MELANOMA CANADA

A GUIDE TO
UVEAL MELANOMA

MELANOMA OF THE EYE

An informative guide
for patients diagnosed with uveal melanoma

WATCH OUR UVEAL VIDEO

ACKNOWLEDGMENTS

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MELANOMA CANADA

Melanoma Canada (MC) is a national, patient- led, charitable organization. The mission of MC is to support individuals whose lives have been changed by melanoma and skin cancer. We are advancing the prevention of melanoma and skin cancer through advocacy and education.

Donations are gratefully accepted to support ongoing publication of this booklet and other educational initiatives.

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CONTENTS

QUICK FACTS

- **Uveal melanoma** (also sometimes called **intraocular melanoma**) is the most common eye cancer in adults. It arises from the middle layer of the eye wall, the uvea.

- According to which part of the uvea the melanoma arises from, the melanoma can be a **Choroidal melanoma**, **Iris melanoma**, or **Ciliary body melanoma**.

- It is called melanoma because it develops from **uveal melanocytes**, similar to **skin melanocytes**, but it is much rarer than melanoma of the skin (cutaneous melanoma).

- Approximately **200 people are diagnosed with uveal melanoma** in Canada each year.

- Common treatment options include radiation therapy and surgery.

- Control of the eye tumour, through treatment discussed on page 16, is highly successful (>90%) in most cases.

- Currently, there is no cure for metastatic uveal melanoma, which **affects between 30-50% of patients with uveal melanoma**. However, there are treatment options.

- If you are diagnosed with uveal melanoma, you are not alone. **Melanoma Canada offers several free support programs to help you through your journey**.

  Visit www.melanomacanada.ca for more information or call 1-877-560-8035

ABOUT THIS BOOKLET

The purpose of this booklet is to help when you are diagnosed with uveal melanoma. This booklet focuses on this form of cancer and how it is treated.

What can I learn from this booklet?

This booklet includes:

- **Treatment options** for uveal melanoma that are available in Canada at the time of publication. Not all treatments apply to every person with uveal melanoma. Diagnostic procedures and treatment may also vary from province to province. Please speak to your healthcare team about the treatment options that may be available to you.
- **Questions to ask your doctor** at different stages of your treatment. To help you learn about the disease and be active in your treatment decisions:
  - Ask questions to make sure you understand your condition and your treatment
  - Take notes so you can remember your questions and the doctor's answers about your condition and treatment
  - Ask for copies of any test results so you have them for easy reference or to review for questions later. Some treatment centres and hospitals may offer online access to your test results, so check with your facility.
  - Bring a friend or family member to your appointments to take notes, listen, or ask questions. Having someone there is helpful and can be a good support for you.

What will I gain from learning about uveal melanoma and its treatment?

The more you know, the more you can be active in making choices about your own care. Being part of your care:

- Helps you feel more in control
- Can lessen the anxiety of a diagnosis
- May help you be more confident with your treatment and communicating with your healthcare team

INTRODUCTION

There are several different types of eye cancer. This informational guide focuses on **uveal melanoma**.

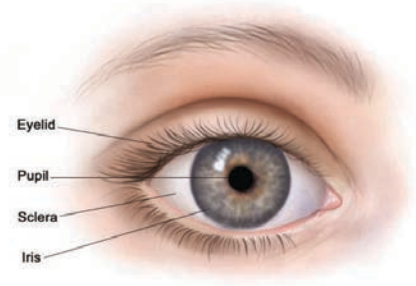
Melanoma occurs when there is a malignant (cancerous) tumour of the melanocytes. **Melanocytes** are pigment or colour-producing cells found in various locations in the body including the skin, hair, and eyes. Melanocytes within the eye are located in the middle and inner layers of the eye.

Melanoma of the skin (cutaneous melanoma) is much more common and is very distinct from melanoma of the eye (uveal melanoma).

An information booklet on melanoma of the skin titled **"Melanoma, What You Need to Know"** is available from Melanoma Canada at melanomacanada.ca

THE EYE:

The eye is a ball with a wall. The wall is made up of three layers:

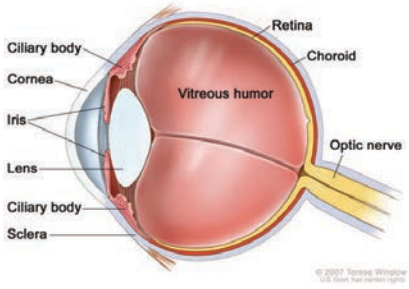


1. **Sclera:** The outer layer is the white visible portion called the sclera and there is a clear portion that covers the front of the eye called the cornea.
2. **Uvea:** The middle layer is called the uvea and is made up of:
    a. The iris, which is visible through the cornea.
    b. The ciliary body.
    c. The choroid, which are behind the sclera.
3. **Retina:** The inner lining layer of the eye is called the retina. It is made up of cells that sense light and transmit this information through the optic nerve to the brain which allows us to see.

THE UVEA:

The uvea (sometimes also called the **uveal tract**) is the middle layer of the eye. The uvea has three parts: the iris, the ciliary body, and the choroid.

1. The iris provides your eye colour that surrounds the pupil
2. The ciliary body is a muscle that controls the size of the pupil and the shape of the lens to help the eye focus
3. The choroid is a layer of blood vessels that provides the eye with nutrients and oxygen



UVEAL MELANOMA:

Uveal melanoma develops when melanocytes of the uvea become cancerous. Melanocytes become cancerous when they multiply and grow rapidly.

This can occur in any part of the uvea: the iris, the ciliary body, and/or the choroid. Therefore, uveal melanoma can also be called Choroidal melanoma, Iris melanoma, or ciliary body melanoma.

Approximately **85%** of uveal melanomas occur in the choroid, approximately **10%** of uveal melanomas occur in the ciliary body, and approximately **5%** of uveal melanomas occur in the iris.

Although uveal melanoma and cutaneous melanoma both affect melanocytes, they are very different cancers. Uveal and cutaneous melanoma are distinct in that they have different genetic mutations, they behave differently, and cutaneous melanoma is much more common than uveal melanoma (nearly 40 times more common).

Having uveal melanoma does not mean that you will develop cutaneous melanoma and having cutaneous melanoma does not mean that you will develop uveal melanoma.

RISK FACTORS AND PREVENTION

The cause of uveal melanoma is unclear. Therefore, we do not know exactly how to prevent it. Unlike cutaneous melanoma, which is often closely linked to overexposure to damaging UV radiation from the sun or other sources of UV radiation such as tanning beds, there is no evidence that UV radiation is what causes uveal melanoma.

However, there are factors that are linked to increased risk for uveal melanoma, which include:

1. Having **light-coloured eyes**, such as blue or green eyes
2. Light **skin colour**, especially those who sunburn easily.
3. Being **older in age** – the median age at diagnosis for a uveal melanoma patient is 55 years old.
4. Having an abnormality or mutation in the **BAP1 gene** which increases the risk of developing uveal melanoma. Speak with your physician regarding the appropriateness of genetic testing for your diagnosis and what may be available to you.

Although research studies have found a connection with these risk factors, it is important to remember that uveal melanoma can occur in any person, regardless of age, gender, or race.

Whilst there is no confirmed research suggesting that uveal melanoma is caused by UV radiation, it is still recommended that you:

- Wear close fitting/wraparound sunglasses with UV 400 or 100% UV protection
- Wear sunglasses any time you are in highly reflective environments, such as snow, water or sand.
- Wear UV protective sunglasses that help to prevent cataract development and/or damage to the eyes.

DETECTION AND DIAGNOSIS

HOW IS UVEAL MELANOMA DETECTED?

A person with uveal melanoma may have no symptoms and the tumor can be discovered during a routine eye exam. However, sometimes a tumor may produce some symptoms.

For a person experiencing symptoms, they may appear as:

- Primary symptoms are **vision changes:**
  - Blurred vision
  - Flashing lights
  - Unexpected seeing of shadows
  - Seeing floating spots
  - Loss of peripheral vision
- Melanoma in the iris may produce these symptoms:
  - A growth in the iris
  - Changes in the colour of the iris
  - A dark spot on the iris
  - Changes in the size and/or shape of the pupil
  - Changes in the position of the eyeball in the eye socket (the eye socket is the space surrounding your eye, including your eyelid, and where your eye sits in your face)
- Symptoms that may develop later can include:
  - Eye pain
  - Eye redness

These symptoms can be similar to many other eye conditions, such as cataracts or glaucoma. An ophthalmic examination (eye examination) should be carried out by an eye specialist, such as an **ophthalmologist or optometrist**, to rule out the presence of melanoma.

It is important to note that not all eye issues or lesions of the eye are necessarily uveal melanoma. but **monitoring any changes or areas of concern** is recommended. Some individuals have abnormalities of the eye, such as freckles or nevi (coloured growth that is similar to a mole). While these are not necessarily uveal melanoma, close monitoring and observation of these freckles or nevi, through your ophthalmologist or optometrist, is recommended.

HOW IS UVEAL MELANOMA DIAGNOSED?

There is no formal screening program for uveal melanoma. Routine eye exams, with an optometrist or ophthalmologist, are the best options for identifying potential issues or areas of concern.

Eye exam: an eye exam is performed by an optometrist or an ophthalmologist and is a painless procedure.

- The outside and inside of the eye are examined for any abnormalities.
- Special eye drops that dilate the pupil (make your pupil larger) may be used to help see the inside of the eye better.
- A diagnosis of uveal melanoma can sometimes be made through an eye exam alone.

Photography: Different types of specialized photographs are used to take pictures of the outside and inside of the eye and can help with the diagnosis of uveal melanoma. Also, by comparing photographs before and after treatment, photographs can also help determine whether the treatment delivered is effective.

Ultrasonography: Ultrasonography uses high frequency sound waves to help see the inside of the eye. Anesthetic (numbing) eye drops may be used so that an ultrasound probe can be placed on the eye's surface. Ultrasonography can be used to determine the tumour size, shape, and location.

Transillumination: Transillumination uses a light that is placed on the eye surface to examine eye structures for any abnormality.

Fluorescein Angiography: Fluorescein angiography is used to see how the blood is flowing in the eye and to see the blood vessels. A fluorescent dye called fluorescein is injected into an arm vein, and the dye travels to the eye in just a few seconds. A special eye instrument can detect this fluorescence to help us see if there is any damage to the eye blood vessels.

Recent Imaging Techniques: These include Optical Coherence Tomography (OCT), and OCT angiography, Infrared Fundus Photography, Indocyanine Green Angiography (ICG), and Fundus Autofluorescence. They are modern sensitive techniques to image subtle changes in the tumour and nearby structures.

Blood tests: A blood sample may be taken by a needle to determine how well organs in your body, such as the liver, are working. Analyzing the blood may help determine whether the tumour has spread to other areas of the body.

Scans: X-rays allow visualizing of internal body structures. A 3D X-ray called Computed Tomography (or CT) may be taken of certain parts of the body to see if there is any spread (or metastasis) of the uveal melanoma tumour. A 2D X-ray of the chest may be taken as an alternative to a CT scan.

Biopsy: A biopsy is a way to get a sample of the tumour cells, sometimes by using a fine needle. It is typically not performed for uveal melanoma diagnosis as other tests are sometimes enough to make a diagnosis. A biopsy may be performed so it can be analyzed by a medical geneticist to study the tumour's DNA or RNA. This information can be useful for determining survival prognosis of the patient and their eligibility for clinical trials.

WHAT IS MY PROGNOSIS IF I AM DIAGNOSED WITH UVEAL MELANOMA?

Prognosis is a term used to help predict the likely outcome for a patient with a health condition, or the likely course of a disease. Prognosis can refer to the likelihood of a patient surviving after the diagnosis of a tumour. A "poor prognosis" typically means that there is a low chance of recovery from a disease.

Control of the eye tumour is highly successful (>90%) in most cases. The following prognostic factors mentioned have an impact on the development of metastasis.

There are several factors that can help determine the prognosis for a patient with uveal melanoma. The most helpful factors to determine prognosis are the **tumour's size, the tumour's location, and genetic testing.**

Factors determining prognosis:

- **Tumour size:** The larger the tumour base and height, the poorer the prognosis.

- **Tumour location:** In general, iris melanomas have a better survival prognosis than ciliary body melanoma. The prognosis for choroidal melanomas is in between iris and ciliary body melanomas.

- **Tumour invasion:** If the tumour has invaded (spread into) the eye wall or spread to other parts of the body (metastasized) then there is typically a poorer prognosis.

- **Return of the tumour:** The tumour can return after treatment, but rarely. This is called **relapse or recurrence.** This is associated with a poorer prognosis as the tumour may no longer respond to treatment and has been shown to have an increased chance of spreading.

- **Genetic factors:** This is the most important factor in determining prognosis and survival. Changes in the DNA and in specific tumour genes may have a role in determining prognosis and can be identified by genetic testing.
    - A biopsy (a sample of the tumour taken using a fine needle) is required to do genetic testing. If you are interested in exploring this possibility and to determine whether you may be a candidate for genetic testing, please speak with your ocular oncologist.

- **The patient:** The patient's age, general health status, and other medical conditions all play a role in determining prognosis. This can be discussed with your doctor.

WHAT WILL HAPPEN TO MY VISION?

Factors that may affect your vision **after treatment** include:

- **Tumor size:** A larger tumour increases the risk of vision loss.
- **Tumour location:** A tumour closer to the optic disk or macula increases the risk of vision loss.
- **Other medical conditions:** Other medical conditions such as certain eye conditions, diabetes, or uncontrolled hypertension, increases the risk of vision loss.

HOW IS UVEAL MELANOMA STAGED?

There have been several staging systems of uveal melanoma according to the tumour dimensions, cellular type, or genetic defects, and the link to the potential for spread (metastases) outside the eye.

The current most practical categorization/staging is the TNM staging.

Stage:

Uveal melanoma stage is described as "TNM":

- **Tumour:** this refers to the tumour size and whether it has invaded nearby tissue.
- **Node:** this refers to whether the cancer has, or has not, spread to lymph nodes (which are organs in the lymphatic system that contain immune cells).
- **Metastasis:** this refers to whether cancer has spread in the body to distant sites (for example, the lungs or liver).

TNM is a staging system that can indicate the prognosis for a patient. The TNM of a patient can be complicated to explain and it is advised that patients discuss the details of their TNM stage with their ocular oncologist.

TREATMENT AND MANAGEMENT

HOW IS TREATMENT DETERMINED?

Treatment is not always recommended for patients diagnosed with uveal melanoma. For example, watchful waiting and close monitoring may be recommended for an elderly, chronically ill patient, who does not have any symptoms and has a small tumour. Otherwise, uveal melanoma should be promptly treated.

Treatment depends on many factors, including the location and size of the tumour, as well as the patient's overall health.

COMMON TREATMENT FOR TUMOURS:

- Small to medium (less than 12mm thick) tumours are:
  - Typically treated with **ocular brachytherapy**
  - **Enucleation** (the removal of the eye) is sometimes chosen by patients who cannot make the follow-up visits required post brachytherapy.
- Large (more than 12mm thick) tumours:
  - Due to the risk of severe vision loss and neovascular glaucoma, as well as potential radiation complications, large lesions are offered **enucleation** or **ocular brachytherapy.**

These treatment options will be discussed in more detailed in the following section.

UVEAL MELANOMA TREATMENT OPTIONS:

The treatment options for uveal melanoma may include radiation therapy or surgery. Some patients will receive both.

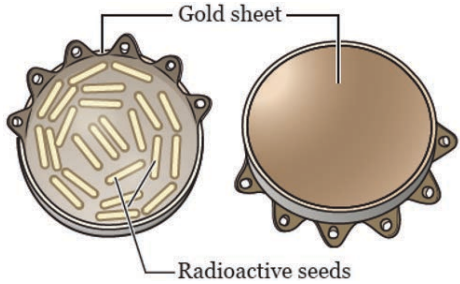
I. Treatment Option: Radiation Therapy

Radiation therapy is used to kill tumour cells.

There are two main forms of radiation therapy to treat uveal melanoma: **Brachytherapy (or Plaque Therapy)** and **External Beam Radiation Therapy EBRT (or Teletherapy).**

a. Brachytherapy (or Plaque Therapy)

Brachytherapy is the most common form of radiation therapy used and is the most widely available. Brachytherapy uses a plaque (a thin gold sheet) that is placed directly on the eye.



Brachytherapy is used to deliver radiation directly (and confined) to the tumour, meaning that the nearby healthy tissue receives less radiation. There are various types of radioactive plaques with different radioactive materials that can be used for Brachytherapy. Each radioactive material differs in its ability to penetrate the tissue of the tumor. The plaque will be placed on the eye during surgery in order to be close to the tumour. The plaque is left on the eye for up to one week and will require a second operation to remove the plaque.

When may it not be used?

- Brachytherapy may not be used when the tumour surrounds the optic disc, which is where part of the optic nerve (the nerve which allows us to see) is situated, and Teletherapy may be used instead.
- Brachytherapy is not used on tumours that are too big (usually greater than 12 mm thick) because the radiation can only effectively penetrate so far. Since Brachytherapy is very precise, many parts of the eye will remain unaffected while the localized radiation treatment will treat the tumor.

What are the potential side effects of Brachytherapy?

Although Brachytherapy is an excellent treatment option for most uveal melanoma patients, it may have some side effects. The risk of these consequences depends upon the size and location of the uveal melanoma inside the eye, as well as the type of radioactive plaque and the radiation dose during treatment. Possible side effects are:

- **Radiation retinopathy –** damage to vessels that supply blood to the retina. This will result in some level of vision loss.
- **Optic neuropathy –** less commonly, damage to the nerve that allows the person to see.
- **Other complications –** increased risk for cataracts, high eye pressure, internal bleeding of the eye and rarely, necrosis (tissue death caused by little blood flow) of the eye tissue.
- **Long-term complications –** poorer vision.

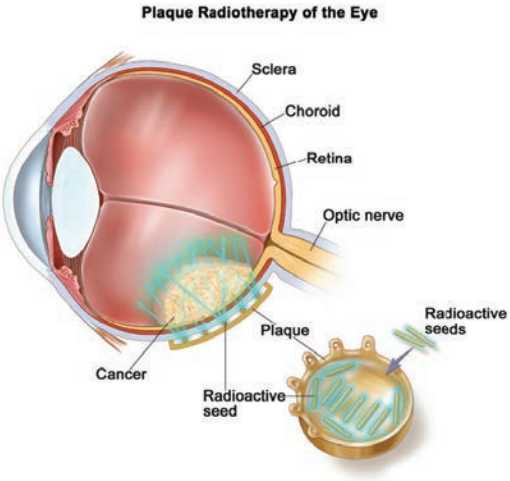


Image source: University of Chicago Medicine

b. External Beam Radiation Therapy (or Teletherapy)

EBRT is also known as Teletherapy. Teletherapy can include charged particle irradiation (e.g., Proton Beam Radiotherapy), Stereotactic Radiotherapy, or Gamma Knife. Different types of EBRT are only available at certain treatment centres in Canada.

Image source: Ohio State University

EBRT uses a machine that delivers radiation treatment from outside the eye. The radiation beams are delivered to the affected part of the eye through the front of the eye only. In the case of Proton Beam Therapy, an eye operation may be required to place metal clips or tags to help the machine know exactly where to deliver the radiation beams.

Who is EBRT for?

EBRT is used to treat patients with medium to large sized tumours that surround the optic disc, where plaque cannot be placed to cover the entire tumour base because of the physical obstruction from the optic nerve. EBRT can also be used for selected cases of tumour recurrence in the eye after plaque radiotherapy.

What are the potential side effects of EBRT?

Complications of EBRT are shared with those of plaque radiotherapy (please refer to previous section), but there may be relatively higher rates in case of Stereotactic Radiotherapy. However, this largely depends on tumour factors, such as its location and size, and possibly the dose of radiation received.

II. Treatment Option: Surgery

Surgical removal of the tumour depends on factors such as the size of the tumor and the location of the tumour.

There are two main forms of surgery to treat uveal melanoma:

a. Removal of the Eye (Enucleation)

Enucleation is considered in cases where radiation therapy may be insuffcient to treat the tumour, such as when the size of the uveal melanoma is particularly large, when the tumour has significant local spreading beyond the white portion of the eye (the sclera) and/or a blind painful eye after very high dose radiation, causing a condition called neovascular glaucoma.

After the eye socket is healed, an artificial eye (or prosthesis) can be customized. This customization process requires a mold to be taken from the eye socket and will take several weeks to create. When ready, the artificial eye is fitted to the patient and should look very realistic and have some movement. Once the eye socket is completely healed, a person living with an artificial eye can do most normal things. It is recommended that goggles be worn during water sports and snow sports.

b. Local Tumour Removal

Local removal of the uveal melanoma tumour may be used only in very specific cases, such as patients who are unable to undergo brachytherapy and do not wish to undergo enucleation. This limitation is due to the possible recurrence from residual cells (a very small number of cancer cells that remain in the body after treatment), as well as the number of complications associated with this surgery, which can affect the retina and cause internal bleeding of the eye.

III. TUMOUR BIOPSY

A tumor biopsy can provide valuable information to determine the risk of developing spread (metastasis). This can be done at the **time of plaque radiation therapy or from a removed eye.** The biopsy sample is performed by your surgeon and sent directly to the laboratory.

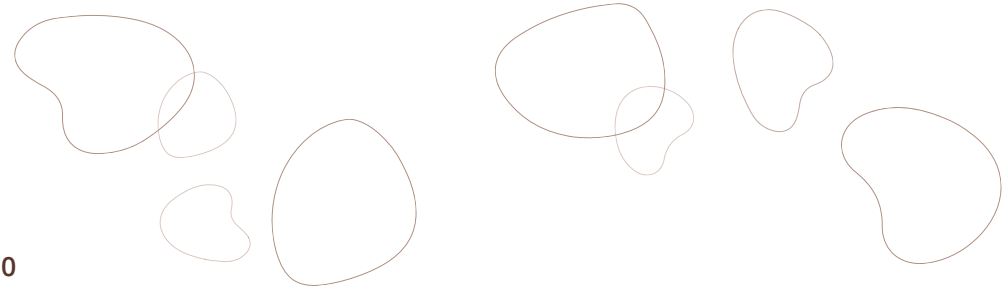
What is genetic testing?

Each cell in the human body contains sets of instructions (genes). These genes are stored in structures called chromosomes. Healthy cells have two copies of each chromosome. Tumour cells that are abnormal may show changes in these chromosomes. These abnormal cells multiply at a higher rate and are considered to be cancer cells. Genetic testing of uveal melanoma tumour cells is performed by obtaining a sample of cells from the eye tumor (biopsy).

What might this mean for me?

One of the most important indicators of poor prognosis in uveal melanoma is partial or complete loss of chromosome 3 (monosomy 3). Metastatic disease develops almost exclusively in patients with this genetic abnormality. Other chromosomes that can be altered in uveal melanoma tumor cells are chromosomes 1, 6 & 8. Others may have specific gene mutations on a chromosome such as BAP1 or SF3B1.

These chromosome changes occur within tumour cells, they are not inherited (passed through the family). These chromosome changes occur by chance in the tumor cell of the eye. They are not present in any other parts of the body, specifically the egg or sperm cells, and therefore cannot be passed on to children.



What are these tests?

The two tumour genetic tests that may be offered are:

1. **Gene Expression Profiling**
2. **Cytogenetic Profile**

Currently, there is no data that suggests one of these tests is better than the other. Please talk to your oncologist about which may be needed, or available and what is covered by your provincial healthcare plan or through private insurance.

What do these tests look for?

1. **Gene Expression Profiling (GEP)**
    a. GEP can identify the risk of metastases for patients with uveal melanoma. GEP classifies patients which are defined as:
        i. Class 1A: Lowest risk of recurrence
        ii. Class 1B/2A: Slightly increased risk of recurrence, but still a good prognosis
        iii. Class 2B: Higher risk of recurrence

2. **Cytogenetic Profile**
    a. Cytogenetic testing is testing that looks closely at chromosomes to determine any abnormalities or mutations.
    b. One of the most important indicators of poor prognosis in uveal melanoma is partial or complete loss of chromosome 3 (monosomy 3).
    c. Another poor prognostic finding is chromosome 8q gain, which you may see in your report.
    d. Other chromosomes that can be altered in uveal melanoma tumor cells are chromosomes 1, 6 & 8.

Other Tests

Blood samples can also be used to identify possible BAP1 mutations which put patients at inherited risk for uveal melanoma, mesothelioma, or kidney cancer. Discuss the role of genetic testing with your ocular oncology team

For further information about testing, what is available to you and covered by your province, and what your results mean for you, speak with your oncologist.

IV. OTHER THERAPIES

Other therapies to treat uveal melanoma exist for specific tumour cases. They include photocoagulation, transpupillary thermotherapy and photodynamic therapy. Speak with your ocular oncologist to learn more about these therapies.

SURVEILLANCE AND MANAGEMENT OF METASTASES

Spreading of cancer cells through blood or the lymphatic system to another part of the body is called metastasis. Uveal melanoma can spread to local structures beside the eye (known as extraocular extension), such as the optic nerve. Uveal melanoma can also metastasize through the blood and develop in the liver, lungs, bones and under the skin.

POST PRIMARY TREATMENT FOLLOW-UP AND SURVEILLANCE:

Uveal melanoma metastases may present years after the primary tumour has been treated. A patient who receives treatment (e.g., brachytherapy, EBRT, or enucleation) can still get metastases from the tumour cells that may have spread beyond the eye prior to treatment.

Less than 1% of patients at the time of initial uveal melanoma diagnosis would show evidence of metastases but between 30-50% of patients with uveal melanoma will develop metastatic disease. A diagnosis of uveal melanoma metastasis has a very poor prognosis and, unfortunately, has a high rate of mortality.

There are several approaches to surveillance for metastases. Because metastases sometimes occur in the liver and in the lung, tests that are performed are focused on these organs. These tests are performed every 6-12 months and can continue for many years or decades. However, there are few standard guidelines or approaches for surveillance as there is no clear consensus amongst experts.

- **Imaging tests –** Magnetic Resonance Imaging (MRI) of the liver or ultrasounds, supplemented with Computed Tomography (CT) are the standard imaging methods.
- **Physical exam –** to detect issues.

The frequency of follow-up and tests depends on the risk of metastasis of each individual tumour as detected by tumour genetic testing and/or tumour size and location. If an abnormality is found on imaging, your physician may recommend a biopsy to rule out metastasis.

MANAGEMENT OF METASTASES:

The development of metastases is a serious complication of this type of melanoma and generally limits patient survival. While treatment options are limited for patients with metastases, they are improving.

There are now new treatment options for metastatic uveal melanoma, in a research landscape that was previously only experimental and investigational. Some of these treatment options may include chemotherapy, immunotherapy, and targeted therapy.

SYSTEMIC THERAPY FOR PATIENTS WITH UNRESECTABLE OR METASTATIC DISEASE:

1. Clinical Trials

Patients should speak with their oncologist to see if enrollment in a clinical trial is possible.

2. Liver Directed Therapy

If the disease is limited to the liver, liver directed therapy could be considered. This would include surgery, ablation by a radiologic procedure, or infusion of chemotherapy or radioactive beads into the liver lesions. Discuss with your physician if this is appropriate for you.

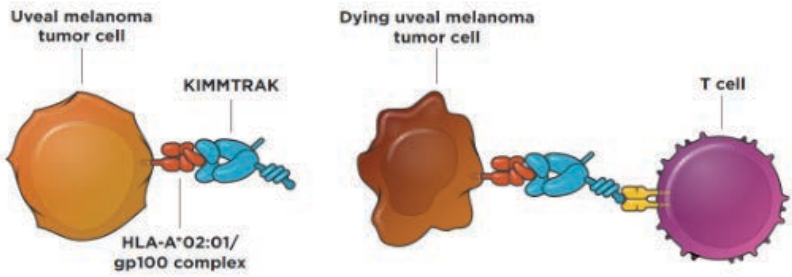
3. Immunotherapies

Immunotherapies are a type of drug that stimulates a person's own immune system (the body's natural defense against disease) to find and destroy cancer cells. Immunotherapy does this by activating the T-cells of your immune system to fight the uveal melanoma tumour cells. T-cells are a type of white blood cell that is found in the immune system. T-cells help the body to fight infection.

Use of the new drug therapy **tebentafusp (brand name Kimmtrak)**, approved by Health Canada, is an immunotherapy treatment for patients with unresectable or metastatic uveal melanoma with positive human leukocyte antigen HLA-A 02:01 haplotype (obtained from a blood sample). Tebentafusp has been proven to improve overall survival rates in many patients.

How does it work?

Tebentafusp is given once weekly as an intra-veinous infusion (IV) over 15-20 minutes. Tebentafusp attaches to the HLA-A*02:01 complex. This helps your T-cells to recognize, attach, and kill the uveal melanoma tumour cell.



To determine if tebentafusp is right for you, you will be required to take a blood test to see if you are HLA-A*02:01 positive. If your HLA status is positive, you will discuss treatment options with your doctor and may be eligible for tebentafusp.

Other immunotherapies

Treatment with the combination of Ipilimumab and Nivolumab or with monotherapies (one drug therapy) of Pembrolizumab or Nivolumab may also be appropriate. Speak with your doctor to discuss your options.

4. Targeted Therapy

Tumour cells sometimes have many mutations (changes) in their DNA (genetic information inside our body's cells). Targeted therapies are drug treatments that target and kill cells with these specific mutations. This can cause tumours to shrink or grow more slowly because a signal has been sent to the cells to stop reproducing and growing. Studies on targeted therapies for uveal melanoma sometimes also use chemotherapy. New targeted therapies are within clinical trial and research phases. Speak with your doctor about whether there are any clinical trials or new treatments available.

5. Chemotherapy

Chemotherapy is the use of chemicals to treat cancer. A trial of chemotherapy may be used only in patients with metastases. There is currently no optimal chemotherapy approach to treat metastases. This means that there are several clinical trials that are investigating which chemotherapy agent, either used alone or in combination with other agents, may be effective in treating metastases.

Outside of a clinical trial, the routine use of palliative cytotoxic chemotherapy is not recommended. The use of chemotherapy for the treatment of patients with metastatic uveal melanoma is associated with very low objective response rates and has never been shown to extend overall survival rates. Sometimes chemotherapy might be used to manage symptoms.

QUESTIONS TO ASK YOUR HEALTHCARE TEAM[1]

ABOUT DISEASE AND TREATMENT:

- What type of cancer do I have?
- What stage is my cancer?
- What are the positives, negatives, and potential side effects of my treatment options?
- What are the expected survival rates with these treatments?
- Will receiving these treatments prevent me from receiving a different type of treatment in the future if I need it?
- Are there any more tests that need to be done before starting treatment?
- Are all of the tests covered by provincial healthcare plans?
- Will there be tests to determine how my disease responds to the treatment?
- How often will these tests be done during and after treatment?
- Will you change my treatment if it does not appear to be working?
- How long will the treatment last?
- How often will I see you during and after treatment?
- What other services are available to help me and my family cope with the disease?
- Are there any clinical trials that I can or should be considering?

ABOUT PROGNOSIS AND SURVIVAL:

- Do you expect these treatments to cure my cancer? If not, what is the goal of this therapy?
- What is the usual life expectancy for this type of cancer?
- What are the best- and worst-case scenarios?

[1] Questions taken from "Questions you may ask" under "Your first appointment" from the Princess Margaret Cancer Centre, the University Health Network (www.theprincessmargaret.ca)

SOCIAL SUPPORT

A diagnosis of uveal melanoma and cancer in general is often filled with uncertainty and anxiety. It is common for people to be upset, scared and angry. Resources are available to support you, they include:

Melanoma Canada Phone & Email Support

Available Monday - Friday, 9 a.m. to 5 p.m. (EST). We aim to respond to all calls and emails within 48 hours. All calls and emails are confidential (private).

For support call 1-877-560-8035 or email support@melanomacanada.ca.

Melanoma Canada Peer-to-Peer Support Program

Connecting with a former patient or caregiver can provide a lot of support. This program connects a trained volunteer who has had a uveal melanoma diagnosis with new and ongoing patients or their caregivers. Patients can ask questions and relieve some of their stress, worries, and fears that come from a diagnosis of uveal melanoma.

This program can connect patients anywhere in Canada and is offered over the phone or email.

If you'd like to become a peer-to-peer volunteer or would like to be matched with a fellow patient or caregiver, please email support@melanomacanada.ca, call 1-877-560-8035 or visit melanomacanada.ca (Note that peer-to-peer support does not replace professional counseling or medical advice.)

Melanoma Canada Private Uveal Facebook Group

This online group provides a virtual space where uveal melanoma patients from across Canada, or their caregivers, can share with others impacted by uveal melanoma. This group is private, and monitored by MC staff, and provides information and insight into the patient journey and a place to discuss the emotional impacts of uveal melanoma.

How to join:
Visit https://www.facebook.com/groups/mncuveal/

Social Media

Connect with Melanoma Canada on Facebook, Twitter, Instagram, and YouTube @melanomacanada

Melanoma Information Sessions

Melanoma information sessions give information and updates on the latest melanoma treatments and support. Patients, their families and friends, and healthcare providers can join these sessions. These sessions are free and are held throughout the year.

To learn more, visit: melanomacanada.ca

Cancer Coaching

A cancer coach can help with emotional, physical, and practical issues that come up during cancer diagnosis, treatment, and management. A cancer coach gives you one-on-one support to identify areas of desired change (i.e., stress reduction or better sleeping habits), set goals, and develop a plan to work towards that change.

To learn more, visit: melanomacanada.ca

Melanoma Research Foundation

(www.melanoma.org)
Cure OM patient online bulletin board is where uveal melanoma patients, caregivers and their loved ones can talk with other diagnosis and challenges with patients and caregivers from around the world.

Scan to join our Uveal Melanoma Support Group

RESOURCES

Eye Plaque Patient Information Booklet

This is a booklet explaining one of the treatments for eye cancer. (UHN Patient Education - Eye Plaque)
https://www.uhn.ca/PatientsFamilies/Health_Information/Health_Topics/Documents/Eye_Plaque.pdf

Cure Ocular Melanoma (the Community United for Research and Education of Ocular Melanoma)

This is an initiative of Melanoma Research Foundation's to increase awareness, education, and research funding for ocular melanoma, while improving the lives of people affected by this disease.
For more information, visit: https://melanoma.org/about-us/programs-initiatives/cure-ocular-melanoma-cure-om/

Vision Registry Platform - The Patient-Powered Platform Focused on a Cure

The Patient Powered Ocular Melanoma Platform unites patients, caregivers, researchers, and physicians across the globe to share knowledge and experience, accelerate progress and advance towards a cure.
For more information visit:
https://melanoma.org/visionregistry/

Eye Cancer Network

This is a dedicated education site for people with eye tumours and their friends and families.
(http://www.eyecancer.com/)

Lost Eye
This site provides support and discussion for people who have lost an eye.
(http://losteye.com/)

Bascom Palmer Eye Institute
This website has information about different eye conditions, including cancer.
(http://bascompalmer.org/)

National Eye Institute
This website has information about eye health and diseases, as well as diagrams of the inside of the eye.
(http://www.nei.nih.gov/)

Impact Genetics
Impact Genetics provides genetic diagnostics for uveal melanoma and other rare diseases.
(http://impactgenetics.com/)

Castle Biosciences
Castle Biosciences provides genetic diagnostics for uveal melanoma and other rare diseases
(https://castletestinfo.com/)

GLOSSARY

Brachytherapy
Uses radioactive material inside your body to treat cancer.

Cancer
Abnormal cells that can divide uncontrollably, invade normal tissues and spread throughout the body.

Choroid
A part of the middle layer of the eye between the sclera (the white part of the eye) and the retina. It has layers of blood vessels that supply nutrients to parts of the eye.

Ciliary body
Located behind the iris and produces a clear fluid in the front of the eye, as well as assisting the eye with focusing at different distances (i.e. accommodation).

Computed Tomography (CT)
Use of X-rays to see into the body.

Cutaneous
Means that it is related to the skin.

Enucleation
The removal of the eye.

External Beam Radiation Therapy (EBRT)
Uses radiation outside of the body to treat cancer.

Iris
The coloured part of the eye that is referred to a person's eye colour.

Magnetic Resonance Imaging (MRI)
Use of radio waves and powerful magnets to see into the body.

Melanocytes
Skin cells that produce a dark pigment called melanin, which is responsible for a person's skin colour.

Melanoma
A cancer of melanocytes.

Metastases
Spreading of cancer throughout the body.

Ocular oncologist
A doctor who specializes in eye cancer.

Oncologist
A doctor who specializes in cancer.

Ophthalmologist
A doctor who specializes in the eye and is a medical doctor (MD).

Optometrist
A healthcare professional who specializes in the eye and is a Doctor of Optometry (OD).

Plaques
Tiny plates.

Pupil
The black dot in the middle of your iris. The pupil changes size to let light into the eye. It gets smaller in bright light and larger when light is dim.

Retina
The inner surface of the eye that senses light.

Tumour
A tissue mass made from an abnormal growth of cells.

Ultrasound
Uses sound waves to see inside the body.

Uvea or uveal tract
The middle layer of the eye which includes the iris, the ciliary body and the choroid.

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Donations are gratefully accepted to support the ongoing publication of this booklet and other educational initiatives.

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