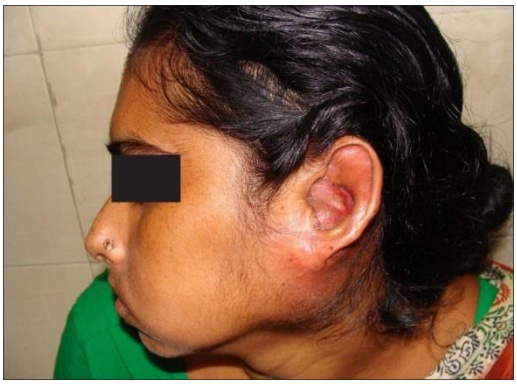
Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet
on
Adenoid Cystic Carcinoma

Introduction

Adenoid cystic carcinoma (ACC) is a rare type of cancer that can exist in many different body sites. It most often occurs in the areas of the head and neck, in particular the salivary glands; but has also been reported in the breast, lacrimal gland of the eye, lung, brain Bartholin gland, trachea and the paranasal sinuses. It is also known as adenocyst, malignant cylindroma, adenocystic, Adenocystic Carcinoma, Cribriform Carcinoma, Cylindroma, ACC or AdCC.



[Picture Credit: Adenoid Cystic Carcinoma – Salivary Gland]

It is the third most common malignant salivary gland tumour overall (after mucoepidermoid carcinoma and polymorphous low grade adenocarcinoma). It represents 28% of malignant submandibular gland tumours, making it the single most common malignant salivary gland tumour. Patients may survive for years with metastases because this tumour is generally well-differentiated and slow growing. In a 1999 study of a cohort of 160 ACC patients, disease specific survival was 89% at 5 years but only 40% at 15 years, reflecting deaths from late-occurring metastatic disease.
(Wikipedia; WebMD).

Signs and Symptoms of Adenoid Cystic Carcinoma (ACC)

ACC tumours are characterised by a distinctive pattern in which abnormal "nests" or cords of certain cells (epithelial cells) surround and/or infiltrate ducts or glandular structures within the affected organ. These structures are typically filled with a mucous-like material or contain abnormal fibrous membranes (hyaline membranes). Such characteristics are apparent during microscopic evaluation of the tumour cells. ACC is considered a low-grade malignancy that has a history of slow growth, but tends to be aggressively invasive and to infiltrate nearby lymph nodes as well as the "sheaths" or coatings surrounding nerve fibres (perineural spaces). This form of cancer may have a tendency to recur later at the site where it first developed (local recurrence) and to spread to distant bodily sites, particularly the lungs, potentially resulting in life-threatening complications.
(WebMD).

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People with ACC may experience the following symptoms or signs. Sometimes, people with ACC do not show any of these symptoms. Or, these symptoms may be caused by a medical condition that is not cancer.

The initial symptoms of ACC depend on the location of the tumour. Early lesions of the salivary glands may appear as painless, usually slow-growing masses underneath the normal lining of the mouth or skin of the face. Because there are many salivary glands under the mucosal lining of the mouth, throat, and sinuses, lumps in these locations could be from this type of tumour. Other symptoms may include:

- A lump on the palate, under the tongue, or in the bottom of the mouth
- An abnormal area on the lining of the mouth
- Numbness of the upper jaw, palate, face, or tongue
- Difficulty swallowing
- Hoarseness
- Dull pain
- A bump or nodule in front of the ear or underneath the jaw
- Paralysis of a facial nerve

If concerned about one or more of the symptoms or signs on this list, please talk with a doctor.

If cancer is diagnosed, relieving symptoms remains an important part of cancer care and treatment. This may also be called symptom management, palliative care, or supportive care. Be sure to talk with the health care team about symptoms that are experienced, including any new symptoms or a change in symptoms.
(Cancer.Net).

Incidence of Adenoid Cystic Carcinoma (ACC) in South Africa
The National Cancer Registry (2013) does not provide information on the incidence of ACC. It only provides information regarding Cancer of the Salivary Gland.

According to the National Cancer Registry (2013) the following number of salivary gland cancer cases was histologically diagnosed in South Africa during 2013:

Group - Males 2013	No of Cases Reported	Estimated Lifetime Risk	Percentage of All Cancers
All males	94	1:1 691	0,26%
Asian males	3	1:2 019	0,37%
Black males	46	1:2 306	0,43%
Coloured males	9	1:2 219	0,22%
White males	35	1:842	0,17%

Group - Females 2013	No of Cases Reported	Estimated Lifetime Risk	Percentage of All Cancers
All females	82	1:3 087	0,22%
Asian females	4	1: 298	0,40%
Black females	43	1:3 957	0,27%
Coloured females	9	1:4 741	0,23%
White females	26	1:1 484	0,16%

The frequency of histologically diagnosed cases of salivary gland cancer in South Africa for 2013 was as follows (National Cancer Registry, 2013):

Group - Males 2013	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	2	4	6	13	22	25	18	4
Asian males	0	0	0	0	0	2	1	0
Black males	1	1	5	8	14	10	6	1
Coloured males	1	0	0	3	1	3	1	0
White males	0	1	2	3	4	16	14	6

Group - Females 2013	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	5	9	9	13	11	12	16	5
Asian females	0	2	0	0	1	0	1	0
Black females	2	4	7	9	3	4	8	2
Coloured females	1	2	1	0	1	1	2	1
White females	2	1	1	2	6	7	4	2

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.

Treatment of Adenoid Cystic Carcinoma (ACC)

The most common treatment protocol and "gold standard" for treating initial ACC tumours is surgical resection with follow-up radiation.

In a fairly large number of cases these two standard treatments do stop the cancer and the patient has no recurrence in their life time. After the surgical removal of a tumour, the tumour sample is reviewed in a laboratory by a pathologist, and they report back that "negative" or clean margins were achieved; meaning all of the observable cancer was removed. If residual cancer is still in the surgical area, the pathologist will report "positive" margins. In learning to understand medical terms, this is one case when "positive" is bad and "negative" is good.

Follow-up radiation treatment for any residual tumour left in the surgical area is the most common recommendation for treatment, with some oncologists recommending follow up radiation even with clean margins due to the tendency of ACC for invisible, microscopic spread.

Because of the of high number of initial cases in the head and neck region, some patients have tumours that are not able to be surgically removed without causing major damage to critical areas, and radiation treatment is the only alternative and recommended choice for treating these unresectable tumours. Post-surgery radiation is always a very important treatment to consider and it is recommended to research the options and gather input from physicians who are familiar with ACC.

In the last 10 years a variety of new, more precise, targeted, computer driven radiation systems have become available and are relatively widely available. Treatment choices and decisions for both primary and metastatic tumours can be varied and complex when taking into account the tumour size, location, number of tumours, adjoining critical organs, infiltration, recommendations from physicians, available treatment centres, financial and insurance resources, and the knowledge and comfort level for the patient.

For years some patients have tried a large variety of chemotherapy or targeted drug treatments by themselves or as part of clinical trials, but no single chemotherapy or drug combination has shown itself to be effective for more than a few patients.
(Adenoid Cystic Carcinoma Organization International).

Staging of Adenoid Cystic Carcinoma
The staging of this condition depends on which excretory cells are involved and where in the body the disease is present.

Questions that One Should Ask Oneself When Reading or Studying Various Cancer Research Reports
Many people with cancer look for information about treatments for themselves. Many people use the internet to try to find out about new treatments. Cancer research is going on all over the world. It is important to understand that a single research paper in isolation will not give one the whole picture about research into a particular type of cancer. It needs to be read in the context of all the other relevant research.

Each time a new treatment makes it through all the stages of research and clinical trials, it will have a large number of published research papers about it. Some of these papers will show it to be a useful new treatment that may contribute to slowing down, or curing a cancer. But there are likely to be one or two papers that show that it did not work better than the existing treatment it was compared to.

The results that seem to contradict the other research papers may have happened by chance. Or there may have been problems with the patient group that was selected. Or there may have been difficulties with giving the treatment.

What doctors and researchers are looking for is evidence that, on balance, the treatment is an improvement when compared to existing treatments. Sometimes statisticians gather together all the results of all the trials and do a meta analysis. This is a process that compares the results of all the relevant trials to give a broader picture. It gives a clearer idea than a single research paper of whether a treatment is helpful or not.

Here are a few questions one might ask

- What type of cancer is being investigated?
- What stage of cancer did the individuals in the study have?
- Is the treatment for early stage or advanced cancer?
- Is the treatment being studied used in combination with another treatment?
- How many patients were involved in the study? The bigger the numbers, the more likely the results are accurate. The fewer there are, the more likely the results happened by chance. The most accurate studies use thousands of people, often in many different countries

- When looking at the results of a clinical trial, what was the aim of the trial? Phase 3 clinical trials compare a new treatment with the current standard treatment. Earlier phase trials look more at things such as what happens to the drug inside the body and what the side effects are

- Was it a controlled trial? This means the treatment was compared with standard treatment (which might be no treatment). Patients were allocated one or other treatment at random to prevent bias. For example, a treatment may seem better because the doctors used it for all the healthier patients and gave the other treatment to all the patients who were more ill

- How much did the new treatment help? Sometimes a new treatment seems really promising when one reads the reports. But when one looks in more detail, people only lived a few weeks longer

- Did the trial look at the people's quality of life? For a treatment to be useful, the benefits need to outweigh any inconvenience or side effects. If the side effects are too severe, quality of life could be made worse than it would be without the treatment. This is especially important if the treatment is only going to slow down or shrink the cancer for a while

- Who carried out the research? Is it a reputable, well known organisation? The quality of research can vary a great deal

- Where was the study reported? Was it in a well known and respected journal? Check with an informed health professional if not sure

(Cancer Research UK).

About Clinical Trials

Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

Types of Clinical Trials

Cancer clinical trials differ according to their primary purpose. They include the following types:

Treatment - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

Prevention - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of

developing a specific type of cancer. Some cancer prevention trials involve people who have had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer

Screening - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

Diagnostic - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

Quality of life or supportive care - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.

Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In these regulations and policies, people who participate in research are usually referred to as "human subjects."

Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different "phase" in the clinical research process. The following phases are used for cancer treatment trials:

Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

Phase I (also called phase 1). These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

Phase II (also called phase 2). These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or “trial arms”: (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.

In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.

Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

Use of Placebos

The use of placebos as comparison or "control" interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often, however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

Possible benefits of taking part in a clinical trial

The benefits of participating in a clinical trial include the following:

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

Potential harms associated with taking part in a clinical trial

The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

Correlative research studies, and how they are related to clinical trials

In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as 'biospecimens') obtained from trial participants before, during, or after treatment.

For example, the molecular characteristics of tumour specimens collected during a trial might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.

Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

When a clinical trial is over

After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical importance and, if so, whether the tested intervention could become the new standard of care.

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care.
(National Cancer Institute).

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 condition or situation. Readers of this document should seek appropriate medical advice prior to taking or refraining from taking any action resulting from the contents of this Fact Sheet. As far as permissible by South African law, the Cancer Association of South Africa (CASNA) accepts no responsibility or liability to any person (or his/her dependants/estate/heirs) as a result of using any information contained in this Fact Sheet.

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Sources and References

Adenoid Cystic Carcinoma Organization International
http://www.accoi.org/faq/what-acc/

Adenoid Cystic Carcinoma – Salivary Gland
http://www.indianjotol.org/article.asp?issn=0971-7749;year=2011;volume=17;issue=2;spage=66;epage=70;aulast=Saha

Cancer.Net
http://www.cancer.net/cancer-types/adenoid-cystic-carcinoma/symptoms-and-signs

Cancer Research UK
http://www.cancerresearchuk.org/about-cancer/what-is-cancer/understanding-statistics-in-cancer-research#tests
http://www.cancerresearchuk.org/about-cancer/what-is-cancer/understanding-statistics-in-cancer-research

National Cancer Institute
http://www.cancer.gov/about-cancer/treatment/clinical-trials/what-are-trials

WebMD
http://www.webmd.com/cancer/adenoid-cystic-carcinoma

Wikipedia
https://en.wikipedia.org/wiki/Adenoid_cystic_carcinoma