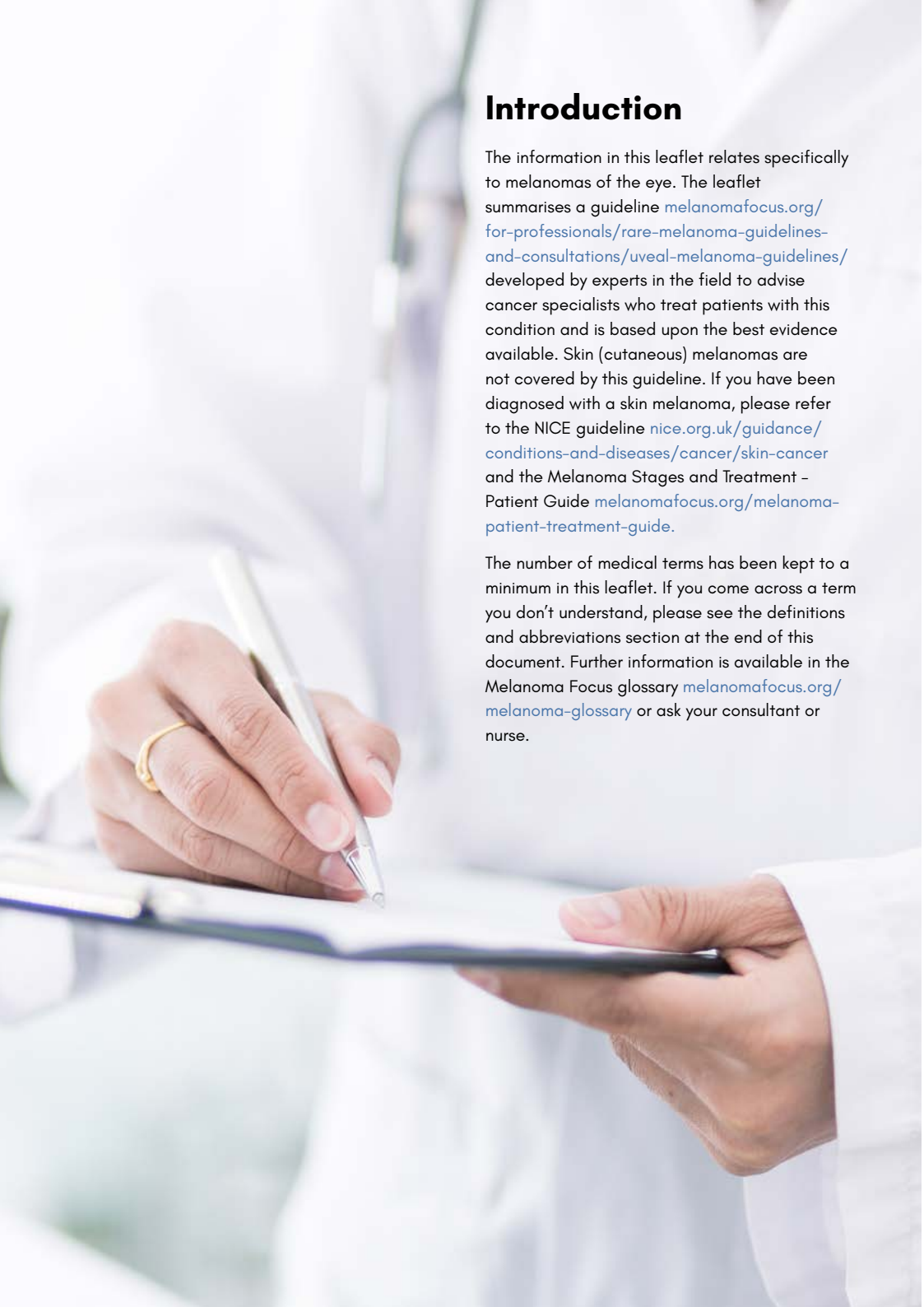
MELANOMA FOCUS

Uveal Melanoma

Information for patients and carers



Introduction

The information in this leaflet relates specifically to melanomas of the eye. The leaflet summarises a guideline melanomafocus.org/for-professionals/rare-melanoma-guidelines-and-consultations/uveal-melanoma-guidelines/ developed by experts in the field to advise cancer specialists who treat patients with this condition and is based upon the best evidence available. Skin (cutaneous) melanomas are not covered by this guideline. If you have been diagnosed with a skin melanoma, please refer to the NICE guideline nice.org.uk/guidance/conditions-and-diseases/cancer/skin-cancer and the Melanoma Stages and Treatment – Patient Guide melanomafocus.org/melanoma-patient-treatment-guide.

The number of medical terms has been kept to a minimum in this leaflet. If you come across a term you don't understand, please see the definitions and abbreviations section at the end of this document. Further information is available in the Melanoma Focus glossary melanomafocus.org/melanoma-glossary or ask your consultant or nurse.

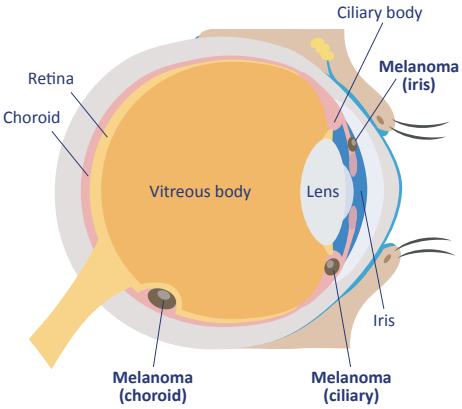
Uveal Melanoma (UM)

What is it?

Uveal melanoma (UM) is a cancer of the eye involving a tumour(s) of the iris, ciliary body or the choroid (known as the uvea). The tumours arise from the pigment cells in the eye called melanocytes.

These melanomas are different in many ways from skin melanomas. For example, the link between too much sun exposure and skin melanoma is strong, while there is no connection between sun exposure and most kinds of UM. Although UM is very rare with about 600-700 new cases in a year in the UK, there are other extremely rare melanomas of the eye and the umbrella term is ocular melanoma. Compare these numbers to melanoma skin cancer with about 17,000 new cases a year in the UK.

Eye Cancer: Melanoma of the Eye



There are certain factors which make getting a UM more likely, these include being older, having lighter colour eyes and/or lighter skin. Very occasionally, there is a faulty gene inherited which may be linked to several types of cancer in the family. Because of these differences some treatments for skin melanomas may not be as effective for UM and the outlook, or prognosis (see glossary), for UMs may not be as good as for skin melanomas. The prognosis will be different depending on a number of factors which are discussed below. If you would like more information about your individual situation, you should discuss this with your medical team.

What to expect from your care

A specific specialist cancer team will look after you during your treatment. The guideline melanomafocus.org/for-professionals/rare-melanoma-guidelines-and-consultations/uveal-melanoma-guidelines/ advises teams on specific ways in which they should work together.

When discussing your diagnosis and treatment you should be told:

- The name and contact details of your consultant and of your Cancer Nurse Specialist (CNS).
- Who your key worker is (this person is your first point of contact should you have questions or problems and is usually the CNS). You should have the contact details including telephone and email address of your keyworker and who to contact should your keyworker not be available.
- How to make an appointment with the consultant quickly should you run into problems.

- About referral to support services (for example, palliative care services) and to other resources such as, for example, Melanoma Focus, OcuMel UK, CRUK, Macmillan, Maggie's should you need them at any point in your treatment. For more information on these organisations, see the list at the end of this leaflet.

What are the symptoms?

Unlike skin melanomas, a UM will not be seen unless it is in the iris and there may not be any symptoms at first. It may be noticed by the optometrist during a routine eye test. If symptoms are present, they might include:

- loss of sight which may be complete or partial
- blurred vision
- seeing new floating spots, squiggly lines, or flashes of light
- change in the size or shape of the pupil in particular a dark spot on the iris
- and, occasionally pain.

What to expect next

Tests and examination

If a UM is suspected, you will be referred to an ophthalmologist with experience of the condition, called an Ocular Oncologist. As it is rare, you may need to travel to a specialist centre, rather than attend your local hospital. UM is treated in three specialised centres in England: Liverpool, London and Sheffield and in Scotland in Glasgow. These are called "supra-regional" centres. UM that has spread (called metastatic UM) requires the input of many different highly-specialised healthcare professionals and may be outside of the supra-regional centres.

Questions you may wish to ask about your visits

How often will I have appointments at the cancer centre?

What sort of support will I need at these appointments?

How long will I be at the centre each time?

What further signs and symptoms should I look out for?

What symptoms should I report urgently?

How and whom should I contact if I need to do so urgently?

Is there psychological support available should I need it?

At the hospital, the consultant* will examine your eye. The most common tests are:

- vision test
- examination of the eye using an ophthalmoscope and/or a slit lamp (see glossary)
- imaging of the eye
- ultrasound scan of the eye

Eye drops are used to dilate the pupils, which helps to see through to the back of the eye. These may blur your vision so you will not be able to drive safely for a few hours.

Diagnosis, staging and prognosis

The cancer team will normally make a diagnosis based on the results of your tests and medical examination and, unlike in skin melanoma, a biopsy will usually not be necessary for diagnosis.

Biopsy

A biopsy removes a small amount of tissue from within the eye to examine in the laboratory. It is either done under a general anaesthetic (where you are put to sleep in hospital) or a local anaesthetic is given to numb the area. You will be able to discuss the options with your medical team. **Note: If the eye is removed (enucleation), a diagnostic biopsy is done routinely, but make it clear to your surgeon if you would like a prognostic biopsy as well.**

Most of the time the diagnosis of uveal melanoma can be made without biopsy, but occasionally, if the diagnosis is not certain from the results of your tests and medical examination, you may be offered a biopsy to confirm the diagnosis. It will provide information about:

- Where the tumour started – although the tumour is in the eye, it may have spread from a tumour somewhere else in the body. If this is the case, treatments may be different depending on where the primary (first) tumour was located.
- What the tumour is made of which will help to confirm a diagnosis as not all intraocular (inside the eye) tumours are melanomas.
- Whether or not the tumour is cancerous. For example, it can be difficult to tell whether a small tumour is a benign mole or a melanoma without examining it under the microscope.

You are likely to also be offered a biopsy to help estimate the chances of tumour spreading – a prognostic biopsy. It may help:

- Estimate the chances of the tumour spreading (metastasis) to other parts of the body. There are certain genes that increase the risk of the cancer spreading to other parts of the body and a biopsy gives an analysis of the gene profile. (See the Staging and Prognosis section on page 4.)
- Inform future treatments – targeted therapies for tumours involving particular genes are continually being developed and knowing the genetic make-up of the tumour may be helpful in determining treatments in future.

The risks of having a biopsy include:

- Minor/temporary changes in vision – there is a 10% chance that the biopsy may result in changes to your vision such as cloudy vision.
- Significant vision loss – rarely, biopsy can result in significant vision loss due to an infection, detachment of the retina, or development of a cataract.
- Very rarely, 'seeding' of tumour cells into tissues around the biopsy area may happen and could theoretically increase the risk of tumour spread elsewhere.
- No result – particularly if the tumour is small there is a 5–10% chance of not getting a result.

* This may be the consultant or another senior doctor on the team.

All four UK centres (Liverpool, London, Sheffield and Glasgow) perform biopsies.

It may take up to 6 weeks to get the results of the biopsy depending on whether you are having the biopsy to aid diagnosis or to assess the chances of tumour spreading.

Staging and Prognosis

Unfortunately, cancers can spread by the blood stream or the lymphatic system to other parts of the body and if UM does spread, it will often spread to the liver.

Determining the prognosis or your chances of recovery (prognostication) involves estimating the chances of developing metastatic disease by analysing 'metastasis predictors' in the eye melanoma.

Prognostication is performed to:

- Identify who has a significant risk of developing metastatic disease and therefore might be considered for regular scans so that any spread (metastasis) is detected as early as possible.
- Identify who is at a low risk of developing metastatic disease so that wellbeing is enhanced by reassurances of their good chance of survival, and they are spared from the stress and inconvenience of repeated liver scans over many years.
- Empower patients to make life choices and prepare for any eventuality while they still feel well.
- Enable participation in any clinical trials evaluating treatments aimed at preventing or delaying the onset of metastatic disease.

Your prognosis is made from a number of factors including your age and sex as well as characteristics of the tumour. See the glossary for more detail.

Questions you may wish to ask about your diagnosis and prognosis

What are you looking for in the biopsies?

What are the risks of a prognostic biopsy?

What are the benefits of having a prognostic biopsy?

Will you offer me an intraocular biopsy? If you do not and I wish to have one, will you refer me to another centre for a second opinion?

If my eye is removed (enucleation) will you do a prognostic biopsy?

When will I get the results of the biopsy?

What stage is my cancer at and what is my prognosis?

Are any gene mutations involved in my cancer and if so, is there a targeted treatment?

What is the best treatment available to me?

What sort of health problems might I have? And what are the plans I need to put in place to be prepared?

What supportive services are available to me and may I have their contact details for future reference?

Can you recommend leaflets or websites with information on my condition?

Are there any clinical trials available that I might be suitable for?

Prognosis is estimated in the UK in the following ways:

- Liverpool Uveal Melanoma Prognosticator Online (LUMPO3) – calculates a risk of metastatic disease score. The LUMPO3 questionnaire which clinicians complete is here mpcetoolsforhealth.liverpool.ac.uk/LUMPONet/LUMPONet.html
- TNM staging system (i.e., Tumour, Node, Metastasis) – more information on TNM staging for Uveal melanoma see cancer.org/cancer/types/eye-cancer/detection-diagnosis-staging/staging.html

If the information is available, your LUMPO3 score should be calculated, and discussed with you should you wish. If not all the information about your tumour is available, it is still possible to predict your risk.

These estimations cannot be 100% accurate, but they can give some idea of the likelihood of the cancer spreading to the liver in the next 10 years.

Having your prognosis can help you plan and make informed life choices.

However, if you and/or a relative or carer don't want to have a full discussion about your prognosis, make this clear to your medical team. If you do not want to know your prognosis the hospital will store the information they have and you can discuss it, if and when you decide.

Whatever your decision, you will be fully supported by your medical team.

Treatment

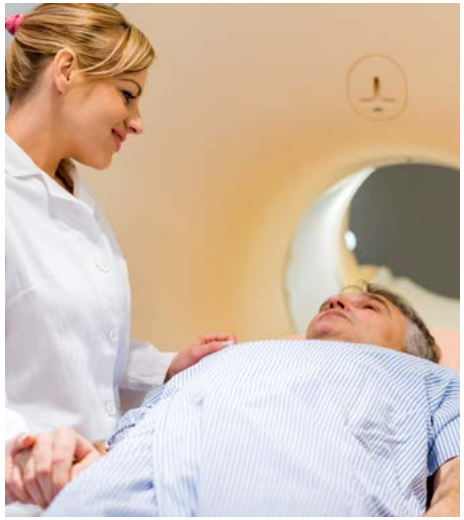
There are a number of different methods for initially treating the primary tumour in the eye. The most common first-line treatments include:

Radiation therapy:
Plaque radiotherapy
Proton beam radiotherapy
Stereotactic radiosurgery

Surgery:
Enucleation

These are defined in the Glossary at the end of this document.

Generally, none of the first-line treatments have been shown to be better than another. On the one hand, you may prefer surgery where treatment is over quickly. On the other, you may prefer a treatment that aims to conserve your eye but may be more involved in terms of requiring more hospital appointments and medical interventions. Depending on where the tumour is located and its size, the consultant may recommend one treatment over another. The options should be discussed fully with you and why a particular treatment is being recommended.



If the UM has not spread, you may not need further treatment (see surveillance after initial treatment). With many types of cancer, adjuvant (extra) chemo or radiation therapy is offered following the primary treatment. However, there is, as yet, no proven benefit of adjuvant therapy for UM. Someone from the cancer team will discuss the options with you and may ask if you would like to enter a clinical trial to help doctors answer this question.

Some questions you may wish to ask about your initial treatment

What size is my tumour?

What are my treatment options?

Are there alternative treatments offered at other centres?

Which treatment do you think is best for me and why?

How will my vision be affected?

How often will I have treatment?

How should I expect to feel after my treatment?

What will the recovery time be?

Will I be able to carry on with life as normal?

What symptoms should I look out for, indicating whether the treatment has worked or not?

Surveillance after initial treatment

'Surveillance' is the term used to keep a close watch on your condition so that signs that a disease has come back or metastasised are detected as early as possible. At the end of your initial treatment, your Ocular Oncologist should put in place a plan for your ongoing surveillance, this should include both surveillance of the eye and a discussion of surveillance of the liver (as there is a risk that uveal melanoma can spread to the liver). You should be copied in on the correspondence between your Ocular Oncologist and the local medical team regarding your follow-up. If you have not heard within 2 months after your treatment has finished, you should contact your Cancer Nurse Specialist or Ocular Oncologist's secretary.

Surveillance of the eye

Unless the eye was removed (enucleation), there is a small chance that the treated tumour may reoccur or that you may get problems related to any radiation used to treat the tumour. You should be seen by an Ophthalmologist approximately every 6 months at first, reducing to annually after 2-5 years depending on your individual situation. You may be monitored locally, instead of going back to the oncology centre. A photo will be taken of the affected eye. If the local medical team cannot get a clear view or if they have some questions, they may refer you back to the Ocular Oncologist. If the tumour has disappeared (completely regressed), you may be discharged to your local Optometrist. If at any time your circumstances change, you can, of course, be referred back to your Ocular Oncologist.

If the eye was removed completely, you can be discharged to your local Optometrist once the socket has healed. To ensure your other eye remains in good health, it is recommended that you have regular examinations with your local Optometrist.

Questions you may wish to ask about your surveillance

What is my risk of metastasis? How accurate is this prediction?

How often will I have a scan and where will it take place?

If I don't hear in 2 months, who should I contact?

Why am I being discharged to a local medical team?

What signs or symptoms should I watch out for?

Can you advise me on how to access psychological services?

Where can I get more information?

Surveillance of the liver

Some uveal melanomas may travel (or metastasise) through the blood stream to the liver and other organs. You should be offered a discussion with an oncologist or other appropriately trained healthcare professional to discuss the potential benefits of surveillance to you. If you do start surveillance this should be co-ordinated through secondary care (the hospital) and not primary care (your G.P.).

A prognostic score should be calculated (see Staging and Prognosis section) and discussed with you should you wish. As with other cancers, if the risk of metastasis is low (less than 10% over ten years), regular surveillance is not needed nor recommended. If not being followed-up regularly worries you, you should be offered access to psychological services.

If your risk is calculated as greater than 10% over the next 10 years, you should be offered regular liver scans for the next 10 years. In rare circumstances, where the genetic SF3B1 mutation has been identified, this should be extended to 15 years.

You will generally have a scan every 6 months for 5 years and then annually for a further 5 years. However, this may vary according to your circumstances. The scans will be either by Ultrasound (US) or Magnetic Resonance Imaging (MRI). Both are generally equally effective for surveillance. If, however, something is detected by ultrasound, you should be offered an MRI as soon as possible. Blood tests monitoring your liver function are not needed and should not be part of your routine surveillance.

If you remain symptom-free during the surveillance period, usually 10 years, you will be discharged to your General Practitioner or local Ophthalmologist at the end of this period. Once again, you can be referred back to the Ocular Oncologist or Oncologist should anything concerning arise.

If the uveal melanoma recurs or spreads (metastasis)

If there is a suspicion that your cancer has spread, you should be looked after by a team of specialists which may be located away from your eye centre. The team should consist of the appropriate specialists and may include a clinical or medical oncologist, an interventional radiologist, a pathologist, a liver surgeon and a clinical nurse specialist. The team should be experienced in treating UM and have direct links to one of the three eye specialist centres in England and one in Scotland. This is because of the rarity of the cancer and the benefits to patients of being seen by those with experience. However, you are also able to choose to be treated nearer home if you prefer. The team should have access to all the treatments and trials available nationally. You can find the clinical trials which are currently running on the Melanoma Focus TrialFinder: melanomafocus.org/melanoma-trialfinder.

The specialist team should give you a variety of scans. Your chest, pelvis and abdomen should be scanned with contrast-enhanced CT or PET CT. Your liver should be scanned with contrast-enhanced MRI with diffusion weighting. In addition, if you have a pain in your bones, you should have a bone scan. You will not have a brain scan unless you have symptoms.

If the cancer has spread outside of the eye, you may be offered anticancer treatment. You should be told of any relevant clinical trials, and these explained to you. If there are no clinical trials available or you do not wish to participate, you may be offered a systemic immune checkpoint inhibitor (ICI). The risks and potential benefits of ICI's should be explained to you. A new drug called tebentafusp is showing promising results for people with a particular immune type (or HLA-type - HLA-A*02:01). At time of publication this has not been approved for use on the NHS. More information about tebentafusp may be found here: melanomafocus.org/about-melanoma/types-of-melanoma/uveal-melanoma/tebentafusp.

If the cancer is only in the liver, surgery (resection) may be the best treatment if you are a suitable candidate. Before your operation you should be given a laparoscopy to check that surgery is possible. If you are not able to have a surgery, your specialists should consider other treatments directly to the liver.

If the disease progresses, there are other options to make you more comfortable, which are used for skin melanomas. General guidance is available in this NICE guidance CSG4 nice.org.uk/guidance/csg4.

Questions you may wish to ask about your treatment and prognosis

What clinical trials are available?

What is the aim of the clinical trial?

What other treatments are available to me?

Is tebentafusp right for me and is it now available on the NHS or privately?

If so, what is the likelihood that it will reduce my symptoms and/or extend my life?

What are the side-effects with this treatment?

What support will I need while on this treatment?

How will I be able to tell whether it's working or not?

If it is not working, how soon can I move on to something else?

Will this treatment prolong my life?

Will I have a reasonable quality of life while on this treatment?

Sources of information and support

Melanoma Focus (melanomafocus.org) is a charity that commissions and funds melanoma research, while providing support & information for patients, carers and healthcare professionals. It funded this booklet and the associated guideline for health professionals, on which this booklet is based. It is here melanomafocus.org/about-melanoma/types-of-melanoma/uveal-melanoma.

OcuMel UK (ocumeluk.org) is a registered charity representing those affected by ocular melanoma. You can contact their Helpline at helpline@omuk.info.

Macmillan (macmillan.org.uk) provides support for people who have cancer.

Although not specific to UM, **Cancer Research UK** has a great deal of information about eye cancer, including treatments and living with cancer, which is relevant to UM: cancerresearchuk.org/about-cancer/eye-cancer.

Maggies (maggies.org) offers support free to anyone with cancer and their families. They have centres alongside NHS hospitals as well as online support.

NHS Choices (nhs.uk) has information on eye cancer treatments and other aspects of care: nhs.uk/conditions/eye-cancer.

Glossary

For further information see melanomafocus.org/melanoma-glossary.

Adjuvant therapy

Adjuvant therapy is is any extra treatment that is given after the complete surgical removal of a cancer. It is used to boost the benefit of first-line treatment by attacking any possible remaining cancer cells circulating in the bloodstream or lymphatic system. The aim is to reduce the possibility that the cancer will come back.

Biopsy

A biopsy is when a small amount of tissue is removed so the cells can be examined under a microscope. There are more details of biopsy on NHS Choices: nhs.uk/conditions/biopsy.

Eye examination

Ophthalmoscope a handheld instrument that shines a light into the back of the eye. It is often used in routine eye examinations.

Slit lamp has a bright light and powerful microscope, so that the eye can be looked at in greater detail.

Genetic factors

From a biopsy, the medical team will be looking at the genes and chromosomes of the tumour. Where some parts are missing or changed the chances of the cancer spreading (prognosis) are higher.

Genetic factors that suggest low risk of the cancer spreading include tumours having:

- Normal number of copies of chromosome 3
- Normal number of copies of chromosome 8.
- Increased amounts of chromosome 6.
- Absence of any loss to the BRCA1-associated protein-1
- No mutations to SF3B1 (Splicing factor 3b subunit 1) gene mutation.

Healthcare professionals you may encounter

Clinical nurse specialist
A nurse who has extra training in a particular speciality.

Clinical oncologist
A doctor with advanced training in cancer who is able to give radiation therapy.

Interventional radiologist
A doctor who uses techniques which rely on the use of radiology to guide them, such as ultrasound-guided biopsy.

Oncologist
A doctor who gives immunotherapy, targeted therapy or chemotherapy.

Ophthalmologist
A doctor specialising in diseases and injuries of the eye and performs surgery on the eye. The Ophthalmologist is likely to be the first consultant you see.

Histopathologist or Pathologist
A pathologist helps to diagnose disease based on the laboratory analysis of bodily fluids such as blood, urine and tissues. If you have a biopsy, a pathologist is the person who looks at the biopsy to help work out what type of melanoma you have.

Immunotherapy
Also called biologic therapy or bio-chemotherapy, stimulates the patient's own immune system to fight cancer.

Immune checkpoint inhibitors
Checkpoint inhibitors block the proteins in the tumour cells that stop the immune system from attacking the cancer cells. For more information see melanomafocus.org/melanoma-patient-treatment-guide/melanoma-treatment/immunotherapy-treatment.

Lesion
An area of tissue that isn't normal. This term can be used when it is uncertain whether the area is cancer (malignant) or not (benign).

Lymph Nodes
Fuller explanation of lymph nodes and cancer is here: cancer.org/cancer/cancer-basics/lymph-nodes-and-cancer.

Melanomas of the Eye
Choroidal melanoma
Uveal melanoma involving the back part of the eye (choroid). This is the most common type of uveal melanoma being about 90% of the total.

Ciliary body melanoma
UM involving the ciliary body which includes the ring of muscle on the inner surface of the front wall of the eye is responsible for providing the fluid that nourishes the lens and cornea of the eye.

Conjunctival melanoma
Melanoma that starts in the outer layer (conjunctiva) of the eye. It has more in common with skin melanoma and is not an uveal melanoma and not covered by this guideline.

Iris melanoma
Uveal melanoma involving the front, coloured part of the eye.

Metastasis/Metastatic Cancer
Metastasis is when cancer cells break away from the original (primary) site, travel through the blood or lymph system, and form a new tumour in other organs or tissues of the body. The new, metastatic tumour is the same type of cancer as the primary tumour. For example, if uveal melanoma spreads to the liver, the cancer cells in the liver are uveal melanoma cancer cells, not liver cancer cells.

Prognosis
Prognosis (outlook) is the prediction of the likelihood the cancer will spread to another part of the body. With UM this is usually the liver. It is calculated based on a number of factors including:

- Age
- Sex
- The location of the tumour
- The size of the tumour
- Whether the ciliary body has been involved
- Whether the tumour has started to grow outside of the eye
- Genetic analysis of the tumour, if available from biopsy, in order to determine what if any changes there have been to the chromosomes – see Genetic Factors.

From this information an estimate of your personal risk for cancer spread can be made. Knowing how the disease is likely to evolve can enable people to plan ahead and understand what may happen. The prognosis, however, is an estimate and will be explained as a percentage risk.

Scans
For more information on the tests mentioned in this leaflet see the Cancer Research UK website link: cancerresearchuk.org/about-cancer/cancer-in-general/tests.

CT Scan
Computerised Tomography (CT) takes x-rays from different angles and the computer then puts them together as a three-dimensional picture. See the Cancer Research UK website link above and nhs.uk/conditions/CT-scan/ for more information.

MRI/MR
Magnetic Resonance Imaging (MRI or MR) takes pictures of the body using magnets and radio waves. These show up soft tissues such as the bowel, liver, lungs etc. better than CT scans. The scan can take up to 1½ hours. See the Cancer Research UK website link above and nhs.uk/conditions/mri-scan/ for more information.

PET-CT
This combines a CT scan (see above) with a Positron Emission Tomography (PET) scan. A mildly radioactive substance is injected, which shows up parts of the body where cells are more active. That is, where a cancer might be growing. See the Cancer Research UK website link above and https://www.nhs.uk/conditions/pet-scan/ for more information.

Staging
Staging is an estimate of how much cancer there is and where is located. Staging is used to plan treatment and future options. Fuller explanation here: melanomafocus.org/melanoma-patient-treatment-guide/melanoma-info-by-stage/melanoma-staging-explained and cancer.org/cancer/types/eye-cancer/detection-diagnosis-staging/staging.html.

Symptom care support services
More information on what forms of home care are available can be found at: nhs.uk/conditions/social-care-and-support/home-care/?tabname=whats-your-situation#types-of-homecare and cancerresearchuk.org/about-cancer/melanoma/advanced-melanoma/support-home-for-you-your-family.

Treatments for primary UM
RADIATION THERAPY

Plaque radiotherapy
Treatment using a radioactive plaque placed on the wall of the eye directly over the tumour in order.

Proton beam radiotherapy
Treatment using pinpoint radiation through the front of the eye targeted at the tumour.

Stereotactic radiosurgery
Treatment using radiation from several directions outside of the eye.

PHOTOTHERAPY
Is rarely done in this country

Transpupillary thermotherapy
Laser treatment involving heating the tumour using an infrared laser beam.

Photodynamic therapy
A treatment using a dye injected into the arm. Infra-red laser is then directed at the tumour in the eye, which activates the dye and kills the tumour.

SURGERY

Enucleation
Removal of the entire eye is the most common operation.

Endoresection
A method used to remove the eye tumour through a hole in the retina. This is rarely done.

Exoresection
A method used to remove the eye tumour through a trapdoor in the wall of the eye. This is rarely done.

ABBREVIATIONS

CNS	Cancer Nurse Specialist sometimes called a Clinical Nurse Specialist
CT	Computed tomography
MRI	Magnetic resonance imaging
mUM	Metastatic uveal melanoma
ICI	Immune checkpoint inhibitors
PET	Positron emission tomography
SNB	Sentinel lymph node biopsy
UM	Uveal melanoma

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