ACC SUPPORT UK

ADRENOCORTICAL CANCER SUPPORT AND INFORMATION

ADRENOCORTICAL CARCINOMA – ACC

PATIENT INFORMATION FOR ADULT PATIENTS

CONTENTS

"It is never easy to accept that you have cancer. A rare one, I think, makes it even more difficult" ACC patient

Being diagnosed with a rare cancer like ACC can be isolating and frustrating. It might be hard to find a medical specialist that can help or anyone else who has been through the same as you. You might not be able to find information to help inform you of what to do or where to go. This booklet has been produced to help answer some of the questions that you may have about your condition.

If you require further information or support please do not hesitate to call or email ACC Support UK (www.accsupport.org.uk). Further details of this and other useful organisations can be found at the end of this booklet.

WHAT IS CANCER?

The body is made up of hundreds of millions of living cells. Normal body cells grow, divide, and die in an orderly way. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn out, damaged, or dying cells.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of this out-of-control growth of abnormal cells. Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells keep on growing and form new cancer cells. These cancer cells can grow into (invade) other tissues, something that normal cells cannot do. Being able to grow out of control and invade other tissues is what makes a cell a cancer cell. Carcinoma is a term used to describe tumours that are cancerous and malignant (having the ability to spread and invade other tissue).

In most cases the cancer cells form a tumour. But some cancers, like leukaemia, rarely form tumours. Instead, these cancer cells are in the blood and bone marrow. Tumours can be benign or malignant. In this booklet 'tumour' refers to a malignant ACC. When cancer cells get into the bloodstream or lymph vessels, they can travel to other parts of the body. There they begin to grow and form new tumours that replace normal tissue. This process is called metastasis.

No matter where a cancer may spread, it is always named for the place where it started. For instance, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is called metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their own kind of cancer. This booklet is looking at Adrenocortical Carcinoma (ACC): what it is, and how it is diagnosed and treated.

WHAT IS ACC?

There are several different types of tumours that can occur in the adrenal gland. They can develop in either the outer part of the gland (the cortex) or the inner part of the gland (the medulla). Tumours can be benign (not cancer) or malignant (cancer).

Benign tumours of the cortex are called adrenocortical adenomas, and malignant tumours are called adrenocortical carcinomas (ACC).

Adrenocortical carcinoma (ACC) is often know simply as adrenal cancer and affects 1-2 people per million per year, making it a rare form of cancer.

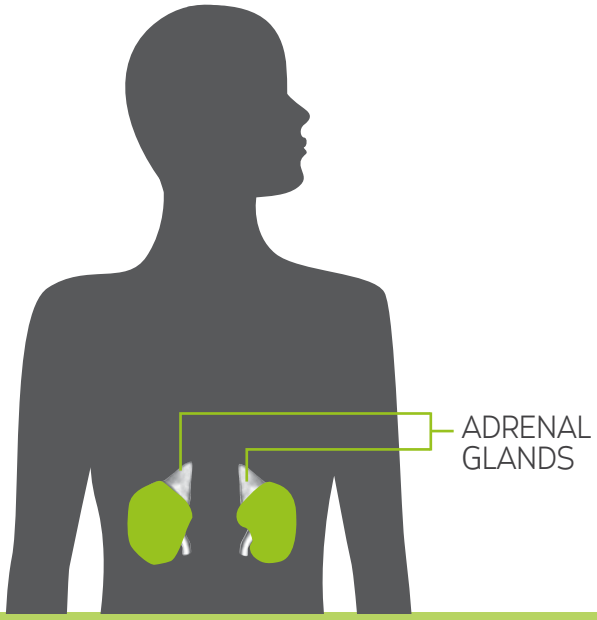
ACC in adults tends to occur in the 4th to the 5th decade of life. Most ACC's occur sporadically (meaning that they do not run in families), but they may sometimes be part of a congenital (present at birth) and/or familial (have a genetic family connection) condition.

WHAT ARE THE ADRENAL GLANDS?

The body has two walnut-sized adrenal glands, one above each of the kidneys ('ad-renal' means 'next to the kidney'). Even though the glands are small they are important as they produce several hormones (the body's chemical messengers) that are important for life.

The adrenal medulla (the inner area of the adrenal gland) produces a number of hormones called catecholamines, mainly adrenaline and noradrenaline. These hormones help the body to maintain blood pressure and deal with sudden stress or threats.

The adrenal cortex (outer area of the gland) produces hormones called steroids, mainly cortisol (also known as glucocorticoid) and aldosterone (also known as mineralocorticoid). These steroids, help the body to maintain blood pressure as well as salt and sugar levels. Cortisol is also an important messenger in our bodies' response to stress and illness.



WHAT ARE THE SYMPTOMS OF ACC?

Adrenocortical carcinomas (ACCs) are usually found because of the symptoms they cause but sometimes they are also discovered by chance if patients undergo a scan arranged for other reasons. ACCs may make higher than normal amounts of cortisol and aldosterone and may also secrete hormones that a healthy adrenal would not produce, such as the male hormone testosterone and the female hormone oestradiol, causing symptoms and even body changes. Some ACCs get very large and although these don't usually produce active hormones (are non-functioning), they may cause symptoms by pressing on other organs.

There are 2 types of ACC:

HORMONE SECRETING

This is when the tumour produces extra quantities of steroid hormones in addition to those already produced by the normal adrenal gland cells.

High levels of these hormones cause symptoms that may include:

- diabetes
- high blood pressure
- sexual dysfunction,
- muscle weakness and wasting,
- weight gain,
- excess facial or body hair in women
- baldness in women
- deepening of the voice in women
- soreness and increase of the size of the breasts in men
- easy bruising,

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- acne,
- early puberty in children,
- osteoporosis,
- reduced immunity (impaired response to infections),
- change in body shape
- mood changes.

NON-FUNCTIONING

These tumours are likely to be found when symptoms occur due to the size of the tumour. Symptoms might include pain or swelling, weight loss or signs that the disease has spread outside of the adrenal gland. They do not produce the symptoms of high hormone levels, although sometimes these hormones are found in the blood or urine. Sometimes tumours are found by chance, for example, during a scan while investigating something unrelated. These tumours are described as 'incidental'. Most adrenal nodules discovered by chance are harmless but larger tumours (usually more than 4cm) need careful checking for cancer.

WHAT CAUSES ACC?

Scientists do not know exactly what causes most adrenocortical carcinomas. Over the past few years, they have made great progress in learning how certain changes in a person's DNA can cause cells in the adrenal gland to become cancer. DNA carries the instructions for nearly all the things our cells do. We often look like our parents because they are the source of our DNA. But DNA affects more than the way we look. DNA changes play a part in our risk for getting certain diseases including some types of cancer. Adrenal tumours are common, but ACCs are not.

Most DNA changes that are seen in cancers happen during life rather than having been inherited. These changes may be caused by exposure to radiation, lifestyle or cancer-causing chemicals. But many of these changes happen for no known reason.

A risk factor is anything that increases a person's chance of getting a disease.

Different cancers have different risk factors. Some risk factors, such as smoking, can be controlled. Others, like a person's age or race, can't be changed. But scientists have found a few risk factors that make a person more likely to get adrenal cancer. Even if a person does have one or more risk factors for adrenal gland tumours, we can't know for sure how large a part they played in causing the cancer.

Family history: Most ACCs do not run in families; however, a number of rare conditions can increase the risk of ACC. Therefore, if an individual with ACC has other members of the family diagnosed with cancer aged 50 years or less, they should ask for referral to their Regional Genetics Service.

HOW IS ACC FOUND?

Very often, ACC tumours are not found until they have grown quite large. This is different for children since they react more to the hormones these tumours make. Sometimes ACC may be found earlier by coincidence when undergoing tests or scans for other unrelated health problems Usually, ACC is found due to the symptoms caused by either the hormones they make or because the tumour has grown large.

WHAT TESTS ARE NEEDED?

These days, the first imaging test to be used is likely to be a CT scan. Other tests may be used to find out more about the size and spread of the tumour to nearby structures such as lymph nodes or to distant areas such as the liver and lungs. These tests enable doctors to determine the 'stage' of the disease, i.e. how advanced it is, and to plan the right treatment or combination of treatments. Not all the tests described need to be performed in every patient. Biochemical tests of urine and blood are also essential to look for hormones that the tumour may be making.

Imaging tests (scans) are ways to take pictures of the inside of your body. One or more of these tests may be done if the doctor thinks you may have an ACC.

CT scans (computed tomography): A CT scan uses x-rays to make detailed pictures of your insides. Instead of taking just one x-ray, the doughnut-shaped CT scanner takes many pictures as it moves around you. A computer then combines these into a picture of a slice of your body. CT scans can show the adrenal glands and can often confirm whether a tumour is present, how large it is, and whether it has spread to nearby sites. CT scans also show the organs near the adrenal glands, as well as lymph nodes and distant organs. This test can

help show if the cancer has spread to the liver or other organs. Before any pictures are taken, or after the first scan, you may also have an IV (intravenous) line put into your arm through which a contrast dye can be given. This helps the outline structures in your body look clearer. The contrast dye can cause some redness and a warm feeling that may last hours to days. A few people are allergic to the dye. Rarely, more serious reactions like breathing problems and low blood pressure can happen. Medicine can be given to prevent and treat these problems. Be sure to tell the doctor if you have ever had a reaction to any contrast substance used for CT scans before. CT scans take longer than regular x-rays and you need to lie still on a table while they are being done.

PET scan (positron emission tomography): For a PET scan, a type of radioactive sugar is injected into your vein. The sugar collects in cancer cells and shows up in the pictures. This test is useful for finding ACC that has spread outside of the adrenal glands.

MRI (magnetic resonance imaging): MRI scans use radio waves and strong magnets to take pictures. The MRI sometimes gives similar information to a CT scan but may be more helpful because it can show views from different angles. In long term follow-up MRI may be used to avoid the repeated exposure to radiation from a CT scan. An MRI scan can take up to an hour to perform. Due to the tube-like shape of the MRI scanner, you might feel quite confined during your scan. If you have problems with tight spaces, tell the doctor before your MRI is set up; you may be able to have the test done using a less confined open MRI scanner. The machine makes loud thumping and clicking noises during the scan as the magnet switches on and off. You will be given earplugs or headphones, sometimes with music, to help block this out.

Chest x-ray: This can show if the cancer has spread to the lungs. This is also often performed to check on your general health status before an operation.

Ultrasound: This test uses sound waves to make pictures of organs inside your body. A computer shows the picture on a screen. This test can show if there is a tumour in the adrenal gland or liver. This would not be the first choice of test as a CT scan would be preferable.

Blood and urine tests:

If there is a suspicion that the tumour is making increased quantities of hormones, then this can be measured in the bloodstream and/or in a urine collection as part of an initial hormonal evaluation. Some hormone tests are done after patients have taken a synthetic steroid tablet called dexamethasone. It may also be possible to measure hormones that do not cause any effect on the body. All of these tests are equally useful after surgery to check that all of the tumour has been removed and, later on, to see if there is any evidence of the tumour returning (follow-up screening). In addition, it may be necessary to do more common blood tests to assess your general level of health.

Other tests:

Biopsy: A biopsy is when a sample of tissue is removed with a fine needle to see whether cancer cells are in it (Fine Needle Aspiration or FNA). FNA should NOT be performed in suspected cases of ACC since it usually does not obtain enough tissue to distinguish the difference between cancer and non-cancerous growths. In addition, it is important that the tumour remains intact and piercing it by a biopsy may lead to tumour spread.

STAGING OF ACC

Doctors use 'staging' to describe the extent of disease. The 'stage' of disease guides the doctors when planning treatment and also gives an idea of likely long term survival. Staging is done using the results of imaging tests together with further information obtained after surgery. It is vital that the staging tests are carried out so that the right treatment option can be offered to you. The stage of ACC depends upon the size of the tumour and how far it may have spread. If you want to know more about how your cancer is staged, please talk to your nurse or doctor.

TREATING ACC

For ACC, the treatment that offers the best chance of a cure is timely surgery by a specialist surgeon. This can be achieved if the tumour is localised (just in one place). Follow-up is essential however even if 'curative surgery' is thought to have been achieved. Even after complete removal the tumour can recur, and your doctor would want to ensure that he/she caught any recurrence in good time. Unfortunately, ACCs can be quite fast growing. They are often diagnosed in the later stages (when they are quite advanced) and this means it can be difficult to cure them. Nevertheless, even if surgery cannot remove all of the tumour, it may sometimes be helpful to reduce the volume to allow other treatments to be used or surgery can be a useful option after other drug treatment has helped to shrink the tumour.

ACCs are rare and treatment should be carried out by specialist teams. Specialist centres that offer surgery and other therapies for adrenal cancer will have a 'multidisciplinary team' that meet regularly to discuss ACCs. Nowadays, all decisions about surgery and other treatments should be taken by a team including a number of doctors of different specialities rather than one individual. You should make sure that you have been referred to a multidisciplinary team experienced in caring for patients with ACC and other adrenal tumours. See the section on Multidisciplinary Teams.

Your doctor may suggest:

- Surgery
- Radiotherapy
- Chemotherapy
- Mitotane
- Combination treatments
- Clinical Trials

SURGERY

If your cancer is diagnosed early enough, surgery to remove the cancer and the adrenal gland is the first choice of treatment and can cure the cancer. This operation is called an adrenalectomy. If your surgeon thinks the cancer may have spread locally, they will remove the tissues immediately surrounding the adrenal gland together with nearby lymph nodes. When tumours are large they may have grown into surrounding structures such as the liver or kidney. In these cases surgery may still be possible but the operation will be larger. Even when the tumour has spread (metastasised) to other organs, it may still be appropriate to remove the initial tumour first and then remove or treat other metastases later. If you need to have one of your adrenal glands removed, your other gland will carry on making all the hormones you need. If you have both adrenal glands removed, you will have to take hormone replacement tablets every day for the rest of your life.

SURGICAL APPROACHES

The procedure your surgeon will use will depend on the type and size of the tumour and also your individual needs. There are different surgical approaches that can be performed to remove malignant ACCs.

Open adrenalectomy

Most frequently, surgeons will make either a horizontal, diagonal or vertical cut to open the tummy, to remove the tumour. Since the tumours are often large, the incisions need to be large too. Sometimes surgeons use an incision in the side just below the ribs.

Laparoscopic Adrenalectomy

In this 'key-hole surgery' operation, a number of small incisions are made in the tummy through which operating instruments and a camera are inserted. This is the preferred approach for small benign (non-cancerous) tumours since it is a smaller operation and generally causes less pain and a shorter hospital stay than other approaches. However, for ACC this is not usually either possible or appropriate and ACCs are usually better treated by a conventional open operation. Laparoscopic adrenalectomy may sometimes be used in cases where the tumour is fairly small and it is not clear if it is a cancer or not.

MITOTANE (LYSODREN)

Your doctor may suggest a drug called Mitotane (Lysodren). It works by damaging both normal and cancerous adrenal cells. Mitotane can be used in four different situations:

1 - Treatment of persistent or recurrent disease

If the initial surgery is unable to remove all of the tumour or the tumour returns later, Mitotane has been proven to reverse the disease and can sometimes lead to complete remission for years. Most doctors would be cautious about claiming that it can 'cure' the condition in this situation. Mostly, Mitotane will be continued for life.

2 - Adjuvant therapy

There is evidence that Mitotane may be useful in preventing cancer returning after 'curative surgery', i.e. if apparently all tumour tissue has been successfully removed. This applies in particular to ACCs considered to have a relatively high risk of returning as judged by examining the tumour tissue obtained at surgery under the microscope. In this situation, it is usually recommended to start a course of two to three years of mitotane treatment, which should start within 12 weeks of the surgery. If the tumour is judged to have a relatively lower risk of returning, then usually the patient is given the choice between close follow-up (observation only) and treatment with mitotane as for this situation no clear evidence of what to do currently exists. In all instances, patients after apparently complete removal of the ACC will be followed by regular blood and urine tests and scan examinations, usually CT scans.

3 - Primary therapy

In some patients the disease is advanced and no surgical treatment can be performed. In this situation, chemotherapy may be used to shrink the tumour(s) and this can be monitored by a scan. In such a situation your doctors may not only recommend chemotherapy but also Mitotane; however, this depends on individual circumstances.

4 - Controlling hormone secretion

Sometimes steroid hormones that cause problems, such as too much cortisol or too much testosterone, remain high after surgery or when surgery cannot be undertaken. Mitotane may be helpful to control the hormone levels and prevent distressing symptoms.

Mitotane may be used alongside chemotherapy. Mitotane can also treat the symptoms of advanced adrenocortical carcinoma. You take Mitotane each day as a number of tablets (often 6-12).

Side effects are common and include nausea, and most often anti-sickness pills are used as well at the same time. Mitotane also causes tiredness and dizziness. Other side effects can occur but generally can be controlled by using a lower dose.

Mitotane kills normal adrenal cells and the normal hormones need to be replaced with tablets. All patients on mitotane require replacement of the normal cortisol levels using hydrocortisone tablets. Hydrocortisone needs to be taken at all times even if mitotane is temporarily stopped or paused. When mitotane is being used in the adjuvant setting (as a temporary therapy to prevent tumour recurrence) and it is stopped after two to three years, the function of the adrenal gland may sometimes recover, but hydrocortisone needs to be continued until blood tests prove that the patient does not need it anymore.

Sometimes patients on mitotane also require replacement of the blood pressure hormone aldosterone, and for this reason will have to take fludrocortisone tablets too. Your doctor will check whether you need fludrocortisone by measuring your blood pressure whilst sitting and standing and by carrying out blood tests.

Mitotane is effective if the level in the body is controlled to a particular level (14-20mg/L). This requires blood samples to be taken every 1-2 months to keep the level high enough to kill the cancer cells, but not to cause side effects. Your doctor will advise you on side effects to be expected from mitotane treatment. If mitotane blood levels are too high the function of the brain can be affected causing problems often described as “trouble talking and trouble walking”. This side effect is fully reversible when mitotane treatment is temporarily stopped.

There is a separate more detailed information leaflet available about mitotane treatment which your doctor will provide you with if you are considered for mitotane treatment.

RADIOTHERAPY

Radiotherapy is sometimes given to the adrenal area after surgery to kill any cancer cells that might remain there. It is also used for ACC that has spread beyond the adrenal glands, in particular if disease has spread to the bones. In this instance, Radiotherapy often helps to control the growth of the bone lesions and alleviate pain. Chemotherapy uses anti cancer (cytotoxic) drugs to destroy cancer cells. You may have just one drug or a combination of more than one drug. Chemotherapy is usually only used to treat adrenocortical carcinomas that have spread to other parts of the body.

CHEMOTHERAPY

Primary chemotherapy (treatment with chemotherapy only) is given when chemotherapy, on its own, is expected to control or cure the cancer; it can be given for acute treatment or long-term control.

Adjuvant Chemotherapy (chemotherapy given after surgery) is used in this manner to decrease the risk of the cancer coming back. This is done even when no clear evidence of cancer can be found, but certain factors (e.g. metastasis to the lymph nodes, large tumour size) predict an increased risk of cancer recurrence.

Neoadjuvant Chemotherapy (chemotherapy given before surgery) is used in this manner to shrink a tumour before surgery, which may allow the surgeon to perform a smaller surgery and/ or remove all visible tumour.

Combined Modality Chemotherapy is the practice of using chemotherapy together with other treatments, such as radiation or surgery or mitotane. Therapies are combined to obtain a greater response rate than could be achieved with a single type of treatment. Today, using more than one treatment modality is common for most cancers. Your doctor will discuss which options are suitable for you.

Some of the chemotherapy drugs used to treat ACC are:

- Cisplatin
- Doxorubicin (Adriamycin)
- Paclitaxel (Taxol)
- Fluorouracil (5FU)
- Vincristine
- Etoposide (VP16

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- Gemcitabine
- Capecitabine
- Streptozotocin

Combination Therapy

In some cases the use of one single chemotherapy treatment is not as effective as combining two different treatments together. Examples of combination treatments are:

- Etoposide + Doxorubicin + Cisplatin + Mitotane (Lysodren)
- Streptozotocin + Mitotane
- Etoposide +Cisplatin + Mitotane
- Gemcitabine + Capecitabine

MULTIDISCIPLINARY TEAMS

ACC care can be complex, and for the patient the journey can encompass not only a whole host of emotions, but also a whole range of investigations, treatments and healthcare professionals.

The very fact that there is often not just one treatment option at diagnosis and throughout the patient journey, means that there has to be a collaboration among many key healthcare professional groups in order to make the best clinical decisions for individual patients.

This collaboration has been termed an MDT (multidisciplinary team) or MPT (Multi-Professional Team). This is a formula that is now being used across the world in the care of cancer patients.

An MDT will usually be formed by a particular specialist with expertise and interest in ACCs and other adrenal tumours. This specialist is commonly an endocrinologist or oncologist.

An ACC patient may see some or all of the following people:

Oncologist (Cancer Specialist)
Surgeon
Endocrinologist (Hormone Specialist)
Radiology staff
Dietitian
Nurse Specialist (including Macmillan Nurses)
Palliative Care Team
Pain Team
General Practitioner/Practice Nurse
Counselling Staff
Various Technicians
Clinic Staff
Hospital Staff
Hospice Team

Patients can feel more confident in the knowledge that all aspects of their care have been discussed and that the best possible treatment plan will be formulated. A well coordinated and disciplined MDT is a very important aspect for care when striving to achieve the best quality of life and the best outcome for ACC patients.

CLINICAL RESEARCH

Research is a step-by-step process that involves collecting and examining information. Research into adrenocortical carcinomas is vital to improve our understanding of the disease and how it can be treated.

Research goals include:

- Understanding what causes ACCs
- Understanding how ACCs form
- Formulating more effective diagnostic scans and tests
- Discovering new treatment options, and ensuring that current treatments are being implemented to provide the best therapeutic benefit

ACCs are a rare form of cancer, and there are only a small number of teams of dedicated medical professionals around the world who treat patients every day. It is important that these specialists are allocated the resources to carry out research within their units, so that our understanding of this disease and how to treat it continues to grow.

In clinical trials, patients agree to try new therapies (under careful supervision) in order to help doctors identify the best treatments with the fewest side effects. Clinical trials may also test the value of new tests to diagnose disease and to help the doctors to detect earlier when the tumour is coming back.

If patients want to take part in a clinical trial, they should discuss this with their specialist, who will know what trials are recruiting patients and whether they are eligible.

All studies are run on strict inclusion and exclusion criteria for the safety of the patients. It can be frustrating for patients to discover that they are not eligible, but no medical professional is able to influence any decisions based on these criteria.

No one should ever include a patient in a clinical trial without his or her knowledge. A doctor, nurse or other researcher

will ask for permission, and they cannot enter a patient into the trial unless that patient has given his or her consent.

To help patients decide whether they want to take part, the researchers should tell them all about the study:

- what it is trying to find out
- how they will be treated
- what they will have to do.

Even after consent has been given, a patient may leave the trial without giving a reason at any time. If a patient is having a new treatment as part of a trial and then leaves the trial, he or she may not be able to continue having the new treatment. In this situation, patients would be given the appropriate standard treatment for their type of cancer.

You can find out more about current trials at:

Current Controlled Trials

This website allows users to search, register and share information about randomised controlled trials. Covers multiple registers, including England, Scotland and the US. **http://www.controlled-trials.com/**

ClinicalTrials.gov

This is a register of federally and privately supported clinical trials conducted in the United States and around the world.

http://www.clinicaltrials.gov

You can also search for research trials available to patients in the UK and Europe on these websites:

www.macmillan.org.uk

www.cancerhelp.org.uk

www.ctu.mrc.ac.uk (The Medical Research Council Clinical Trials Unit)

www.ncrn.org.uk (National Cancer Research Network)

www.eortc.be/ (European Organisation for Research and Treatment of Cancer)

USEFUL ORGANISATIONS

"It's nice just to have a cuppa and a chat with other people in a similar position" ACC patient

ACC SUPPORT UK

(A NET Patient Foundation / AMEND partnership funded by Macmillan Cancer Support)

To speak with someone in person, please contact either organisation

www.accsupport.org.uk

ACC SUPPORT UK
ADRENOCORTICAL CANCER SUPPORT AND INFORMATION

AMEND

(Association for Multiple Endocrine Neoplasia Disorders)

Patient information, support and counselling service

01892 516076

www.amend.org.uk

AMEND

NET PATIENT FOUNDATION

Patient information, support and specialised nurse advice line

0800 434 6476

www.netpatientfoundation.com

NET Patient Foundation
incorporating Living with Carcinoid

RARER CANCERS FOUNDATION

www.rarercancersfoundation.org

0800 434 6476

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NOTES

visit www.accsupport.org.uk
or scan the QR code below