MRF MELANOMA RESEARCH FOUNDATION

CURE OCULAR MELANOMA

OCULAR MELANOMA PATIENT GUIDE

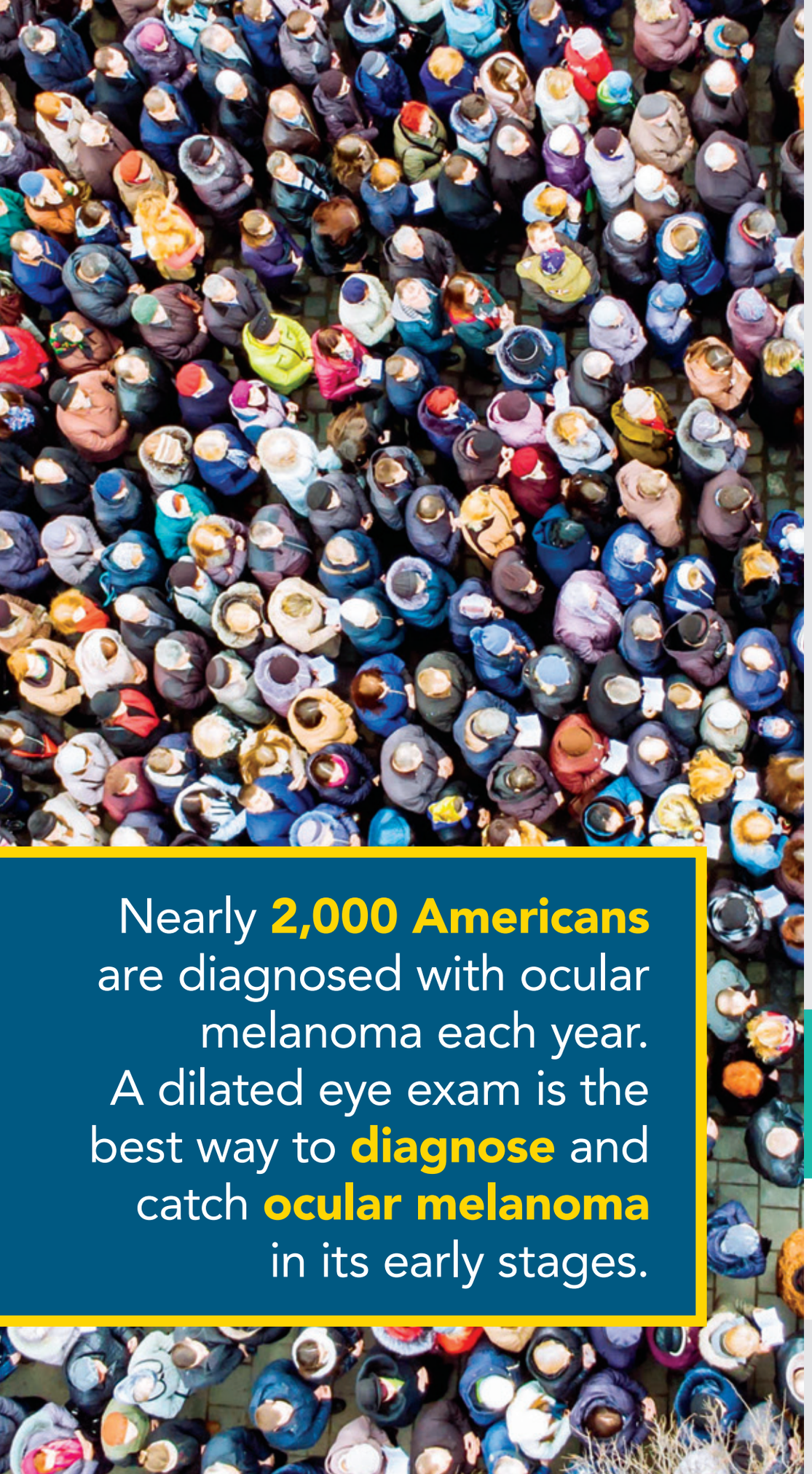
Guiding You Along the Way

PRIMARY UVEAL MELANOMA

METASTATIC UVEAL MELANOMA

CONJUNCTIVAL MELANOMA

LIVING WITH OCULAR MELANOMA



Nearly **2,000 Americans** are diagnosed with ocular melanoma each year. A dilated eye exam is the best way to **diagnose** and catch **ocular melanoma** in its early stages.

Just Diagnosed With Ocular Melanoma…

Now What?

An ocular melanoma (OM) diagnosis can be a scary and overwhelming experience, and it's important to learn all you can about your diagnosis. The truth is, informed and empowered patients live longer, better lives. By arming yourself with knowledge, you'll better understand what you're up against.

Soon, you will likely know more about melanoma than you ever thought possible. You will become familiar with terms and language you never knew before. You will understand the importance of regular skin exams, eye exams, the difference between an optometrist and ophthalmologist and even advances in melanoma research. As a result of all of this knowledge, you may even help prevent someone you love from receiving a melanoma diagnosis.

This is not a community anyone *wants* to join. However, it is important to know that YOU ARE NOT ALONE. At the end of this section, you will find ideas on how to connect with others who have been diagnosed and, if you'd like, ways to get involved in the fight against this disease.

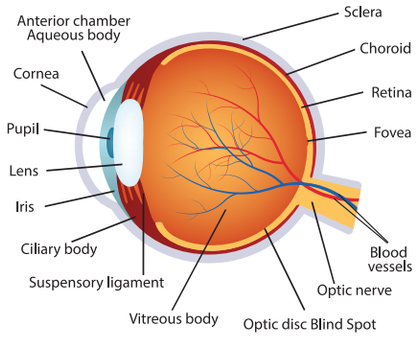
WHAT YOU NEED TO KNOW

- In the U.S. it is estimated that approximately 2,000 new ocular melanoma cases are diagnosed each year.
- Ocular melanoma is the most common primary tumor of the eye in adults.
- Although OM is more common in Caucasian men with light-colored eyes, it does not discriminate by age, race or gender. Everyone is at risk.

Ocular Melanoma — The Basics

Melanoma is a type of cancer, most often of the skin. However, melanoma can also occur in the mucous membranes of the body (mucosal melanoma) and in the eye (ocular melanoma).

Ocular melanoma, or melanoma of the eye, is the most common primary eye tumor in adults. It is the second most common form of melanoma with around 2,000 new cases diagnosed each year in the United States. Like all forms of melanoma, OM begins in melanocytes — the cells that color the skin and eyes, and make moles.



WHAT YOU NEED TO KNOW

So what do you do if you have just been diagnosed with OM?

1 Take a breath and try to stay calm.

2 RESEARCH. EDUCATE. ADVOCATE.

Types of Ocular Melanoma

Different types of melanoma of the eye include:

UVEAL MELANOMA

The uveal tract is made up of three main sections: the choroid, the iris and the ciliary body. Uveal melanoma (UM) can form in any of these layers and is named for where it forms:

- **Choroidal melanoma** begins in the layer of blood vessels — the choroid — beneath the retina.
- **Iris melanoma** occurs in the front, colored part of the eye.
- **Ciliary melanoma** occurs in the back part of the eye — in the ciliary body.

CONJUNCTIVAL MELANOMA

The conjunctiva is the clear tissue that covers the white part of the eye, as well as the inside of the eyelids. Conjunctival melanoma is very rare. It often appears as a raised tumor and may contain little or even no pigment. Conjunctival melanoma most commonly occurs in the bulbar conjunctiva — the mucous membrane that covers the outer surface of the eyeball. Unlike other forms of ocular melanoma that spread most often to the liver, when conjunctival melanoma spreads, it most often spreads to the lymph nodes and lungs.

Ocular Melanoma vs. Cutaneous Melanoma

Cutaneous (skin) melanoma and **ocular** melanoma are distinct conditions that share the same name but are biologically and genetically very different from one another. Both forms of melanoma begin in melanocytes but, beyond that, there are many differences and only a few similarities:

INCIDENCE

Cutaneous and conjunctival melanoma have increased in frequency over the last several decades, but this trend is not evident in UM. Cutaneous melanoma occurs in approximately 153 per one million Americans each year. On the other hand, about six Americans per one million are diagnosed with melanoma of the eye each year.

PROGNOSIS AND METASTASES

The size of the tumor and the degree of invasion are major factors in determining the prognosis — or outcome — in melanoma. When the disease spreads, however, it spreads differently. Uveal melanoma tends to spread through the blood, while cutaneous and conjunctival melanoma tend to spread through the lymphatic system. UM metastasizes in about half of all cases and when it spreads, it spreads to the liver almost 90% of the time. Cutaneous and conjunctival melanoma are less predictable and can spread to the lymph nodes, liver, lungs, brain, bone and soft tissue.

Diagnosing Ocular Melanoma

Ocular melanoma is most often detected by an optometrist or an ophthalmologist during a dilated eye exam. Often, OM is asymptomatic until the tumor grows large enough to create visual disturbances. Iris and conjunctival melanoma may sometimes be diagnosed by external — from the outside — examination. Detection of choroidal or ciliary melanoma requires a thorough dilated eye exam.

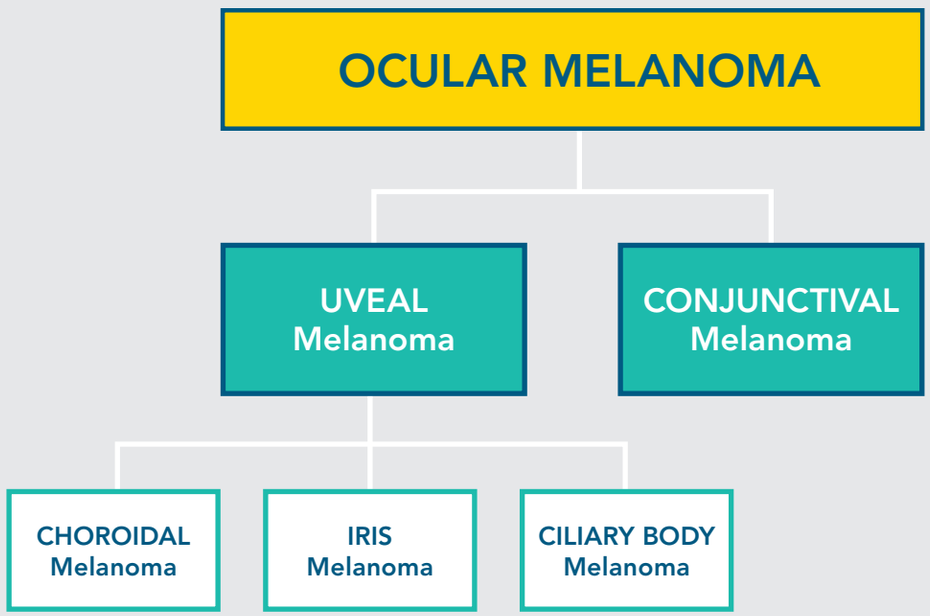
After an OM diagnosis, your doctor will take an x-ray, MRI, CT scan and/or PET scan to check the body for signs of cancer beyond the eye.

Unlike cutaneous melanoma, a biopsy is not usually taken to diagnose OM. Rather, OM tends to be a clinical diagnosis — meaning it is often made based on signs and symptoms.

REMINDER

WHAT YOU NEED TO KNOW

- Educate yourself and loved ones about your diagnosis.
- Find a support system. Family, friends, strangers, in-person, online, phone support — choose one (or more) that is best for you.
- Ocular melanoma survival statistics describe a group of similar patients…but they may have nothing to do with your individual chance of survival.
- Every patient is different. There is no "blanket" treatment plan.
- It is important to be an active participant in your treatment. Seek out an OM specialist. Be your own advocate.



Genetic Testing, Tumor Size and Metastatic Risk

Once ocular melanoma is diagnosed, several items should be discussed with your treatment team that will help everyone learn more about your specific diagnosis. While treating the primary eye tumor remains the most important clinical issue, determining a patient's risk for developing metastatic disease is also important.

THE AMERICAN JOINT COMMITTEE ON CANCER (AJCC)

The *AJCC Cancer Staging Manual* is a resource that can help guide your treatment team in assessing the extent of the tumor, lymph node involvement and distant metastasis. This classification system organizes these individual factors into prognostic stages. Each stage indicates different risk for possible metastasis and mortality.

Common Genetic Tests in OM

Healthcare providers can determine a patient's risk for metastatic disease based upon the size and location of the tumor. From a biopsy, they can also test the genes in the tumor itself to help determine the risk of cancer recurrence and metastasis. The results of these tests can help your treatment team develop an appropriate and individualized surveillance plan and, if necessary, a treatment plan.

Timing is critical because:

- **These genetic tests must be performed on a biopsy sample of the tumor.**
- **The biopsy sample must be taken before the tumor is treated with radiation.**

Two different types of genetic testing may be performed:

1. CHROMOSOME ANALYSIS (KAROTYPING)

Abnormalities in chromosomes 1, 3, 6 and 8 may indicate an increased risk of uveal melanoma metastasis. About half of UM tumors will show an alteration of chromosome 3 and metastatic UM occurs almost exclusively in patients with a loss of chromosome 3 *(monosomy 3)*.

2. GENETIC EXPRESSION PROFILE (GEP) TESTING

This test measures the gene expression profile (GEP), or molecular signature, of the tumor. It is based on a 15-GEP test and groups the tumor into low-, medium- or high-risk for metastasis over the next five years.

Class 1A tumors have a very low risk of metastasis.

Class 1B tumors have an intermediate risk of metastasis.

Class 2 tumors have a high risk of metastasis.

Should I have my tumor tested?

Studies have shown that, if given the opportunity, most patients prefer to know their risk. Patients often feel that they can make more informed decisions and have reported that knowing the results of the genetic test were valuable regardless of the results. Ultimately, the hope with genetic testing is that individual clinical follow-up can be tailored to a patient's risk of metastasis and, perhaps, lead to earlier detection and therapy.

As with any genetic testing, this is a personal decision and many factors must be considered. Speak with your doctor about how long it will take to find out the results and whether or not insurance will cover the cost of the test(s). Speaking with a certified genetic counselor may also be helpful.

Tumor Size

The size of the eye tumor may also impact the prognosis and risk of metastasis. For example, a large tumor has a higher risk of spreading than a small tumor.

Small: 1.0–2.5 mm in height; greater than 5 mm at the base

Medium: 2.5–10 mm in height; less than or equal to 16 mm at the base

Large: greater than 10 mm in height; greater than 16 mm at the base

Genetic Mutations in OM

A variety of genetic mutations have been found in OM. Although no therapies are currently approved by the FDA for the treatment of metastatic OM, several are being studied in clinical trials. Therefore, knowing your mutation status may be helpful. The following mutations are thought to "drive" the disease:

- **GNAQ and GNA11**
  The GNAQ and GNA11 mutations are the most common mutations in uveal melanoma, appearing in more than 80% of all cases. These mutations do not seem to be associated with patient outcomes or risk of metastasis.
- **BAP1**
  The BAP1 mutation is found in about half of uveal melanoma cases. It is most often associated with older patient age and high risk for metastasis. The BAP1 mutation is strongly associated with a Class 2 gene expression profile (GEP).
- **BRAF**
  The BRAF mutation is common in cutaneous melanoma but is rare in uveal melanoma. It is found in about 30% of conjunctival melanoma cases.

Speak with your oncologist about what your mutation status could mean and when your tumor should be tested.

What does this mean for treatment?

Currently, this does not impact treatment for primary OM. These results may impact surveillance and/or adjuvant therapy available in clinical trials.

GLOSSARY AND RESOURCES

Common Terms

ADJUVANT THERAPY
Used after the primary treatment, such as surgery, to decrease the chance of the ocular melanoma returning or spreading.

BIOPSY
The removal of cells or tissues for examination under a microscope.

BONE SCAN
Imaging test that uses radioactive material to check for bone involvement.

CT SCAN
Rather than just one picture like an x-ray, CT scanners can help detect melanoma in soft tissues, like internal organs and the liver, by taking many pictures that provide a detailed image of the body.

EXTENSION
The melanoma has spread outside the eye by extending through the wall of the eye.

MALIGNANT
A term often used in melanoma, meaning invasive, cancerous or capable of metastasis.

MEDICAL ONCOLOGIST
A doctor who specializes in diagnosing and treating cancer. A medical oncologist often is the main healthcare provider for someone who has cancer. He or she may also give supportive care and coordinate treatment given by other specialists.

METASTATIC
The spread of the melanoma from the original site to other places in the body.

MRI
Imaging test used primarily to determine if melanoma has spread to the brain, spinal cord or liver. Unlike x-rays and CT scans, MRIs use radio waves and magnets to create pictures of the body.

OCULAR ONCOLOGIST
An eye cancer physician who provides comprehensive care for patients with eye tumors. Ocular oncologists are trained in ophthalmology and have completed specialized training in eye cancers. Ocular oncologists diagnose, treat and research a variety of malignancies that include the eye, eyelid and surrounding tissue.

OPHTHALMOLOGIST
A medical or osteopathic doctor who specializes in eye and vision care. An ophthalmologist diagnoses and treats eye diseases and is licensed to practice medicine and surgery. Many ophthalmologists are also involved in scientific research in eye diseases and disorders.

OPTOMETRIST
A health professional who provides primary vision care, sight testing and management of vision changes. An optometrist can perform eye exams, vision tests and detect certain eye abnormalities. An optometrist does not perform surgery.

PATHOLOGIST
A specialist in pathology who interprets and diagnoses the changes caused by disease in tissues and body fluids.

PET SCAN
Imaging test that looks for metabolically active areas in the body. PET scans are not as detailed as CT or MRI scans but can provide helpful information about the whole body.

RECURRENCE
The return of the melanoma.

SURGICAL ONCOLOGIST
A doctor who performs biopsies and other surgical procedures in cancer patients.

SYSTEMIC TREATMENT
Treatments that travel through the bloodstream, affecting cells throughout the body. Examples include immunotherapy and chemotherapy.

ULTRASOUND
A procedure that uses high-energy sound waves to look at tissues and organs inside the body. May also be used to evaluate a tumor.

X-RAY
Imaging test most often used to determine if melanoma has spread to the lungs.

FREE PATIENT RESOURCES

Online Patient Forum (MPIP)	The MRF's online community for melanoma patients can be found at www.mpip.org.
Ask a Nurse	The MRF's nurse provides free, personalized answers to melanoma questions and can be emailed at askanurse@melanoma.org.
Melanoma Treatment Center Finder	An interactive map listing melanoma centers of excellence and treatment centers which have experience treating melanoma. Visit www.melanoma.org to learn more.
Educational Resources and Recordings	View webinars, slides and recordings from educational events at www.melanoma.org/educational-recordings.
Support Groups	The MRF partners with a variety of organizations who offer patient and caregiver support. Email cureom@melanoma.org to learn more.
Social Media	Follow CURE OM on Facebook and the MRF on Facebook, Twitter and Instagram.

PRIMARY UM

What do I need to know?

DEFINITION

Primary uveal melanoma means that the tumor originated in the eye.

TREATMENT OF THE PRIMARY TUMOR

The goals of treating the primary tumor are to stop tumor growth, spare the eye, preserve vision and improve patient survival. Treatment most often includes a combination of radiation and surgery but depends on the size and location of the tumor, among other factors.

SOMETHING TO CONSIDER:

A melanoma diagnosis of any kind is never easy. Patients who have been diagnosed with UM often feel a variety of emotions ranging from denial to anger. A UM diagnosis can be especially difficult. You may find yourself continuously wondering whether or not your melanoma has spread, or will spread, to other places in your body. Know that these feelings and emotions are normal. Meeting others, joining support groups and learning about this disease may help you during this difficult time.

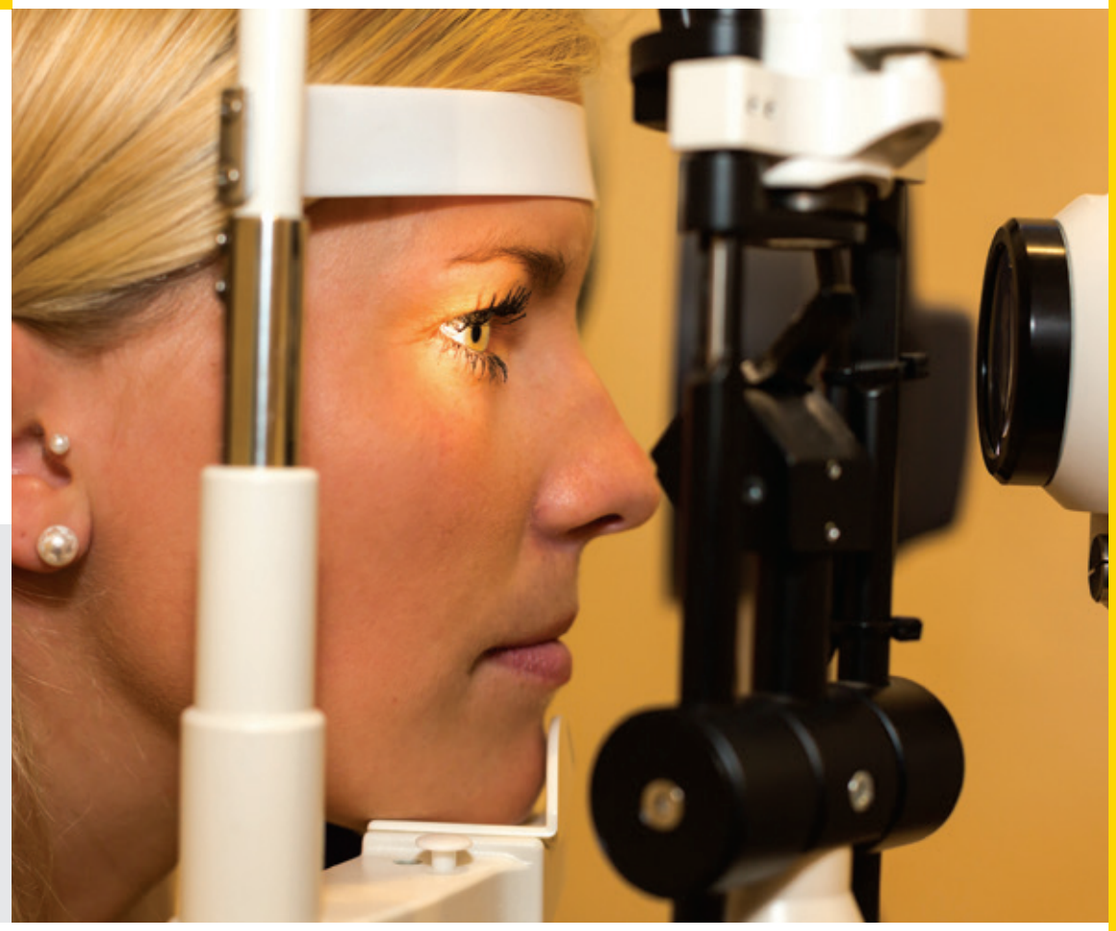
Radiation

For most small and medium-sized tumors, radiation is the recommended treatment. There is currently no evidence that one form of radiation is better than the other.

The different types of radiation therapy include:

- **Plaque Brachytherapy (Radiotherapy)**
  A thin piece of metal, called a plaque, is sewn onto the outside wall of the eye. The radioactive seeds in the plaque give off radiation, which aims to kill the tumor. The treatment usually lasts a few days and the plaque is removed at the end of treatment. This is the most common therapy in the United States for posterior (choroidal and ciliary body) ocular melanoma and is considered the standard of care for most UM patients with small or medium-sized tumors. After this treatment, removal of the eye is not usually necessary, and many patients, depending on the tumor location, are able to retain some degree of visual function.

- **Proton Beam Radiotherapy**
  Clips are surgically placed onto the eye at the tumor base and an external beam of radiation is aimed at the tumor, most often through the front of the eye. Treatment is usually finished after 3–5 daily outpatient treatments.



Surgery

In some cases, the recommended treatment for ocular melanoma is surgical removal of the tumor. Surgery is often recommended for tumors of large size and for iris melanomas. Surgery may also be recommended after radiation.

Types of surgery include:

- **Enucleation**
  Removal of the eye is sometimes recommended in cases involving large tumors. Following enucleation, an artificial eye may be placed in the socket and, with the help of an ocularist, made to look like a natural eye.
- **Iridectomy**
  Removal of part of the iris where the tumor is present.
- **Iridocyclectomy**
  Removal of part of the iris (iridectomy) as well as the ciliary body (cyclectomy) where the tumor is present.
- **Trans-Scleral Local Resection**
  Removal of the tumor through an opening in the wall, or the white part, of the eye. This is often used when the tumor is large. A radioactive plaque may be placed over the treated area to reduce the risk of tumor recurrence.

Other Possible Treatments

- **Transpupillary Thermotherapy**
  The temperature of the tumor is slowly raised, killing cancer cells and shrinking the tumor. This treatment is most often used for small tumors in the retina and choroid.
- **Cryotherapy**
  The temperature of the tumor is lowered since melanocytes are susceptible to freezing.
- **Gamma Knife**
  A focused, single dose of radiation is given to the tumor, sparing healthy tissue in and around the eye.
- **Intraocular Injections**
  Injections in the eye are used to administer medications to treat a variety of ocular conditions. These medications may include steroids for inflammation and or anti-angiogenic factors, which shrink blood vessels. Intraocular injections might be used if changes have occurred to the retina and optic nerve (retinopathy) due to radiation.

Adjuvant Treatment

In skin melanoma, adjuvant treatment is treatment used after the primary treatment (most often, surgery), to prevent the spread of disease. It can also refer to treatment used in addition to the primary form of treatment. Currently, in ocular melanoma, all adjuvant treatments are in the clinical trial stage and nothing yet has been proven to show beneficial results.

Clinical Trials

There is some important information you should know about clinical trials in ocular melanoma:

- Trials help physicians determine which patients should receive which drugs in which order (sequence).
- Trials may provide you access to therapies not yet approved by the FDA but that may be more effective.
- Trials are usually (but not always) free to participate in and you may have more diagnostic tests while participating than you otherwise would have during regular treatment. Be sure you understand your health insurance policy and the coverage of the clinical trial so you are fully aware of what is covered and what is not.
- You can choose to stop participating in a trial at any time.

Visit **www.melanoma.org/clinical-trials** to explore a database of clinical trials that may be right for you.

QUESTIONS TO ASK YOUR DOCTOR

> Do I need to have my eye removed?
> What are the dimensions of the tumor? What does this mean for treatment options?
> Will you do a biopsy of the tumor? Why or why not?
> Will you test my tumor for genetic mutations?
> Do mutations affect the risk for metastasis?
> How do mutations affect treatment?
> How will you determine if the cancer has spread?
> What are my treatment options and what are the differences?
> Should I get a second opinion or explore another treatment center with more experience with ocular melanoma?
> Which treatment do you recommend?
> What are the side effects of each treatment? How soon will those side effects emerge?
> Will my vision be affected?
> How will this diagnosis affect my normal, daily life?

METASTATIC UM

What do I need to know?

Treatment of Metastatic UM

If UM has spread beyond the eye, it is considered *metastatic*. Approximately half of UM patients will develop metastatic disease, although each person's individual risk is based on factors such as tumor genetics and other clinical characteristics. When UM metastasizes, it first spreads to the liver nearly 90% of the time.

It is important to note that the treatment of uveal melanoma can be very different from that of cutaneous melanoma. While some treatments are used both in cutaneous melanoma and UM, the diseases are very different. It is important for your treatment team to understand the differences.

Although there are currently no FDA-approved treatments for metastatic UM, clinical trials exploring a variety of treatment options are emerging all the time. Visit **www.melanoma.org** to find an ocular melanoma specialist who can discuss all possible treatment options with you, including clinical trials.

QUESTIONS TO ASK YOUR DOCTOR

- Where has the UM spread?
- Do I need additional scans to determine the extent of the disease?
- Have you tested for genetic mutations? How will this affect treatment?
- Do you recommend liver-directed therapy or systemic therapy?
- Can different treatments be combined?
- Should I consider clinical trials? If so, which ones?
- What are the side effects of each treatment?
- Do I have to travel for the treatment or can I receive it close to home?
- How will this diagnosis and the treatment affect my day-to-day life?
- If I choose no treatment for my metastatic disease, what is my life expectancy?
- Do I need scans on a regular basis? If so, what type of scans do you recommend?
- What should my follow-up plan be?
- Will I be able to continue my normal daily life?
- Should I seek a second opinion?

Treatments Targeting the Liver

These treatments may be used in conjunction with systemic (full body, or through the bloodstream) treatments, so be sure to discuss them with your treatment team.

Note: OM specialists are often asked if liver transplants are an option when the melanoma has metastasized. Unfortunately, this is not an option.

LOCALIZED TREATMENTS FOR INDIVIDUAL TUMORS IN THE LIVER AND OTHER ORGANS

- **Resection**
  Surgical removal of the tumor. Resection is mainly used when a single tumor is present. It is often reserved for patients who are several years out from a primary eye tumor diagnosis and repeated imaging studies show only one tumor. Since liver resection can sometimes remove some healthy tissue along with the tumor, it is reserved for select cases.

- **Ablation**
  Ablation involves inserting small probes into tumors and heating (i.e., radio frequency ablation, microwave ablation) or freezing (cryoablation) the tumors to kill them. This can be done through the skin or surgically. Like resection, this is typically not recommended if multiple tumors are present. Ablation can be used in other areas of the body beyond the liver, such as the lung, kidney and soft tissue.

- **Radiation**
  Targeted radiation can be used to treat liver disease. This includes treatments such as stereotactic radiosurgery (Gamma Knife and Cyber Knife) that can be used to target specific tumors while sparing normal tissue. Radiation can be used to treat other areas of the body including lung, bone and brain, and can be used to treat isolated metastases or to relieve symptoms caused by a specific lesion.

These treatments may be used in conjunction with other treatments.

Transarterial Catheter-Directed Liver Therapies

REGIONAL LIVER-DIRECTED THERAPIES THAT AFFECT THE ENTIRE LIVER INCLUDE:

- **Immunoembolization**
  Immunotherapy drugs called cytokines are injected into the hepatic arteries (the arteries that supply the liver). This is combined with embolization of the hepatic artery. Embolization blocks off the blood supply to the tumors using injections into the arteries. The goal is to induce an inflammatory response in the tumor. This process may also stimulate the immune system outside the liver, which could help suppress tumor growth in other areas of the body.

- **Chemoembolization** (TACE)
  A chemotherapy drug is injected into the hepatic arteries. The goal is to block off the blood supply to the tumors.

- **Radioembolization**
  Small beads, embedded with a radioactive material, are injected into the hepatic arteries. These microspheres emit high doses of radiation to the tumor cells to destroy them. This treatment is sometimes referred to as Y-90 radioembolization, SIR-Spheres or TheraSpheres.

  Embolization treatments can be safely performed because the liver gets its blood supply from both the hepatic artery and a separate vein, called the portal vein. Tumors preferentially get their blood supply from the artery, and the healthy liver from the vein. That is why the blood supply can be cut off through the hepatic artery and not cause significant damage to the healthy liver.

- **Hepatic Arterial Chemoinfusion** (HAI)
  Infusion of chemotherapy into the liver through a specialized infusion system in which a catheter is placed into the hepatic artery to directly and continuously deliver the chemotherapy to the liver. Before this procedure, patients must have a surgery to isolate the liver's blood supply so the infused chemotherapy does not leak out of the liver. This direct infusion allows for fewer side effects of chemotherapy and allows high doses to be delivered.

- **Isolated Hepatic Perfusion** (IHP)
  In IHP, a catheter is placed into the hepatic artery and another is placed into the vein that takes blood away from the liver. This temporarily separates the liver's blood supply from blood circulating through the rest of the body and allows high doses of chemotherapy to be directed only to the liver. When this is done percutaneously, or through the skin, it is referred to as Percutaneous Hepatic Perfusion (PHP). This procedure is currently only available on clinical trials.

These treatments may be used in conjunction with other treatments.

Systemic Treatments

Although there are currently no FDA-approved systemic treatments for metastatic uveal melanoma, some clinicians recommend treatment with therapies that have been FDA-approved for cutaneous melanoma. In addition, ongoing clinical trials may give patients access to systemic agents before they are approved.

- **Immunotherapy**
  A type of systemic treatment given to activate a person's immune system so that it will destroy melanoma cells within the body. Several immunotherapies are FDA-approved for cutaneous melanoma and some are being studied in uveal melanoma. However, success with these treatments in UM has been limited so far. Clinical trials are currently underway to better understand immunotherapies in UM.

- **Targeted Therapy**
  A form of treatment in which drugs are developed with the goal of destroying cancer cells while leaving normal cells intact. These drugs are designed to interfere with the specific molecules, genetic mutations in the tumor itself, that are driving the growth and spread of the tumor.

  Common mutations in cutaneous melanoma (such as BRAF) are not often found in UM. The most common mutations in uveal melanoma are the GNAQ, GNA11 and BAP1 genes. Clinical trials are currently underway to better understand these mutations and possible treatment options.

- **Chemotherapy**
  Overall, chemotherapy has not been shown to be effective for uveal melanoma. However, it may still be recommended in some cases.

Clinical Trials

There is some important information you should know about clinical trials in uveal melanoma:

- Trials help physicians determine which patients should receive which drugs in which order (sequence).
- Trials may provide you access to therapies not yet approved by the FDA but that may be more effective.
- Trials are usually (but not always) free to participate in and you may have more diagnostic tests while participating than you otherwise would have during regular treatment. Be sure you understand your health insurance policy and the coverage of the clinical trial so you are fully aware of what is covered and what is not.
- You can choose to stop participating in a trial at any time.

Visit **www.melanoma.org/clinical-trials** to explore a database of clinical trials that may be right for you.

Managing Side Effects

Unfortunately, side effects are a reality of every treatment option. Side effects vary by treatment and by individual. Some patients experience every possible side effect while others experience very few, and sometimes no side effects from their treatment.

Common side effects of certain immunotherapy and targeted therapy melanoma treatments include, but are not limited to:

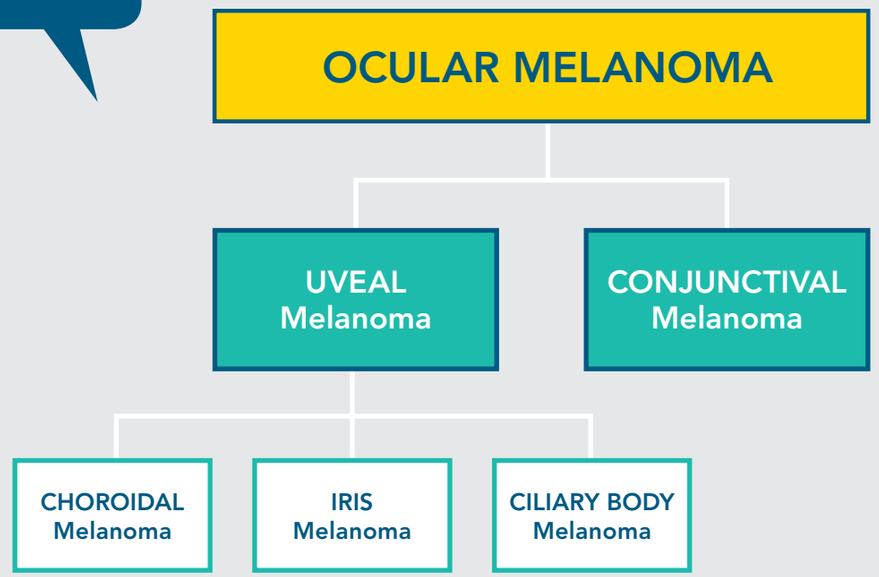
- Diarrhea
- Lymphedema
- Itching
- Nausea
- Vitiligo (loss of pigment)
- Thyroid issues
- Fever
- Constipation
- Skin rash
- Colitis
- Fatigue
- Joint pain

Be sure to **talk to your doctor about all side effects that you experience** as soon as you begin experiencing them. This will allow your treatment team to manage the side effects more effectively.

TIPS TO REMEMBER

1. Never hesitate to mention your side effects to your treatment team. Keeping your treatment team informed of all side effects as soon as they occur is of the utmost importance.
2. Experiencing few or no side effects does not mean the treatment isn't working.
3. It's impossible to know how you will react to any given treatment.
4. There is no one-size-fits-all treatment for ocular melanoma — everyone's case is different.

REMINDER



CONJUNCTIVAL MELANOMA

What do I need to know?

What is Conjunctival Melanoma?

The conjunctiva is the clear tissue that covers the white part of the eye, as well as the inside of the eyelids. Conjunctival melanoma often appears as a raised tumor and may contain little or no pigment. Conjunctival melanoma most commonly occurs in the *bulbar conjunctiva* — the mucous membrane that covers the outer surface of the eyeball.

Conjunctival melanoma is very rare, making up only 2% of all eye tumors and 0.25% of all melanomas. According to registry data from five countries, overall incidence is between 0.24 to 0.8 cases per million. However, incidence appears to be increasing, just as incidence rates are increasing in melanoma of the skin, suggesting a possible association between conjunctival melanoma and ultraviolet (UV) exposure.

Diagnosing Conjunctival Melanoma

A conjunctival melanoma diagnosis usually begins with a thorough examination of the eye and all conjunctival surfaces, including the inside of the eyelids. It is recommended that photographs be taken before a biopsy is taken. This allows the doctor to properly document the extent of the melanoma and may assist in planning for treatment and follow-up.

A biopsy of the tumor and examination of the tissue under a microscope will rule out or diagnose conjunctival melanoma. If conjunctival melanoma is diagnosed, the extent of disease and treatment plan should be discussed with a trained ocular oncologist.

Primary Management and Treatment

Surgery is the most common type of treatment for conjunctival melanoma. Enucleation, or removal of the eye, has been used for the treatment of extensive conjunctival melanoma. However, data does not currently indicate that this improves overall survival. Therefore, wide local excision and biopsy is the current standard approach.

Excision is often followed by one or more types of adjuvant therapy in an effort to prevent the melanoma from spreading, or metastasizing. Types of adjuvant therapies could include cryotherapy (using freezing or near-freezing temperatures), topical chemotherapy or radiation therapy.

Long-term follow-up of patients with conjunctival melanoma is recommended in order to detect recurrences or metastatic disease. Patients should be monitored for recurrence by a trained ocular oncologist.

Living with Conjunctival Melanoma

Please take a moment to review the final tab of this booklet — Living with Ocular Melanoma — for helpful information regarding follow-up care, coping with vision issues and living with monocular vision.

Prognosis and Metastases

Conjunctival, uveal and cutaneous melanoma are distinct from one another. Therefore, they each require different treatment strategies. While there is no standardized treatment for uveal or conjunctival melanoma, significant advances have been made in our understanding of these rare melanoma subtypes. This has led to novel targeted therapy and immunotherapy approaches.

When conjunctival melanoma spreads, it often behaves more closely to cutaneous melanoma in that it usually spreads through the lymph nodes. From there, it has the ability to spread to the lungs, liver, soft tissues, bone and brain. When uveal melanoma spreads, it most often spreads to the liver and doesn't usually spread through the lymph nodes.

Because conjunctival melanoma usually spreads through the lymph system, sentinel lymph node biopsy (SLNB) may be considered and discussed with your treatment team. Risk factors for metastasis include tumor thickness, ulceration and mitotic rate. These are known risk and prognostic factors for cutaneous melanoma and were incorporated into staging criteria.

Metastatic Treatment of Conjunctival Melanoma

Although there are currently no FDA-approved systemic treatments for conjunctival melanoma that has metastasized, some clinicians recommend treatment with therapies that have been FDA-approved for cutaneous melanoma. In addition, ongoing clinical trials may give patients access to systemic agents before they are approved.

- **Immunotherapy**
  A type of systemic treatment given to activate a person's immune system so that it will destroy melanoma cells within the body. Several immunotherapies are FDA-approved for cutaneous melanoma and some are being studied in ocular melanoma.
- **Targeted Therapy**
  A form of treatment in which drugs are developed with the goal of destroying cancer cells while leaving normal cells intact. These drugs are designed to interfere with the specific molecules, genetic mutations in the tumor itself, that are driving the growth and spread of the tumor.

  For example, the BRAF mutation, which is found in about 50% of cutaneous melanomas, is also present in about 30% of conjunctival melanomas. Therefore, some clinicians may recommend targeted therapy for the treatment of conjunctival melanoma in which the BRAF mutation has been found.
- **Chemotherapy**
  Overall, chemotherapy has not been shown to be effective for ocular melanoma. However, it still may be recommended in some cases.

- **Clinical Trials**
  Clinical trials should be explored as a treatment option for anyone diagnosed with conjunctival melanoma.

  Here's why:

  – Trials help physicians determine which patients should receive which drugs in which order (sequence).

  – Trials may provide access to therapies not yet approved by the FDA but that may be more effective.

  – Trials are usually (but not always) free to participate in and you may have more diagnostic tests while participating than you otherwise would have during regular treatment. Be sure you understand your health insurance policy and the coverage of the clinical trial so you are fully aware of what is covered and what is not.

  – You can choose to stop participating in a trial at any time.

Visit **www.melanoma.org/clinical-trials** to explore clinical trials that may be a good fit for you.

QUESTIONS TO ASK YOUR DOCTOR

> What is my risk of the melanoma spreading?
> How will you determine if the cancer has spread?
> What is adjuvant therapy?
> Should I consider adjuvant therapy or explore clinical trials?
> Do you recommend immunotherapy or targeted therapy?
> Do I need scans on a regular basis? If so, what type of scans do you recommend?
> Has my melanoma been tested for genetic mutations, such as the BRAF mutation?
> What should my follow-up plan be?
> Will I be able to continue my normal, daily life?
> Should I seek a second opinion?

Survivorship

Follow-Up Care

Follow-up care is different for every person. Factors to consider can be anything from the results of the tumor biopsy to the location of the tumor and even the medical provider.

Follow-up care will consist of ongoing monitoring and surveillance, including:

- **Scans** (MRI/CT/PET scan/x-ray/ultrasound) — Scans are a way to monitor the spread of the disease. Scans are likely to be scheduled on a recurring basis, usually every three to six months, but will depend on your doctor's recommendations.
- **Routine visits** with your ophthalmologist and medical oncologist.

Coping With Vision Issues

Depending on the treatment received, vision loss or monocular vision may become your new normal. Adjusting to monocular vision or vision loss will take time, so try not to get discouraged.

Support services from social workers, therapists and loved ones may be helpful when adjusting to the loss of vision. It is normal to experience a period of grief due to these new changes and challenges. Always remember that there are people trained to assist you during this time.

Resources for vision loss include adaptive services for reading, installing track lighting in areas that might need more light, services that perform home assessments and transportation plans if driving is affected. Employers may be able to help with lighting, reading assistance, screen shields or lens filters for more sensitive eyes. In addition, occupational therapists may be able to assist with visual perception issues.

QUESTIONS TO ASK YOUR DOCTOR

- What is my risk of the melanoma spreading?
- How will you determine if the cancer has spread?
- Are there any symptoms I should be aware of that could signal that the cancer has spread?
- Are there changes to my diet or lifestyle that will make a difference in my cancer battle?
- What is adjuvant therapy?
- Should I consider adjuvant therapy or explore clinical trials?
- Do I need scans on a regular basis? If so, what type of scans do you recommend?
- What should my follow-up plan be?
- Will I be able to continue my normal, daily life?
- Should I seek a second opinion?

Living With Monocular Vision

Losing vision in one of your eyes takes some adjustment, both physically and emotionally. It takes time, so be gentle on yourself during this adjustment period.

Depth perception might be affected in some of the following ways:

- judging distances while walking and using the stairs
- catching objects in the air
- judging the heights of steps and the widths of entrances
- pouring liquids into containers
- judging how close people are as they move in and out of your field of vision

Double vision may also become a challenge and is a known side effect of radiation therapy. Your brain will eventually start to assist you in compensating for the change in vision. Most day-to-day tasks and activities should fall back into place after an adjustment period. Be sure to work with your optometrist if you use corrective lenses to ensure your remaining eye is receiving the assistance it needs.

Driving is still an option but be patient as you adjust to your new condition. Take the time to use your mirrors, become comfortable with the size of your vehicle and the blind spots that may occur while driving. Stopping, turning and changing lanes could be more challenging than they were before.

THANK YOU TO THE MANY PATIENTS, CAREGIVERS AND CLINICIANS WHO PROVIDED WISDOM, EXPERIENCE AND RECOMMENDATIONS AS THIS GUIDE WAS DEVELOPED.

JOIN THE FIGHT AGAINST MELANOMA

Melanoma does not discriminate by race, age or gender. It knows no boundaries and is being diagnosed at alarming rates in children, teens, women and men.

You can join the fight by visiting **www.melanoma.org/get-involved.**

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