CENTRAL RETINAL VEIN OCCLUSION

Treatment of Macular Oedema Causing Loss of Vision in Central Retinal Vein Occlusion (CRVO)

Ozurdex versus Lucentis Pictogram

What is CRVO?
Central Retinal Vein Occlusion is a blockage of the main vein in the retina at the back of the eye. It can cause macular oedema, which is swelling of the central part of the retina. Macular oedema is typically associated with loss of vision, particularly loss of sharpness of vision, such as the ability of reading or recognising faces and objects.

Can CRVO cause additional problems during the course of the disease?
In addition to loss of sharp vision Central Retinal Vein Occlusion can also cause loss of blood supply to the retina and reactive growth of new abnormal blood vessels at the back of the eye (Proliferative Retinopathy) or at the front of the eye (Rubeotic Glaucoma). These are complications of CRVO that are explained in more detail further on.
What causes CRVO?
The cause of CRVO is not well known. However, that are known risk factors such as age, smoking, raised cholesterol and lipids (fat) in the blood, raised blood pressure and in younger patients, inflammation or clotting disorders. The risk factors contribute to hardening of the retinal arteries. Retinal arteries and veins are lodged in a tight space at the origin of the optic nerve from the eye. Individual variation in the anatomy (shape and size) of the optic nerve at its origin add to the risk factors in causing progressive sludge of blood flow and eventually clotting of the main retinal vein in the optic nerve.

What happens without treatment?
It’s important to remember that each case of retinal vein occlusion is unique and that macular oedema is the main cause of loss of vision in CRVO.

Occasionally patients may get better without treatment. For this reason a few weeks of observation period may be appropriate to identify patients that recover spontaneously and may not need any treatment. However, this happens only in 1 in 10 or less of affected eyes and even when this happens usually patients are left with some degree of permanent visual abnormalities, such as slightly blurred visions.

The majority of patients with CRVO do not recover vision and often get worse if left untreated for several months. There is some evidence that delaying treatment for months may reduce the chances of visual recovery once treatment is started.

How is CRVO treated?
The current main options are about a choice between Lucentis and Ozurdex.
There is an impression that Lucentis may be superior to Ozurdex when comparing results from the pivotal clinical trials for each drug. However, these studies had different design and did not truly compare the two treatments head-to-head. Therefore it is not possible to conclusively know if Lucentis is superior to Ozurdex or viceversa.

Head-to-head comparative studies of Lucentis versus Ozurdex are under way. One of them is being conducted at the Macular Unit at the Hospital of St Cross, Rugby, with Mr Pagliarini being the Principal Investigator.

Is there a restriction in using Lucentis in the NHS?
Lucentis is licensed for treating macular oedema in retinal vein occlusions. However, it has yet to be approved by NICE for its use in the NHS, although it is currently being evaluated. Lucentis can be used in private practice or as part of an ethically approved clinical research study.

**What is Ozurdex?**

**Ozurdex** is a biodegradable implant containing the steroid Dexamethasone. Ozurdex is licensed for treating macular oedema in retinal vein occlusions and is approved by NICE for use in the NHS. The Ozurdex implant is injected into the eye with a variant of a procedure called **intravitreal injection**.

**How is Ozurdex injected into the eye?**

The implant is a small rod injected into the eye with a special technique that creates a self-sealing wound “shelved” through the eye wall, on the white of the eye approximately 3.5-4.0 mm behind the iris. The implant is injected using a special applicator device shaped like a pen. The tiny rod-shaped implant rests into the vitreous, the gel-like material that fills the eye. The implant slowly dissolves gradually releasing dexamethasone. The steroid dexamethasone blocks chemical pathways that lead to inflammation and leakage from retinal blood vessels.

**How many injections of Ozurdex would I need?**

It’s important to remember that each case of retinal vein occlusion is unique. We do not have long term data on the benefit of Ozurdex. The manufacturer indicated that Ozurdex last for 6 months. However, clinical experience suggests that the benefit of Ozurdex lasts for only 2-3 months.

It seems that 80% of patients need more than 1 Ozurdex implant. How many it is unclear.

It is recommended that patients being treated in centres that take part in research using prospective anonymised data collection to understand the benefit and safety of Ozurdex take part into research, if offered, to help their ophthalmologists understand better how to use Ozurdex in CRVO.

**What are the side effects of Ozurdex?**

Approximately 1:6 to 1:8 treated eyes experience raised eye pressure or glaucoma and need treatment with eye drops. Usually this resolves as the effect of Ozurdex wanes off. Approximately 1:1000 patients may require glaucoma surgery.

**Risks associated with the intravitreal injection procedure**
Common side effects of the intravitreal procedure and advice include:

- You may experience temporary visual blurring after receiving an injection and should not drive or use machines until this has resolved.
- You are likely to have some discomfort for the first 24 hours. If the discomfort does not ease off and turns into pain contact the ophthalmologist or the nearest eye casualty

Uncommon complications related to the injection procedure, i.e. not related to the injected drug, include:

- Endophthalmitis, a severe infection inside the eye
- Retinal detachment
- Traumatic cataract
- Large bleeding inside the eye or within the eye wall.
- Bleeding on the surface of the eye at the site of injection is common but it is not a reason of concern as it disappears within 2 to 10 days without causing any problem.
- Corneal abrasion, a painful “scratch to the eye” due to excessive penetration in the cornea of the disinfectant used to reduce the risk of endophthalmitis, occurring in 1:100 injections

Some of the complications may be severe and require hospital admission, such as endophthalmitis and retinal detachment.

Fortunately, complications related to the injection are rare. This means they occur in 1:2000 injections or less. To put things into perspective cataract surgery, a procedure deemed to be safe, has more than double the risk of severe complications than intravitreal injections.

**What should I do if I develop pain after an intravitreal injection?**

The general advice is to contact the ophthalmologist or the nearest eye casualty if there is pain after the intravitreal injection procedure.

Endophthalmitis is the most dreaded complication because it can cause severe and permanent loss of vision and requires emergency hospital
admission.

The main two reasons for having pain after an intravitreal injection procedure are:

- corneal abrasion
- endophthalmitis

Corneal abrasions cause sharp pain within the first 24 hours of the procedure. The pain is worse with blinking and is associated to intense tearing and intolerance to light. The pain may give the patient a bad night sleep but starts easing off with time.

Corneal abrasions are self-healing over a few days. However, they heal faster with an ointment and an eye pad. Therefore, if the post-injection discomfort turns into pain it is recommended to contact the ophthalmologist or the nearest eye casualty.

The main feature of endophthalmitis is pain that gets worse rather than better. If the pain starts between day 1 and 7 after the injection it must be considered to be endophthalmitis until proven otherwise and must be reported immediately by the patient to the ophthalmologist or the nearest eye casualty.

What is Lucentis?
Lucentis is part of a class of drugs grouped under the general term of anti-VEGF. Other anti-VEGF drugs used in eye disease are Avastin and Aflibercept.

Anti-VEGF drugs work by blocking chemical pathways based on VEGF (Vascular Endothelial Growth Factors). These are small proteins that when produced in excess into the eye cause leakage of fluid and blood from the retinal vessels. VEGF also cause growth of abnormal blood vessels at the back of the eye or at the front of the eye resulting in two dreaded complications of CRVO known respectively as Proliferative Retinopathy and Rubeotic Glaucoma.

How Lucentis or other anti-VEGF drugs are injected into the eye?
Anti-VEGF drugs are injected into the vitreous, the jel-like substance that fills the eye. The injection is placed through the eye wall, on the white of the eye approximately 3.5-4.0 mm behind the iris. Anti-VEGF are fluid drugs. The needle used to inject fluid drugs is tiny and much smaller than the needle of the Ozurdex device. The needle is not seen by the patient during the
injection. However, whilst the drug is injected fluid may be seen swirling around into the eye.

**Aflibercept (VEGF Trap-eye or VTE)** is a newer drug which has been shown to have a similar effect to Lucentis in retinal vein occlusions. It seems it lasts longer in the eye than Lucentis, potentially requiring less frequent eye injections. It is currently undergoing the regulatory process of licensing in Europe and will be soon available in the UK, although not in the NHS until NICE approval.

**Avastin** is an anti-VEGF drug licensed to treat cancer but not eye disease. However, given the much lower cost than Lucentis or Aflibercept it has been used worldwide as a “low cost” alternative to treat a variety of eye diseases. NICE does not review unlicensed drugs. Therefore Avastin is not approved by NICE for treatment of CRVO.

**Is there any other potential benefit of using Lucentis or other anti-VEGF drugs for treating CRVO?**

Lucentis and Avastin have been used to treat complications of central retinal vein occlusions such as rubeotic glaucoma with excellent results. There are anecdotal reports that Lucentis reduces the risk of CRVO complications such as proliferative retinopathy and rubeotic glaucoma in patients with treated with Lucentis for their macular oedema.

**What are the complications of Lucentis and other anti-VEGF drugs?**

**Laser treatment** has no role in treating macular oedema in CRVO and in restoring vision.

However, laser treatment can be very effective in treating complications of CRVO that, if untreated, may cause further vision loss or a painful eye:

- **Rubeotic Glaucoma**
- **Proliferative Retinopathy**.

These are complications that may occur in the first few months after the onset of CRVO and only rarely a few years later.
In **Proliferative Retinopathy** abnormal blood vessels grow onto the retina. These vessels are frail and at risk of bleeding inside the eye.

If proliferative retinopathy is detected during follow-up, scattered retinal laser photocoagulation is applied to the affected areas to reduce the risk of bleeding. This type of laser treatment is referred to as **Panretinal Photocoagulation (sector PRP)** or **Scattered Retinal Photocoagulation**.

In **Rubeotic Glaucoma** abnormal blood vessels grow at the front of the eye where water is drained out of the eye. They cause raised eye pressure that is difficult to control.

Raised eye pressure may cause chronic pain. **Rubeotic glaucoma can cause a blind and painful eye.**

Laser treatment with panretinal photocoagulation (PRP) reduces the chances of the eye becoming painful, but it cannot restore vision for patients with rubeotic glaucoma.

**Panretinal photocoagulation (PRP) laser treatment** is offered to those patients who develop high risk features for progression to rubeotic glaucoma during follow up.

The laser procedure used to treat raised eye pressure in rubeotic glaucoma is referred to as **cyclodiode laser**.

**Disclaimer**

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