

## **COMPLICATIONS FROM THE MEDICATION AND INJECTION**

Complications when Avastin® is given to patients with cancer

When Avastin® is given to patients with metastatic colorectal cancer, some patients experienced serious and sometimes life-threatening complications, such as gastrointestinal perforations or wound healing complications, hemorrhage, arterial thromboembolic events (such as stroke or heart attack), hypertension, proteinuria, and congestive heart failure.

Patients who experienced these complications not only had metastatic colon cancer, but were also given 400 times the dose you will be given, at more frequent intervals, and in a way (through an intravenous infusion) that spread the drug throughout their bodies.

Complications following Lucentis®

The prescribing information for intravitreal Lucentis® contains a warning about arterial thromboembolic events: “Although there was a low rate (<4%) of arterial thromboembolic events observed in the LUCENTIS clinical trials, there is a theoretical risk of arterial thromboembolic events following intravitreal use of inhibitors of VEGF.

Genentech, the company that manufactures both Avastin® and Lucentis®, has advised ophthalmologists “of a higher incidence in one LUCENTIS study of strokes in the 0.5-mg dose group compared with the 0.3-mg dose group (1.2% versus 0.3%, respectively;  $P=0.02$ ).”

One study showed that patients who have had a stroke are at greater risk of having one again. The causal relationship between Lucentis and strokes is unclear, and patients with AMD are already at risk for stroke.

It must be noted that whenever a medication is used in a large number of patients, a small number of coincidental life-threatening problems may occur that may have no relationship to the treatment.

Risk when Avastin® or Lucentis® is given to treat patients with eye conditions

Ophthalmologists believe that the risk of these complications for patients with eye conditions is low. Patients receiving Avastin® for eye conditions are healthier than the cancer patients, and receive a significantly small dose, delivered only to the cavity of their eye. While there are no randomised controlled trials about the use of Avastin® in the eye that prove it is safe and effective, Lucentis®, a similar drug, was recently licensed for AMD. One study of patients who received Avastin® through an intravenous infusion reported only a mild elevation in blood pressure. Another study of patients treated like you will be with intravitreal Avastin® (that is, Avastin® injected into the eye) did not have these elevations or the other serious problems seen in the patients with cancer.

However, the benefits and risks of intravitreal Avastin® or Lucentis® for eye conditions are not yet fully known. In addition, whenever a medication is used in a large number of

patients, a small number of coincidental life-threatening problems may occur that have no relationship to the treatment. For example, patients with diabetes are already at increased risk for heart attacks and strokes. If one of these patients being treated with Avastin® or Lucentis® suffers a heart attack or stroke, it may be caused by the diabetes and not the Avastin® or Lucentis® treatment.

There is the risk that Avastin® or Lucentis® reduce even further the blood supply in eyes suffering from conditions where the blood supply is already compromised, such as diabetic retinopathy or central or branch retinal vein occlusion.

#### Known risks of intravitreal eye injections

Your condition may not get better or may become worse. Any or all of these complications may cause decreased vision and/or have a possibility of causing blindness. Additional procedures may be needed to treat these complications. During the follow up visits or phone calls, you will be checked for possible side effects and the results will be discussed with you.

Possible complications and side effects of the procedure and administration of Avastin® include but are not limited to retinal detachment, cataract formation (clouding of the lens of the eye), glaucoma (increased pressure in the eye), hypotony (reduced pressure in the eye), damage to the retina or cornea (structures of the eye), and bleeding. There is also the possibility of an infection inside the eye infection (endophthalmitis). You will receive eye drops with instructions on when to use them to reduce the possibility of this occurring. Any of these rare complications may lead to severe, permanent loss of vision or blindness and in extreme cases, even loss of the eyeball. You may require to be admitted into hospital for treatment that could include, between others, further injections into the eye or surgery. The prognosis in such event is usually guarded.

Patients receiving an injection of Avastin® or Lucentis® may experience less severe side effects related to the pre-injection preparation procedure (eyelid speculum, anaesthetic drops, dilating drops, antibiotic drops, povidone-iodine drops and the injection of the anaesthetic). These side effects may include eye pain, subconjunctival haemorrhage (bloodshot eye), vitreous floaters, irregularity or swelling of the cornea, inflammation of the eye, and visual disturbances.

#### PATIENT RESPONSIBILITIES

You must immediately contact Mr Stanga or his team if any of the following signs of infection or other complications develop: pain, blurry or decreased vision, sensitivity to light, redness of the eye (compared to immediately after the injection), or discharge from the eye. You should not rub my eyes or swim for three days after each injection. Please keep all post-injection appointments or scheduled telephone calls so that Mr Stanga or his team can check for complications.

Although the likelihood of serious complications affecting other organs of your body is low, you should immediately contact your GP doctor or go to the Accidents and

Emergency Room if you experience abdominal pain associated with constipation and vomiting, abnormal bleeding, chest pain, severe headache, slurred speech, or weakness on one side of the body.

As informed by Mr Stanga and his team, symptoms of stroke include sudden changes in vision; sudden numbness or weakness of the face, arm, or leg, especially on one side of the body; sudden confusion, trouble speaking or understanding; sudden trouble walking, dizziness, loss of balance or co-ordination; sudden, severe headache with no known cause.

Please notify Mr Stanga or his team about any of these problems.

Please read the section Vitrectomy and posturing if undergoing this type of surgery.

**Please remember that each patient is different and the information here provided is only a general guide. If you require further advice or information please contact Mr Stanga or a member of his team.**