About Eye Cancer

Overview and Types

If you have been diagnosed with eye cancer or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- What Is Eye Cancer?

Research and Statistics

See the latest estimates for new cases of eye cancer and deaths in the US and what research is currently being done.

- Key Statistics for Eye Cancer
- What’s New in Eye Cancer Research and Treatment?

What Is Eye Cancer?

Cancer starts when cells in the body begin to grow out of control. Cells in nearly any part of the body can become cancer, and can spread to other areas of the body. To learn more about how cancers start and spread, see What Is Cancer?

An eye cancer starts in the eye. There are different types of eye cancers. To understand eye cancers, it helps to know something about the parts of the eye and what they do.

Parts of the eye

The eye has 3 major parts: the eyeball (globe), the orbit, and the adnexal structures.
Eyeball

The main part of the eye is the eyeball (also known as the globe), which is mostly filled with a jelly-like material called vitreous humor. The eyeball has 3 main layers: the sclera, the uvea, and the retina.

Sclera: The sclera is the tough, white covering over most of the outside of the eyeball. In the front of the eye it is continuous with the cornea, which is clear to let light through.

Uvea: The uvea is the middle layer of the eyeball. It is where most melanomas of the eye develop. The uvea has 3 main parts:

- The iris is the colored part of the eye (most often blue or brown). It surrounds the pupil, the small opening that lets light enter the eyeball.
- The choroid is a thin, pigmented layer lining the eyeball that nourishes the retina and the front of the eye with blood.
- The ciliary body contains the muscles inside the eye that change the shape of the lens so that the eye can focus on near or distant objects. It also has cells that make aqueous humor, the clear fluid in the front of the eye between the cornea and the lens.

Retina: The retina is the inner layer of cells in the back of the eye. It is made up of specialized nerve cells that are sensitive to light. These light-sensing cells are connected to the brain by the optic nerve. When light enters the eye it passes through
the lens, which focuses it on the retina. The pattern of light (image) appearing on the retina is sent through the optic nerve to an area of the brain called the visual cortex, allowing us to see.

Cancers that affect the eyeball are called intraocular (within the eye) cancers.

**Orbit**

The orbit consists of the tissues surrounding the eyeball. These include muscles that move the eyeball in different directions and the nerves attached to the eye.

Cancers of these tissues are called orbital cancers.

**Adnexal structures**

Adnexal (accessory) structures include the eyelids and tear glands. Cancers that develop in these tissues are called adnexal cancers.

**Cancers in the eye (intraocular cancers)**

Two types of cancers can be found in the eye.

**Primary intraocular cancers** start inside the eyeball. In adults, melanoma is the most common primary intraocular cancer, followed by primary intraocular lymphoma. These 2 cancers are the focus of this document.

In children, retinoblastoma (a cancer that starts in cells in the retina) is the most common primary intraocular cancer, and medulloepithelioma is the next most common (but is still extremely rare). These childhood cancers are discussed in Retinoblastoma.

**Secondary intraocular cancers** start somewhere else in the body and then spread to the eye. These are not truly “eye cancers,” but they are actually more common than primary intraocular cancers. The most common cancers that spread to the eye are breast and lung cancers. Most often these cancers spread to the part of the eyeball called the uvea. For more information on these types of cancers, see our documents on them.

**Intraocular melanoma (melanoma of the eye)**
Intraocular melanoma is the most common type of cancer that develops within the eyeball in adults, but it is still fairly rare. Melanomas of the skin are much more common than intraocular melanomas.

Melanomas develop from pigment-making cells called melanocytes. When melanoma develops in the eye, it is usually in the uvea, which is why these cancers are also called uveal melanomas.

About 9 out of 10 intraocular melanomas develop in the choroid or ciliary body (which are parts of the uvea). Choroid cells make the same kind of pigment as melanocytes in the skin, so it’s not surprising that these cells sometimes form melanomas.

Most of the other intraocular melanomas start in the iris (also part of the uvea). These are the easiest for a person (or their doctor) to see because they often start in a dark spot on the iris that has been present for many years and then begins to grow. These melanomas usually are fairly slow growing, and they rarely spread to other parts of the body. For these reasons, people with iris melanomas generally have a good prognosis (outlook).

Intraocular melanomas are generally made up of 2 different kinds of cells.

- **Spindle cells:** These are long, thin cells.
- **Epithelioid cells:** These cells are almost round but with some straight edges.

Most tumors have both kinds of cells. The outlook is better if the tumors are mostly spindle cells as opposed to mostly epithelioid cells. Epithelioid tumors are more likely to spread to distant parts of the body (such as the liver). If you have intraocular melanoma, your doctor can tell you which type of cells were found.

**Primary intraocular lymphoma (lymphoma of the eye)**

Lymphoma is a type of cancer that starts in immune system cells called lymphocytes. Most lymphomas start in lymph nodes, which are bean-sized collections of immune system cells scattered throughout the body. Lymphomas can also start in internal organs such as the stomach, lungs, and rarely, in the eyes.

There are 2 main types of lymphoma: Hodgkin disease and non-Hodgkin lymphoma. Primary intraocular lymphoma is a type of non-Hodgkin lymphoma. Most people with primary intraocular lymphoma are elderly or have immune system problems such as AIDS. Primary intraocular lymphoma is often seen along with lymphoma of the brain, known as primary central nervous system (CNS) lymphoma.
Orbital and adnexal cancers

Cancers of the orbit and adnexa develop from tissues such as muscle, nerve, and skin around the eyeball and are like their counterparts in other parts of the body. These are described in our other documents on cancers of muscle, nerve, skin, etc. For example, cancers of the eyelid are usually skin cancers, which are described in our documents on skin cancers (Melanoma Skin Cancer and Skin Cancer: Basal and Squamous Cell). Muscle cancer is described in Rhabdomyosarcoma.

Most of the rest of this document focuses on intraocular melanomas and lymphomas.

- References
  See all references for Eye Cancer

Key Statistics for Eye Cancer

The American Cancer Society’s estimates for eye cancer in the United States for 2018 are:

- 3,540 new cancers (mainly melanomas) of the eye and orbit: 2,130 in men and 1,410 in women
- 350 deaths from cancers of the eye and orbit: 190 in men and 160 in women

Primary eye cancers can occur at any age, but the risk for most types increases as people get older. The rate of eye melanomas has been fairly stable over the past few decades. Cancers that spread to the eye from another part of the body (secondary eye cancers) are actually more common than primary eye cancers.

Most cancers of the eye and orbit in adults are melanomas, with lymphomas being the next most common. Both of these cancers start more often in other parts of the body. More than 9 out of 10 melanomas start in the skin, while most lymphomas begin in lymph nodes.
What’s New in Eye Cancer Research and Treatment?

Many medical centers around the world are doing research on the causes and treatment of eye cancers. These are challenging diseases to study because they are not common. But each year scientists find out more about what causes them and how to improve treatment.

Genetics

Learning more about the gene changes that make eye cancer cells different from normal cells will likely play an important role in treating eye melanomas, lymphomas, and other eye cancers in the future.

Using genes to help find people at higher risk

As we learn about the gene changes in these cancers, we may be able to develop tests to identify people who are more likely to get them and then carefully screen those people.

For example, in recent years, researchers have found that some families have a change
(mutation) in the BAP1 gene that makes them more likely to develop melanoma of the eye. While this gene change affects only a small portion of people with eye melanoma, researchers might be able to study it to learn more about how eye melanomas develop.

Using genes to help predict prognosis (outlook)

The genetic changes in tumors may also help predict the likelihood of them spreading. For example, in uveal melanoma, certain genetic changes, such as the loss of one copy of chromosome 3, have been linked to an increased risk of cancer spread.

Recently, researchers have found that patterns of gene expression in tumor cells appear to be an even better way to tell if an eye melanoma is likely to spread. Based on these gene patterns, a little more than half of eye melanomas are shown to be “Class 1” tumors. These cancers have a low risk of spreading. The remaining eye melanomas fall into the “Class 2” category, which have a very high risk of spreading.

Some doctors now offer a test (DecisionDx-UM) for these gene changes, and some patients may want to have them to learn if their cancer is likely to spread. If a patient is found to be at high risk, the doctor might follow them more closely to try to detect cancer spread as early as possible. But other doctors are not as keen on using the test at this time, because we don’t yet have proven ways to prevent the cancer spread or alter the outcome in people who are in the high risk group.

Using genes to help find new treatments

Identifying gene changes in eye cancer cells might also provide specific targets for newer drugs. For example, most eye melanomas have changes in either of 2 related genes, GNAQ or GNA11. The proteins made by these genes are part of the MAPK signaling pathway inside cells that helps them grow. It’s not yet clear if drugs will be able to target these proteins directly, but drugs that target other proteins in the MAPK pathway are now being studied for use against eye melanomas, and some have shown early promising results (see Targeted therapy below).

Immunotherapy

Immunotherapies are treatments that boost the body’s immune system to try to get it to attack the cancer. Cytokines, monoclonal antibodies, cancer vaccines, and other immunotherapies are among the most promising approaches for treating melanoma and lymphoma. Although most clinical trials of these treatments include people with melanomas of the skin and lymphomas that begin in lymph nodes, results of these
studies might help treat people with eye melanomas and lymphomas as well.

One example is ipilimumab (Yervoy), a type of drug called a *monoclonal antibody* that boosts the overall activity of the immune system. This has been shown to help some people with advanced melanomas of the skin live longer, although it can also have some serious side effects. Some doctors now use it to treat melanomas of the eye as well, although its benefits against this cancer are still being studied in clinical trials.

Newer drugs such as nivolumab and pembrolizumab (Keytruda), which boost the immune response against cancer cells in a slightly different way, have shown even better results against skin melanomas in early studies. These drugs might prove to be useful against eye melanomas as well.

**Targeted therapy**

As researchers have learned more about some of the changes in cells that cause them to become cancer, they have begun to develop drugs that target these changes. These new targeted drugs work differently from standard chemo drugs. They might work in some cases when chemo drugs don't, and they tend to have different (and often less severe) side effects.

Most eye melanomas have changes in the *GNAQ* or *GNA11* genes. Proteins made by these genes are part of the MAPK gene signaling pathway that helps cells grow. Selumetinib is a drug that targets the MEK protein, which is also part of the MAPK pathway. Selumetinib has been shown to slow the growth of advanced eye melanomas in a clinical trial. While it does not cure these cancers, it often shrinks them for a time. For now, this drug is only available through clinical trials.

Other drugs might also be useful in treating cancers with these gene mutations. For example, some early research suggests that sotrastaurin (AEB071), a drug that targets protein kinase C, might be effective against cells with a *GNAQ* mutation. This is now being studied in clinical trials.

Some newer drugs, such as vemurafenib (Zelboraf®), dabrafenib (Tafinlar®), and trametinib (Mekinist™), target cells with a mutation in the BRAF gene. This mutation is found in about half of patients with skin melanoma, but only in about 5% of patients with eye melanoma. Still, these or similar drugs might help people whose cancer cells have these mutations.

Many targeted drugs are already used to treat other types of cancer. Some of them are now being studied for use against melanoma of the eye as well, including sunitinib.
(Sutent®, sorafenib (Nexavar®), vorinostat (Zolinza®), and everolimus (Afinitor®)).

Other drugs target the blood vessels that tumors need to grow. These are known as *anti-angiogenesis drugs*. One example is bevacizumab (Avastin®), which is already used to treat some other types of cancer. It may help prevent some radiation side effects, which might help people retain more vision after treatment. This drug is also being studied for use along with chemotherapy in people with advanced eye melanomas.

- References
See all references for Eye Cancer

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