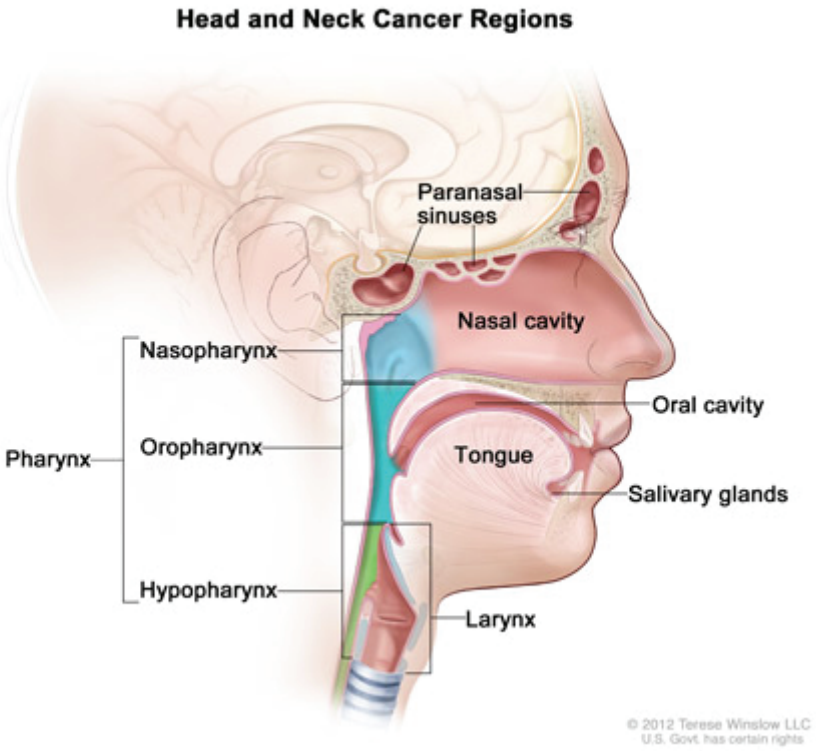
- Stage I and stage II head and neck cancer are called localized or early stage cancers as they are less than 4 cm in diameter and have not spread to any lymph node.
    - Radiotherapy* and surgery are similarly effective to treat the tumour.
    - Modern techniques of radiotherapy* allow to substantially limit damages to healthy tissues surrounding the tumour.
- Stage III and IV head and neck cancers are respectively called locally advanced and metastatic cancer as they either are larger than 4 cm in diameter, have spread to lymph nodes* or, have spread to distant organs. The main question at these stages will be to evaluate if the tumour can be entirely removed by surgery without compromising too much the quality of life of the person.
    - If the tumour is considered resectable (operable), the treatment proposed is surgery to remove the tumour, followed by reconstructive surgery and radiotherapy*. Analysis of the tumour removed during surgery will provide additional information to decide if chemotherapy* should be proposed afterwards.
    - In some cases, a drug called cetuximab* which causes fewer side effects may be used instead of chemotherapy*.

Follow-up

- Follow-up is important to detect side effects associated to treatment such as swallowing or breathing problems. The thyroid gland function is evaluated at 1, 2 and 5 years in patients that received radiotherapy to the neck.
- Physical examination and medical imaging will be performed on a regular basis mainly to detect recurrence of the cancer.

DEFINITION OF HEAD AND NECK CANCERS

Head and neck cancers are a group of cancers that originate from the upper aerodigestive tract (lips, tongue, mouth, throat and larynx or voice box), the salivary glands, the nasopharynx* (area that connects the nose and the upper part of the throat) or the sinuses and nasal cavity. Almost all cancers in these areas are squamous cell carcinomas*. Rare cancers such as those originating from the salivary glands, nasopharynx*, paranasal sinuses, and nasal cavity and those with a histologic type* other than squamous, have special recommendations and are not included in this guide.



Head and neck cancer regions. This drawing illustrates location of paranasal sinuses, nasal cavity, oral cavity, tongue, salivary glands, larynx, and pharynx (including the nasopharynx*, oropharynx*, and hypopharynx*).

ARE HEAD AND NECK CANCERS FREQUENT?

Head and neck cancers represent 4% of all cancers worldwide. The location most frequently affected is the oral cavity, counting for 41% of all head and neck cancers followed by pharynx and larynx cancers with 22% and 24% respectively.

In Europe, oral cavity cancers are diagnosed every year in 48 individuals out of one million, followed by nasopharyngeal* cancers and salivary glands tumours diagnosed in 28 and 13 cases per million respectively.

In Europe, the risk of developing head and neck cancer is higher for men than for women. There are some differences between countries especially in the male population. 20 to 30 men out of 100000 will develop mouth, tongue, oropharynx*, or hypopharynx* cancers at some point in their lives while in women, 8 to 10 out of 100000 will develop mouth or tongue cancers and 2 to 3 oropharynx* or hypopharynx* cancers. In general, the risk is higher in France and Switzerland and lower in some areas of Italy and the UK. Nevertheless, the risk of hypopharynx* cancer in women is lower in some areas of Switzerland.

Other types of tumours like epithelial tumours of nasal cavities, nasopharynx*, eye and adnexa*, and middle ears occur in less than 5 people per million. These cancer types are categorized as rare cancer of head and neck.

WHAT CAUSES HEAD AND NECK CANCERS?

Tobacco consumption and alcohol drinking have been linked to more than 70% of head and neck cancers. Some other risk factors* have been identified as well. A risk factor* increases the risk of cancer occurring, but is neither necessary nor sufficient to cause cancer. A risk factor* is not a cause in itself.
Some people with these risk factors* will never develop head and neck cancers and some people without any of these risk factors* may nonetheless develop head and neck cancers.

The main risk factors* of head and neck cancers are:

- **Tobacco consumption:** The risk is directly linked to the time and quantity of tobacco consumption. It has been found, however, that the risk decreases in time after quitting its use. Second hand smoking (passive smoking) also increases the risk. Not only tobacco smoking but the consumption of smokeless tobacco, such as chewing tobacco and snuff, has been associated to oral cancer. In some Asian countries the combination of tobacco with betel quid is linked to oral, tonsil and pharynx cancers. Even the use of betel quid alone increases the risk of getting oral cancer.

- **Alcohol:** Alcohol and tobacco consumption have been associated to the majority of cases of head and neck cancer. The risk associated to alcohol drinking increases in time and proportionally to the quantities of alcohol consumed. Heavy drinkers are at higher risk, 5-fold for oral cancer and 7-fold for pharyngeal cancers.
- **Human papilloma viruses* (HPV):** Evidence of infection with HPV, particularly HPV16, has been found in cancers of the oropharynx*, much less in oral cavity and larynx. Moreover, sexual behaviours have shown to be correlated to head and neck cancers, such as earlier age at sexual debut and multiple sexual partners.

Having a first-degree relative (parents, siblings or children) affected and low socio-economic status have also been correlated with head and neck cancers. However, they could only be reflecting the variability of exposure to alcohol and tobacco consumption.

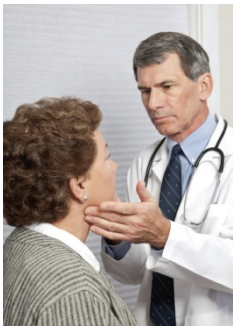
Other important risk factors* are diet high in animal fats and low in fresh fruit for all types of head and neck cancer, prolonged exposure to sunlight for lip cancer; gastro-oesophageal reflux disease for larynx and pharynx cancers, radiation* exposure for salivary glands cancer and yerba mate* drinking for oral cavity cancers. There are also some pre-cancerous conditions such as white and red patches (leukoplakia* and erythroplakia* respectively) associated to tobacco use or other conditions that increase the risk of developing a cancer in the mouth.

Other factors like coffee consumption, body leanness or being underweight have been suspected to be associated to an increased risk of head and neck cancers, but the evidence is inconclusive.

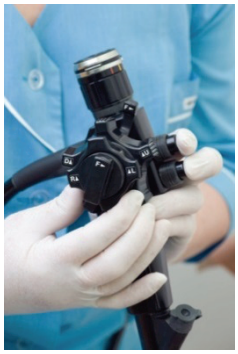
HOW ARE HEAD AND NECK CANCERS DIAGNOSED?

Head and neck cancers can be suspected with the appearance of symptoms depending on the cancer's specific location. Lump in neck, tongue sore, bleeding area, white or red patch in mouth, pain in the throat, painful swallowing, persistent hoarseness, blocked nose on one side and/or bloody discharge from the nose are symptoms that, when persistent for more than 3 weeks, should be investigated by your doctor.

The diagnosis of head and neck cancers is based on the following examinations:



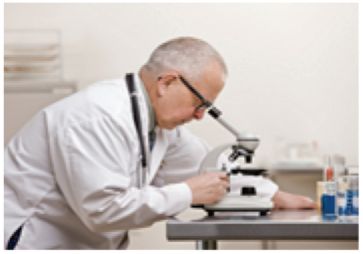
1. **Physical examination.**
   The physical examination may include visual inspection of the mouth, nose and neck, using a light and a mirror for clearer view. Observation and palpation of the lips, the cheeks, gums, and neck are performed to investigate for lumps or other abnormalities, as described previously. The conclusions of these observations will guide further diagnostic procedures.



2. **Endoscopy*.**
   While the oral cavity and oral pharynx may be inspected directly, visualising the nasopharynx*, hypopharynx*, and larynx requires the use of indirect mirror laryngoscopy* and/or endoscopy*, a procedure to examine the areas inside the body using a thin, lighted and flexible tube called endoscope. In this procedure you won't need to stay long at the doctor's office and no anaesthetic* is necessary. Another procedure called panendoscopy* encompasses the use of direct laryngoscopy*, bronchoscopy* (to evaluate airways in the lung), and oesophagoscopy* to map eventual tumour involvement of oesophagus. Panendoscopy* is performed under general anaesthesia*.

3. **Radiological examination.**
   Computed tomography* (CT scan) and Magnetic Resonance Imaging* (MRI) are used to know the size and shape of the primary tumour. CT scan* can show soft tissues, including lymph nodes*, bony structures and blood vessels at the same time, however MRI* has better resolution to picture details of soft tissues. Hence, MRI* is the preferable staging procedure for every tumour sub-site except laryngeal and hypopharyngeal* cancers.
   Chest X ray* is recommended to evaluate eventual presence of metastases* in the lung or a primary tumour in the lung. In that regard, CT scan* of the chest may be performed in larger tumours.

4. **Histopathological examination.**



This is the laboratory analysis of the tumour tissue. It is performed using a microscope to examine the material obtained through biopsy*. Tissue biopsy* can be done via endoscopy* and depending on tumour location also simply by opening the mouth or in some cases by taking a sample from an enlarged lymph node* in the neck. The histopathological information will confirm the diagnosis of cancer and reveals specific characteristics of the tumour. The pathological diagnosis is made according to the World Health Organization classification of head and neck tumours. Tumours could be less or more aggressive than the most common type, squamous*, so it is important to know this information. For example, papillary* and verrucous carcinomas* are less aggressive whilst basaloid* and spindle cell* variants are more aggressive. Further details that should be reported by the pathologist are going to be explained in the treatment chapter.

WHAT IS IMPORTANT TO KNOW TO GET THE OPTIMAL TREATMENT?

Doctors will need to consider many aspects of both the patient and the cancer in order to decide on the best treatment.

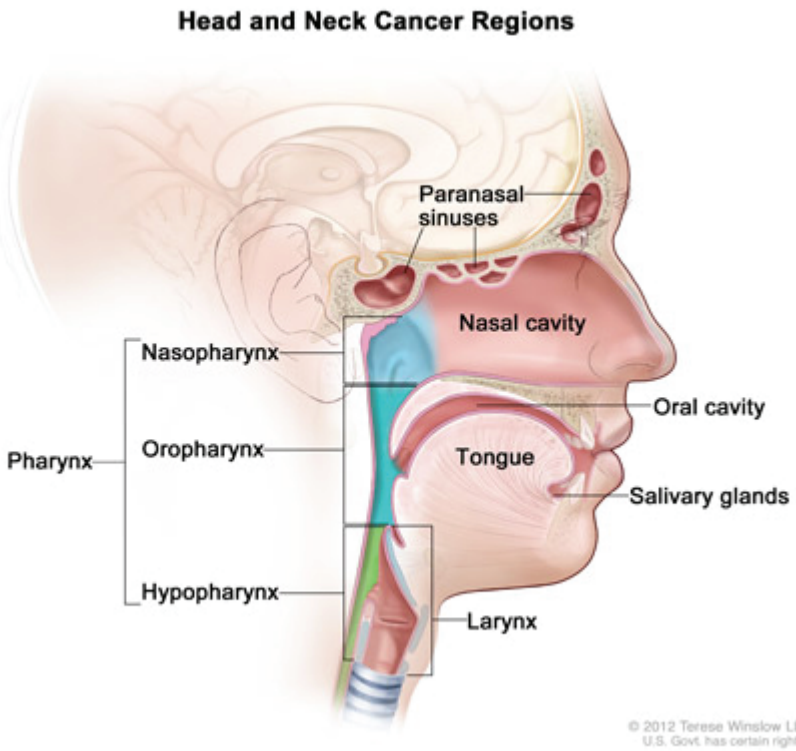
Relevant information about the patient

- Personal medical history
- Family history of cancer
- Alcohol and tobacco use
- Results from the clinical examination by the doctor
- General well-being
- Weight and nutritional status
- In addition to clinical examination, other exams may be performed to assess the risks of complications due to the treatment. Particularly assesments of kidney function and dental health status are conducted, as some treatment options might affect these.

Relevant information about the cancer

- **Location of the tumour**
  The location of the tumour will influence the treatment decisions as head and neck cancers affect relatively small and visible organs and the treatment could affect their functionality and physical appearance.

  Head and neck cancers involve most of the small but functional organs in head and neck with few exceptions. Thyroid, eyes, and brain are not included.
  In this particular guide, paranasal sinuses, salivary gland, nasal cavity, and nasopharynx* cancers, in spite of being head and neck cancers, are not presented because the treatment recommendations for these are very specific.
  As previously stated, the recommendations in this guide are appropriate for mouth, lips, tongue, palate, pharynx (excluding its upper part or nasopharynx*), and larynx.



Head and neck cancer regions. This drawing illustrates location of paranasal sinuses, nasal cavity, oral cavity, tongue, salivary glands, larynx, and pharynx (including the nasopharynx*, oropharynx*, and hypopharynx*).

- **Staging**

  Doctors use staging to assess the extension of the cancer and the prognosis* of the patient. The TNM staging system is commonly used. The combination of T (size of the tumour and invasion of nearby tissue), N (involvement of lymph nodes*), and M (metastasis* or spread of the cancer to other organ(s) of the body), will classify the cancer into one of the stages explained later.

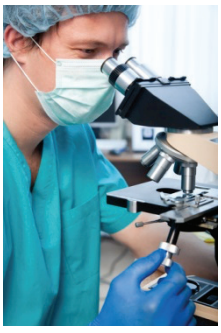
  The stage is fundamental in order to make the right decision about the treatment. The lower the stage, the better the prognosis*. Staging is usually performed twice: after clinical and radiological examination and after surgery. If surgery is performed, staging may also be influenced by the laboratory examination of the removed tumour.

  Staging is very particular for each cancer location as the structures affected are not the same. It is not the purpose of this guide to provide detailed information, however you must be aware that the table presented below only provides very general explanations to give you an overview of head and neck cancer stages. It is recommended to ask your doctors for the details on each particular case.

Stage	Definition
Stage I	• *Tumour size and infiltration:* 2 cm in diameter or less with no infiltration of contiguous tissues. • *Lymph nodes* involved:* No. • *Distant organs involved:* No.
Stage II	• *Tumour size and infiltration:* Tumour of more than 2 cm but no more than 4 cm or already involving neighbouring sites. • *Lymph nodes* involved:* No. • *Distant organs involved:* No.
Stage III	• *Tumour size and infiltration:* Tumour of more than 4 cm. OR • *Lymph nodes* involved:* Yes and 3 cm maximum. • *Distant organs involved:* No.
Stage IVA	• *Tumour size and infiltration:* Any size and infiltration. • *Lymph nodes* involved:* Yes and between 3 and 6cm. • *Distant organs involved:* No.
Stage IVB	• *Tumour size and infiltration:* The tumour invades the space in front of the spine in the neck, the carotid artery* or structures in the area between the lungs called mediastinum*, such as the trachea* and oesophagus. OR • *Lymph nodes* involved:* Yes and sized more than 6 cm. • *Distant organs involved:* No.
Stage IVC	Regardless the size of the primary tumour and the lymph nodes* involved if any, a distant organ is involved (distant metastasis*).

- **Results of the biopsy***

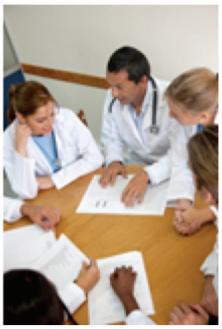
  The biopsy* will be examined in the laboratory. This examination is called histopathology*. The second histopathology* involves the examination of the tumour and the lymph nodes* after surgical removal. It is very important to confirm the results of the biopsy* and to provide more information on the cancer. Generally, the more lymph nodes* are affected and the more downwards in the body they are located the less favourable the prognosis* is. Results of the examination of the biopsy* should include:



  - **Primary site:** The prognosis* is different depending on the area of the head and neck affected.
  - **T stage:** This means the tumour dimensions and the presence or absence of adjacent invasion. The T stage is used to assess the staging of the disease explained previously. The higher the T stage, the less favourable the prognosis*.
  - **Histological type*:** Most head and neck cancers are squamous carcinomas*. Particular subtypes are papillary* and verrucous carcinomas* that have better prognosis* or basaloid* and spindle cell carcinomas* that are more aggressive.
  - **Depth of invasion:** Invasion to adjacent tissues superior to 4 mm has less favourable prognosis*.

- **Pattern of infiltration:** Cohesive pattern means that the tumour is growing as a unique mass pushing adjacent tissues. Its prognosis* is indeed better than the non-cohesive pattern in which broad strands and sheets of tumour invade adjacent tissues.
- **Grade:** Head and neck cancers are graded from 1 to 4. The higher the grade, the less favourable the prognosis*.
  GX: The grade cannot be assessed by the pathologist
  G1: Well-differentiated, in which the cancer cells look a lot like healthy cells from which the cancer is originating.
  G2: Moderately differentiated, the cells are less identifiable but still their origin can be determined.
  G3: Poorly differentiated, the cells are barely identifiable.
  G4: Undifferentiated, cancer cells cannot even be compared to the healthy cells from which they originated.
- **Tumour margins:** Margins are theedges or borders of the tissue removed in cancer surgery. The margin is described as negative or clean when the pathologist finds no cancer cells at the edge of the tissue, suggesting that all of the cancer has been removed. The margin is described as positive or involved when the pathologist finds cancer cells at the edge of the tissue, suggesting that all of the cancer has not been removed. For head and neck cancers, when cancer cells are found up to 1 mm from the border of resection, the margins are considered positive. It is considered that cancer cells might have been left behind in the area from which the tumour was removed.
- **Vascular and perineural infiltration:** Analysis of the biopsy* may show that tumour cells infiltrate the surrounding nerves (perineural) and vessels (vascular). This infiltration indicates an elevated risk of recurrence of disease after treatment compared to tumour with no such infiltration.
- **HPV* infection:** Investigating HPV* infection so far does not influence treatment decision making. Nevertheless, its assessment is recommended as it might be relevant for prognosis* and for patients who are interested in understanding more about their disease.

WHAT ARE THE TREATMENT OPTIONS?



Planning of the treatment involves an inter-disciplinary team of medical professionals. This usually implies a meeting of different specialists, called multidisciplinary opinion* or tumour board review. In this meeting, the planning of treatment will be discussed according to the relevant information mentioned before.
It is recommended that patients should quit habits considered as risk factors* for head and neck cancers, such as tobacco consumption and alcohol drinking. They are also encouraged to keep a healthy nutritional status before starting the treatment as swallowing may be made more difficult by the cancer and any treatments, therefore the intervention of a dietician is recommended. Dental treatment is also highly recommended before starting treatment, radiotherapy* to the head will make teeth decay, and this process could be enhanced by a poor dental health. Good oral hygiene is very important to reduce the risk of sore mouth (mucositis*) and oral infections.

The treatment will usually combine therapies that:

- Treat the cancer locally, such as surgery or radiotherapy*
- Treat cancer cells all over the body by systemic therapy* such as chemotherapy* (cisplatin* or carboplatin*, 5-Fluorouracil*, docetaxel*) and targeted*, biologic therapy* (cetuximab*).

The extent of the treatment will depend on the stage of the cancer, on the characteristics of the tumour and on the risks for the patient.

The treatments listed below have their benefits, their risks and their contraindications*. It is recommended that patients ask their doctors about the expected benefits and risks of every treatment in order to fully understand the treatment. For some treatments, several possibilities are available and the choice should be discussed according to the balance between benefits and risks.

After describing the different treatment options that can be used to treat head and neck cancers, the recommended treatment plans according to the stage are presented.

Treatment options used for head and neck cancers

Surgery

Surgery will be performed under general anaesthesia*. The surgeon will remove the tumour and some lymph nodes* could be removed during the same operation. As the aesthetic* and functionality of the organs in head and neck can be importantly affected, surgery should try to spare healthy structures as much as possible, this is called conservative surgery. Reconstructive (plastic) surgery could be performed during the same procedure to replace missing tissue with pieces of tissue from other parts of the body (tissue flap). The skin could also be shifted to cover up the lesion (skin graft). The ultimate goal of reconstructive surgery is to restore the appearance and function of the removed tissues as much as possible.

Radiotherapy*

Radiotherapy* is the use of radiation* to kill cancer cells. Generally, cancer cells are less capable of recovering from radiation damage than normal cells.

Radiotherapy* in head and neck cancer aims to destroy cancer cells locally using high-energy radiation* produced by a radiotherapy* device. In external radiotherapy*, radiation is produced by an external source and directed to the area in head or neck where the tumour is, including lymph vessels* and lymph nodes* in some cases. A mask is used to support the head and keep the patient still while the treatment is delivered. Once the mask is placed onto the patient's head and neck, it is attached to the table where the patient is lying on. It is easy to breathe through the mask, however, if you do not feel comfortable with the idea of wearing a mask you must communicate it to your medical team, they will make sure you overcome any stress you may have.

Chemotherapy*

Chemotherapy* aims to kill the tumour cells. Chemotherapy* for head and neck cancer is given through a vein, and therefore acts systemically* (through the blood circulation). Several drugs are active against head and neck cancers such as cisplatin*, paclitaxel*, docetaxel*, 5-Fluorouracil* (5-FU) and others. They may also be used in combination. Sometimes chemotherapy* is delivered concomitantly to radiation* therapy to potentiate the action of radiation*.

Biologic therapy*

Biologic therapy refers to the therapeutic use of substances that are specifically designed to interfere with the growth of cells.
Cetuximab* is a monoclonal antibody* which acts against epidermal growth factor receptor* (EGFR), a structure on the surface of all normal cells that helps them grow. Head and neck cancer carries a high amount of EGFR on the cell surface, and binding of cetuximab* to EGFR* interferes with the growth of tumour cells and causes them to die.

Treatment plan for stage I and II

The primary tumour is smaller than 4 cm in diameter. In larynx it could affect partially the vocal cords, but invasion of surrounding tissues is limited. Lymph nodes and distant organs present no sign of disease.*

In stages I and II, radiotherapy* or conservative surgery give similar results concerning local control of the tumour, even though no direct comparison of the efficacy of radiotherapy* versus surgery has ever been done. Modern radiotherapy* techniques, where real-time images and real-time modulation of beams to delineate the tumours are created, help the radiation* beams to be delivered more precisely to the tumour, avoiding as much as possible healthy tissues that surround the tumour.

Treatment plan for stage III and IV

The primary tumour is larger than 4 cm, invading surrounding tissues in a way that could compromise functionality for example paralyzing the vocal cords in larynx cancer. Other than that, there could be invasion of lymph nodes and/or distant organs.*

In general, a tumour could be considered operable or resectable when there is certainty that once the tumour is removed no cancerous cells are left behind, preserving the functionality of the organs affected and providing a good cosmetic result with or without reconstructive surgery. Some tumours could be affecting structures that could be technically very difficult to operate, so that the surgeon considers that the tumour is unresectable. Other tumours could be technically resectable, but the outcome might not be acceptable for the patient from an aesthetic* and functional point of view. For example a large tumour in the tongue, would not represent a big challenge technically for the surgeon, but the removal of the tongue might not be acceptable for the patient.

Treatment for advanced stages III and IV, when a tumour is considered resectable, include surgery often with reconstructive surgery plus radiotherapy* afterwards. When the margins of the tumour are positive (infiltrated by the tumour) or it spreads beyond the external lining of the lymph nodes* (extracapsular nodal spread*), postoperative chemoradiotherapy (radiotherapy* and chemotherapy* given concomitantly) with a single platinum-based* drug (cisplatin* or carboplatin*) is recommended.

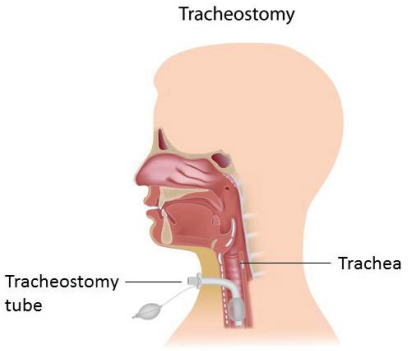
Weighing up the expected outcome considering the site affected by tumour, the extension of the disease, the patients' personal preferences amongst other factors help to make the choice between surgery and radiotherapy*. Alternatively to chemoradiotherapy, radiotherapy* administered concomitantly with cetuximab* could be chosen. In fact, although these two regimens have not been compared formally, it has been observed that radiotherapy* plus cetuximab* cause fewer side effects than chemoradiotherapy. However, the efficacy of these regimens in patients older than 65 years is still to be studied.

Administration of therapies before the local treatment with the purpose of reducing the size of the tumour and improve its curability with surgery or radiation* are called induction therapies. Chemotherapy* regimens using docetaxel* plus cisplatin* plus 5-Fluorouracil* are an option for induction therapy. To date there is no clear evidence that induction chemotherapy improves survival. It can be used within organ preservation protocols for some selected laryngeal and hypopharyngeal* cancers in order to avoid laryngectomy.

WHAT ARE THE POSSIBLE SIDE EFFECTS OF THE TREATMENTS?

Risks and side effects of surgery

Surgery aims to remove the tumour and a bit of the surrounding healthy tissue in an effort to make sure that no cancerous cells are left behind. Considering the structure and visibility of the organs affected, some functional and body image issues may arise depending on the tumour site.



Normal voice and speech may be affected temporarily or permanently. Other problems include shoulder weakness, difficulty chewing and swallowing, hearing loss, thyroid gland malfunction. A feeding tube may be required to maintain nutrition; this may be passed through the nose into the stomach or directly through the skin into the stomach. The complete removal of the larynx will need the creation of an opening (stoma) at the basis of the neck to allow normal breathing because there is no longer a connection between the nose and mouth and the trachea* (windpipe). A tracheostomy tube is placed in this opening to keep the stoma open. A tracheostomy tube requires special daily care and cleaning and the patient himself is responsible for it with appropriate training from doctors and nurses.

Depending on the location of the tumour removed some patients may experience facial disfigurement. Reconstructive surgery is offered to help appearance and maintain body functions.

Risks and side effects of radiotherapy*

Early complications

The area of the skin through which the radiation* beams pass could turn red, irritated and/or swollen; damage to salivary glands could result in dry mouth or thickened saliva. The lining of the mouth could be swollen, painful and sometimes ulcerated, this is called mucositis*. Radiation* can also affect the lingual buds and cause changes in taste. Oral infections, especially candidiasis (thrush) are another side effect of radiation* to the head and neck. Adequate pain control and maintenance of good oral hygiene are very important.

Late complications

Late side effects of radiotherapy* depend on the damage to the structures close to the area treated. Radiotherapy* can cause damage to the teeth and changes in blood supply to the jawbones, however it could be prevented with adequate dental treatment before starting the radiotherapy* sessions.

Swelling and/or scarring caused by radiotherapy* could lead to pain and swallowing problems, voice changes, changes in taste, and consequently loss of appetite.

Earwax build-up or ear canal scarring could cause hearing loss. Since the thyroid gland is located immediately in front of the neck, it can also be affected. In this case, it produces less thyroid hormones* and the patient could feel tired and sluggish. Blood tests for thyroid gland function should be monitored after the treatment with radiotherapy*.

During follow-up, the healthcare team will regularly assess for the presence of these complications.

Side effects of anticancer drugs

Cisplatin* and carboplatin* (Platinum-based* drugs)

Kidney damage is a side effect that will require adjustment of doses. Nerve damage may lead to blurred vision and hearing loss. Nausea and vomiting, electrolyte imbalance*, blood cells (red blood cells*, white blood cells* and platelets*) counts are also frequently affected.

Carboplatin* can cause hair thinning and hair loss. Although it is unlikely that the hair loss is complete, patients receive advice from the medical team to cope with it.

Docetaxel*

It sometimes causes fluid retention, temporary nail discoloration and an itchy skin rash. Some people also develop hand-foot syndrome (soreness of the palms of the hands and soles of the feet with tingling, numbness, pain, dryness and possibly peeling) or numbness and tingling in hands and feet alone, mucositis* and hair loss among others. About one in four patients will suffer from an allergic reaction during the first or second infusion with docetaxel*. This is why antihistamines* are given to patients prior to administration of docetaxel*.

5-Fluorouracil*

Severe side effects may occur in individuals who have the inborn condition dihydropyrimidine dehydrogenase (DPD) deficiency*: these individuals have low levels of the enzyme dihydropyrimidine dehydrogenase needed by the body to break down this drug.

Skin sensitivity to sunlight: sun exposure should be avoided for at least one year following completion of treatment.

Hand-foot syndrome (also called palmo-plantar erythema): the skin of palms and soles shows reddening and feels sore; the skin may peel. The syndrome is usually mild.

Damages to the heart and mucositis* are also important possible side effects of 5-Fluorouracil*.

Cetuximab*

Some well-known side effects associated to the use of cetuximab* are acne-like skin rash, fatigue, electrolyte imbalance* (low magnesium levels* in blood), inflammation of the skin surrounding a fingernail or toenail.

Although these are known side effects of chemotherapy*, there are interventions that may help prevent or treat these. Side effects will be regularly assessed and monitored by the multi-disciplinary team to ensure appropriate measures are put into place as early as possible.

Side effects of chemoradiation

The use of two approaches such as chemotherapy* and radiotherapy* concomitantly, increases the possibilities of side effects. The side effects of one are additional to the side effects of the other.

Psychological and social effects

All therapies used to treat head and neck cancer have also negative effects with a deep impact on psychological and social aspects. These could be perceived in higher or lower intensity according to the patient's personality and if he considers himself healthy or ill after the treatment.

Visible scars have an important impact compared to others. In the case of laryngectomies and their families the main trouble occurs due to voice loss. Here all the oral communications abilities, so necessary for the social relationships, must change along with the physical personal image. All changes due to a head and neck cancer produce some uncertainties and complexes. In most cases the anxiety for adjustment to a quite unknown new situation may be increased by doubts on the success of the treatment received. Thus inducing confusion, excess of disability, loss of self-esteem and withdrawal into oneself.

The social area of course is where most of the problems occur, but inside the family and workplace some problems are rising up as well.

About the family

Conflicts may occur within the core of the family as the patient is confronting a very challenging new situation and needs the support and attention of his family. Family members are also going through a difficult situation in which they do not know what the patient is expecting from them.
When the disease is lived as an obstacle to the usual family life, because too much attention is requested, the consequent issues are:

- Couple clashes
- Sexual relationship troubles
- Behavior changes

Therefore, three different family environments might be present only because of the disease, the family might strengthen their ties, sometimes pre-existing troubles could substantially worsen and sometimes things just follow their natural course and the family is able to continue with their lives as if nothing happened.

About the workplace

Becoming temporary or definitely disabled means the income lowering with a contemporary increase of medical expenses for medicines, necessary aids, prosthesis and so on. Consequently the social reintegration is not always so simple and feasible.

About the social relationships

Often the patient perceives attitude changes from old friends. The patient feels the marginalization due to insensitivity and, in case of laryngectomy, due to repulsion from most people. Overcoming this status needs the patient attitude to be changed, but contemporary the social attitude must change through awareness campaigns, dissemination of information about head and neck cancer and its implications.

WHAT HAPPENS AFTER THE TREATMENT?

It is not unusual to continue to experience treatment-related symptoms once the treatment is over.

- It is common that anxiety, fatigue, sleep problems or depression continue in the post-treatment phase; patients suffering from these symptoms may need psychological support.
- Poor memory and difficulty in concentrating are not uncommon side effects of chemotherapy* and are generally reversible within a few months.
- Other side effects of the treatment should be carefully treated as some of them would limit some body functions such as hearing, talking, dry mouth and even tasting food. Concerns about physical appearance could be a cause of stress and depression.

Follow-up with doctors

After the treatment has been completed, doctors will propose a follow-up aiming to:

- detect possible relapse
- evaluate adverse effects of the treatment and treat them
- provide psychological support and information to help patients return to normal life

Imaging tests and physical examination are important during follow-up of patients for potentially curable recurrence and to survey new tumours appearing. They are fundamental if there is any suspicion of recurrence.

CT scan* and MRI* are diagnostic tests that are frequently used to evaluate the results of the treatment given. Sometimes a diagnostic test called PET-CT* is used in addition to these procedures. PET-CT* uses a substance that contains glucose*; this is injected to the patient. This glucose-based substance is absorbed by any cancerous cells and shows as a 'hot spot' on the scan. Having a PET-CT* scan positive does not always mean that there is residual cancer, your doctor might ask for further tests to be sure, however when PET-CT* scan is negative there is, under certain circumstances, a high probability that there is no residual disease and no further examinations are needed.

The follow-up is also important to detect side effects of the treatment given to the patient, for example swallowing and breathing problems.

Chest X-ray may be included on a yearly basis. The evaluation of the function of the thyroid gland through a laboratory test is recommended at 1, 2 and 5 years, in patients whose neck received radiotherapy*.

Returning to normal life

It can be hard to live with the idea that the cancer can come back. From what is known today, no specific way of decreasing the risk of recurrence after finishing treatment can be recommended. As a consequence of the cancer itself and of the treatment, return to normal life may not be easy for some people.

It is necessary to stimulate the patient's desire to believe "that a future exists and that it can even be better than it was expected before the diagnosis".

Questions related to body-image, fatigue, work, emotions or lifestyle may be a concern to you. Some problems may emerge in case of a laryngectomy. In general work can be resumed but may require adaptation of the working environment in case of noisy, dusty, polluted, too cool or too hot environments, or when work involves lifting heavy weights. Outdoor activities may also be limited and swimming and extreme sport activities should usually no longer be practiced. Interpersonal relationships could also be challenging at the beginning for reasons such as the noise made by breathing, a possible smell of the stoma, not being properly heard while speaking or children staring at the stoma. In any case, discussing these questions with relatives, friends, other patients, nurses or doctors may be helpful. The experience of people who eventually got used to the new situation can provide an invaluable help to live a normal life. Support from patients organisations providing advice such as on managing effects of treatments, as well as psycho-oncology services, websites, or telephone info-lines are available in many countries.

What if the cancer comes back?

If the cancer comes back it is called recurrence. Treatment with chemotherapy* is the standard choice for the majority of patients. It can reduce the symptoms and improve quality of life. The first option could include a combination of cetuximab* with cisplatin* or carboplatin* and 5-Fluorouracil*. In patients for whom it is anticipated that a treatment with more than one drug will not be well-tolerated, weekly methotrexate* alone or cetuximab* alone could be offered. Both options have shown limited side effects and both can help to reduce symptoms.

In selected cases of localized recurrence, surgery (if operable) or re-irradiation can be considered.

DEFINITIONS OF DIFFICULT WORDS

5-Fluorouracil
A drug used to treat cancers of the breast, stomach, pancreas, and certain types of colorectal, head and neck cancers. It is also used in a cream to treat basal cell skin cancer and actinic keratosis (a skin condition that may become cancer). It is being studied in the treatment of other conditions and types of cancer. 5-Fluorouracil stops cells from making DNA and it may kill cancer cells. It is a type of antimetabolite. Also called 5-FU and fluorouracil.

Aesthetic
In this context, relating to beauty and physical appearance.

Anaesthesia
Reversible state of loss of awareness in which the patient feels no pain, has no normal reflexes, and responds less to stress, induced artificially by the employment of certain substances known as anaesthetics*. It can be complete or partial and allows patients to undergo surgery.

Anaesthetic
Substance that causes lack of feeling or awareness. It can be local (causing loss of feeling in a part of the body) and general (putting the person to sleep).

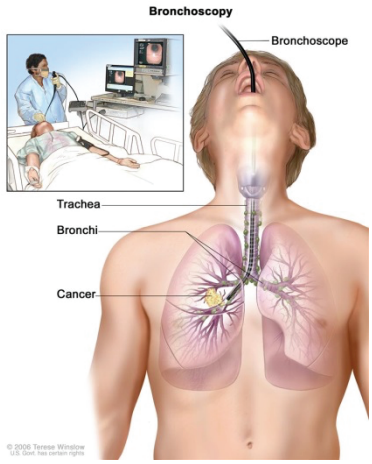
Antihistamine
A type of drug that blocks the action of histamine, which can cause fever, itching, sneezing, a runny nose, and watery eyes. Antihistamines are used to prevent fevers in patients receiving blood transfusions and to treat allergies, coughs, and colds.

Basaloid carcinoma of head and neck
Aggressive type of head and neck cancer that starts in cells that resemble basal cells (basaloid) in the epidermis. The epidermis or external layer of the skin has five layers of different types of cells; basal cells are in the deepest layer. But head and neck cancers do not include skin cancers, rather cancer of internal structures.

Biologic therapy
Treatment to stimulate or restore the ability of the immune system to fight cancer, infections, and other diseases. Also used to lessen certain side effects that may be caused by some cancer treatments. Also called immunotherapy, biotherapy, or biological response modifier (BRM) therapy.

Biopsy
The removal of cells or tissues for examination by a pathologist. The pathologist may study the tissue under a microscope or perform other tests on the cells or tissue. There are many different types of biopsy procedures. The most common types include: (1) incisional biopsy, in which only a sample of tissue is removed; (2) excisional biopsy, in which an entire lump or suspicious area is removed; and (3) needle biopsy, in which a sample of tissue or fluid is removed with a needle. When a wide needle is used, the procedure is called a core biopsy. When a thin needle is used, the procedure is called a fine-needle aspiration biopsy.

Bronchoscopy
A procedure that uses a bronchoscope to examine the inside of the trachea, bronchi (air passages that lead to the lungs), and lungs. A bronchoscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue to be checked under a microscope for signs of disease. The bronchoscope is inserted through the nose or mouth. Bronchoscopy may be used to detect cancer or to perform some treatment procedures.



Carboplatin
A drug that is used to treat advanced ovarian cancer that has never been treated or symptoms of ovarian cancer that has come back after treatment with other anticancer drugs. It is also used with other drugs to treat advanced, metastatic, or recurrent non-small cell lung cancer, and head and neck cancer. It continues to be studied in the treatment of other types of cancer. Carboplatin is a form of the anticancer drug cisplatin* and causes fewer side effects in patients. It attaches to DNA in cells and may kill cancer cells. It is a type of platinum compound.

Carotid artery
A major artery that carries blood from the heart to the head. There is a carotid artery on each side of the neck, and each one splits into two branches. The interior branch carries blood to the brain and eyes, and the exterior branch carries blood to the face, tongue, and outside parts of the head.

Cetuximab
A drug used to treat certain types of head and neck cancer, and a certain type of colorectal cancer that has spread to other parts of the body. It is also being studied in the treatment of other types of cancer. Cetuximab binds to a protein called epidermal growth factor receptor* (EGFR), which is on the surface of some types of cancer cells. This may stop cancer cells from growing. Cetuximab is a type of monoclonal antibody.

Chemotherapy
A type of cancer treatment using drugs that kill cancer cells and/or limit their growth. These drugs are usually administered to the patient by slow infusion into a vein but can also be administered orally, by direct infusion to the limb or by infusion to the liver, according to cancer location.

Cisplatin
A drug used to treat many types of cancer. Cisplatin contains the metal platinum. It kills cancer cells by damaging their DNA and stopping them from dividing. Cisplatin is a type of alkylating agent.

Computed tomography (CT scan)
A form of radiography in which body organs are scanned with X-rays and the results are synthesised by a computer to generate images of parts of the body. Also called CT scan.

Contraindication
Condition or symptom that prevents the administration of a given treatment or procedure to the patient. Contraindications are either absolute, meaning the treatment should never be given to patients with this condition or symptom, or relative, meaning that the risk can be outweighed by the benefits in some patients with this condition or symptom.

Dihydropyrimidine dehydrogenase (DPD) deficiency
Genetic disorder in which the enzyme DPD is decreased or absent. DPD deficiency can cause neurologic symptoms or be asymptomatic. DPD enzyme breaks down certain chemotherapy drugs, in its absence these drugs build up and patients can be severely affected by toxicity associated to them.

Docetaxel
Docetaxel belongs to the group of anticancer medicines known as the taxanes. Docetaxel blocks the ability of cells to destroy the internal 'skeleton' that allows them to divide and multiply. With the skeleton still in place, the cells cannot divide and they eventually die. Docetaxel also affects non-cancer cells such as blood cells, which can cause side effects.

Electrolyte imbalance
Electrolytes are minerals such as calcium, potassium and sodium. They are present in the blood, body fluids and urine. They are ingested with food, drinks, and medicines and supplements. Electrolytes play an important role keeping the normal functioning of the body, so that they should be kept in an even balance. Their diminished or excessive ingestion, or diminished or excessive elimination from the body cause electrolyte imbalance and consequently malfunctioning of the body.

Endoscopy
A medical procedure where a doctor puts a tube-like instrument into the body to look inside. There are many types of endoscopy, each of which is designed for looking at a certain part of the body.

Epidermal growth factor receptor (EGFR)
The protein found on the surface of some cells and to which epidermal growth factor binds, causing the cells to divide. It is found at abnormally high levels on the surface of many types of cancer cells, so these cells may divide excessively in the presence of epidermal growth factor. Also called EGFR, ErbB1, and HER1.

Erythroplakia
An abnormal patch of red tissue that forms on mucous membranes in the mouth and may become cancer. Tobacco (smoking and chewing) and alcohol may increase the risk of erythroplakia.

External radiotherapy
External radiotherapy aims high-energy X-ray beams, electrons or particle beams, such as protons, at the cancer from outside the body, and is given as a series of short and daily treatments. External radiotherapy can be administered after surgery, or before surgery with the intent of reducing the size of the tumor to make its surgical removal easier. It can also be used alone (without surgery) as the main treatment for cancer, or to relieve symptoms caused by metastases or massive tumors.

Extracapsular nodal spread
Infiltration of cancer cells beyond the capsule (outer tissue layer that surrounds the lymph nodes) of the metastatic lymph node.

Eye adnexa
Accessory visual structures such as the eyelids, lacrimal apparatus and orbital tissue.

Gastro-esophageal reflux disease
The backward flow of stomach acid contents into the oesophagus (the tube that connects the mouth to the stomach). Also called oesophageal reflux, gastric reflux or acid reflux.

Glucose
Glucose is a monosaccharide sugar that occurs widely in plant and animal tissue. It is the major energy source of the body.

Histologic(al) type
The category in which a tumour is grouped, considering the characteristics of its cells and other structures under the microscope.

Histopathology
The examination and study of tissue and cells using a microscope. Tissue obtained from the body by biopsy or surgery is placed in a fixative and transported to the laboratory. Here, it is cut into thin sections, stained with various dyes and then studied under the microscope. A histopathologist is a doctor interpreting sections of tissue including tumour tissue.

HPV (Human Papilloma Virus)
The HPV represents a family of viruses that cause local skin or mucosal infection. There are two subgroups of HPV types infecting the genital tract, the low-risk types causing warts in the genital areas and the high-risk types causing cancers of the cervix, vagina, vulva, and anus in women, and cancers of the penis and anus in men.

Hypopharynx/hypopharyngeal
The bottom part of the throat. Cancer of the hypopharynx is also known as hypopharyngeal cancer.

Laryngoscopy (direct/indirect mirror)
Examination of the larynx (voice box) with a mirror (indirect laryngoscopy) or with a laryngoscope (direct laryngoscopy).

Leukoplakia
An abnormal patch of white tissue that forms on mucous membranes in the mouth and other areas of the body. It may become cancer. Tobacco (smoking and chewing) and alcohol may increase the risk of leukoplakia in the mouth.

Lymph nodes
A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Lymph nodes filter lymph and they store lymphocytes. They are located along lymphatic vessels. Also called lymph gland.

Lymph vessel
A thin tube that carries lymph (lymphatic fluid) and white blood cells through the lymphatic system. Also called lymphatic vessel.

Magnesium level
Concentration of the mineral magnesium in blood, measured through a laboratory test. Magnesium is a mineral used by the body to help maintain muscles, nerves, and bones. It is also used in energy metabolism and protein synthesis.

Magnetic Resonance Imaging (MRI)
An imaging technique that is used in medicine. It uses magnetic resonance. Sometimes a fluid is injected that enhances the contrast between different tissues to make structures more clearly visible.

Mediastinum
The area between the lungs. The organs in this area include the heart and its large blood vessels, the trachea, the oesophagus, the thymus, and lymph nodes but not the lungs.

Metastasis
The spread of cancer from one part of the body to another. A tumour formed by cells that have spread is called a metastatic tumour or a metastasis. The metastatic tumour contains cells that are like those in the original tumour.

Methotrexate
A drug used to treat some types of cancer, rheumatoid arthritis, and severe skin conditions, such as psoriasis. Methotrexate stops cells from making DNA and may kill cancer cells. It is a type of antimetabolite. Also called amethopterin, MTX, and Rheumatrex.

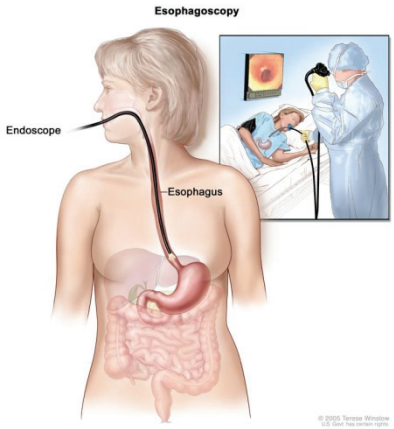
Monoclonal antibody
Monoclonal antibodies are antibodies that are exactly the same because they are produced by clones of the same parent cell.

Mucositis
Inflammation of the lining of the digestive system. Often seen as sores in the mouth.

Multidisciplinary opinion
A treatment planning approach in which a number of doctors who are experts in different specialties (disciplines) review and discuss the medical condition and treatment options of a patient. In cancer treatment, a multidisciplinary opinion may include that of a medical oncologist (who provides cancer treatment with drugs), a surgical oncologist (who provides cancer treatment with surgery), and a radiation oncologist (who provides cancer treatment with radiation). Also called tumour board review.

Nasopharynx/ Nasopharyngeal
The upper part of the throat behind the nose. An opening on each side of the nasopharynx leads into the ear.

Oesophagoscopy
Examination of the esophagus using an oesophagoscope. An oesophagoscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue to be checked under a microscope for signs of disease.



Oropharynx
The part of the throat at the back of the mouth behind the oral cavity. It includes the back third of the tongue, the soft palate, the side and back walls of the throat, and the tonsils.

Paclitaxel
A drug used to treat breast cancer, ovarian cancer, and AIDS-related Kaposi sarcoma. It is also used together with another drug to treat non-small cell lung cancer. Paclitaxel is also being studied in the treatment of other types of cancer. It blocks cell growth by stopping cell division and may kill cancer cells. It is a type of antimitotic agent. Also called Taxol.

Panendoscopy
Panendoscopy of head and neck is the combined examination of the nose, mouth, throat and upper part of the airways (trachea and bronchi). It is performed using a lightened flexible tube to visualize properly those parts of the body. A biopsy of any suspicious areas can be done during this procedure.

Papillary carcinoma/Papillary squamous carcinoma of head and neck
Subtype of cancer of head and neck. It is a variant of squamous cell carcinoma. Its name (papillary) refers to the pattern of its growth, it has nipple-shaped protuberances or papillae. This subtype of cancer has good prognosis.

PET-CT
A procedure in which a small amount of radioactive glucose (sugar) is injected into a vein, and a scanner is used to make detailed, computerized pictures of areas inside the body where the glucose is used. Because cancer cells often use more glucose than normal cells, the pictures can be used to find cancer cells in the body. Also called positron emission tomography scan.

Platelet
Small cell fragments that play a fundamental role in the formation of blood clots. Patients with a low platelet count are at risk of severe bleeding. Patients with a high count are at risk of thrombosis, the formation of blood clots that can block blood vessels and result in stroke or other severe conditions, and can also be at risk of severe bleeding because of platelet dysfunction.

Platinum-based drug/therapy
Treatment that uses drugs that are derived from the element platinum. It includes cisplatin, carboplatin and oxaliplatin.

Prognosis.
The likely outcome or course of a disease; the chance of recovery or recurrence.

Radiation
Can be defined as energy travelling through space. Examples of radiation include UV, and x-rays, which are commonly used in medicine.

Radiotherapy
A therapy in which radiation is used in the treatment of cancer always oriented to the specific area of the cancer.

Red blood cell
The most common type of blood cell. It is the substance that makes the blood appear red. The main function is the transport of oxygen.

Risk factor
Something that increases the chance of developing a disease. Some examples of risk factors for cancer are age, a family history of certain cancers, use of tobacco products, being exposed to radiation or certain chemicals, infection with certain viruses or bacteria, and certain genetic changes.

Spindle cell carcinoma
A type of tumour that contains cells called spindle cells, based on their shape. Under a microscope, spindle cells look long and slender. Spindle cell tumours may be sarcomas or carcinomas. Spindle cell carcinomas begin in the skin or in tissues that line or cover internal organs whereas spindle cell sarcomas begin in the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissues.

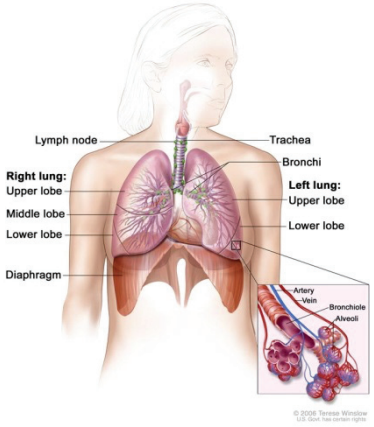
Squamous cell carcinoma
Cancer that begins in squamous cells. Squamous cells are thin, flat cells that look like fish scales, and are found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body, and the lining of the respiratory and digestive tracts. Most cancers of the anus, cervix, head and neck, and vagina are squamous cell carcinomas. Also called epidermoid carcinoma.

Systemic therapy
Treatment using substances that travel through the bloodstream, reaching and affecting cells all over the body. Chemotherapy and immunotherapy are examples of systemic therapy.

Targeted therapy
A type of treatment that uses drugs or other substances, such as monoclonal antibodies, to identify and attack specific cancer cells. Targeted therapy may have fewer side effects than other types of cancer treatments.

Thyroid hormone
A hormone that affects heart rate, blood pressure, body temperature, and weight. Thyroid hormone is made by the thyroid gland and can also be made in the laboratory.

Trachea
The airway that leads from the larynx (voice box) to the bronchi (large airways that lead to the lungs). Also called windpipe.



Verrucous carcinoma
A rare variant of squamous cell carcinoma, which is a low-grade malignancy unlikely to present with distant metastasis.

White blood cell
Cells of the immune system that are involved in the body's defence against infections.

X ray
X-rays are a form of radiation used to take images of the inside of objects. In medicine, X-rays are commonly used to take images of the inside of the body.

Yerba maté
A plant that is used to make a warm beverage (infusion) called maté. Maté is traditionally consumed in many countries of South America and in some Arabic countries.

The ESMO / Anticancer Fund 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. These guides are produced by the Anticancer Fund in close collaboration with the ESMO Guidelines Working Group and the ESMO Cancer Patient Working Group.

For more information please visit www.esmo.org and anticancerfund.org

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