Bilateral Anti-VEGF Treatment

Background
Intravitreal injection is the most commonly performed ophthalmic procedure, and injection of anti-VEGF agents is the gold-standard treatment for many retinal vascular disorders. Clinical trials and real-life experience have demonstrated that single intravitreal injections carry a very low risk of serious complications when proper procedures and precautions are followed. However, many patients present with bilateral disease, meaning that both eyes require treatment. Treating each eye at separate, staggered visits adds significantly to the burden of anti-VEGF therapy, essentially doubling both clinic time and cost. There is potential to substantially reduce this burden by treating both eyes concomitantly at the same patient visit. Furthermore, several studies have highlighted that patients prefer receiving treatment in this manner.

Viewpoint
1. It is possible and reasonable to conduct bilateral injections while observing appropriate procedures and precautions
Bilateral treatment can be defined as simultaneous or consecutive administration of anti-VEGF treatment, with both injections administered during the same patient visit. While some feel that this may pose an enhanced risk of local injection-related complications, there is no evidence to date suggesting that there is an increased risk of ocular adverse events with bilateral treatment compared with unilateral treatment. Furthermore, while there may be a theoretical risk of systemic adverse events associated with intravitreal injection of anti-VEGF agents, there is also no evidence that treating both eyes concomitantly alters this risk.

To manage the risks associated with the injection procedure, it is recommended to follow the guidance outlined in points 2–4 below in cases where bilateral treatment is deemed to be appropriate.

2. The second injection should be treated as a separate procedure within the same visit
To minimize the risk of procedure-related complications or cross-contamination between treatments, each injection should be treated as a completely new procedure. After the first injection, the patient should be prepared again, following the recommended procedure for intravitreal injections. In brief, this should include:
- Surgical disinfection of the surgeon’s hands and/or application of new sterile gloves
- Application of povidone-iodine* to the conjunctival sac
- Cleaning of the periocular skin, eyelid margins and eyelashes with povidone-iodine*
- The use of sterile equipment, including masks, eyelid speculum, forceps, and ophthalmic drape (if used)

*Or suitable alternative, such as chlorhexidine
3. Where possible, products should not be from the same batch

It is essential to avoid the risks of a contaminated product being administered to both eyes. This is especially important with compounded agents, where sterility may be compromised due to the additional steps required to aliquot them into individual doses.

To minimize this risk, the products administered to each eye should be from different batches.

Commercial products are supplied in packages for single use only. These are produced in very large lot sizes, so use of different batches may not be feasible. Where this is the case, separate packages from the same batch may be used.

4. Extra care is required for patients who require bilateral injections at the first visit

As it may be an intimidating prospect to receive injections in both eyes at the first visit, the preference of the patient should always be taken into account when deciding whether to treat both eyes at this time. Furthermore, as there is a small risk that an idiosyncratic hypersensitivity response may occur after the first treatment, additional considerations apply at the first visit:

- If possible, avoid bilateral injections until the tolerability of the agent has been ascertained.
- If it is essential to administer bilateral treatment at the first visit, consider separating the injections to allow time for acute hypersensitivity responses to manifest by administering the first injection at the beginning of clinic and the second at the end

Further considerations

There is variation in opinion on how to address the needs of patients with bilateral disease who are following a treat-and-extend or as-needed regimen. When extending treatment intervals, the needs of each eye should be considered separately, as the ideal treatment interval for one eye may be different to the fellow eye. To reduce clinic burden, it may be preferable to treat both eyes according to the needs of the eye that requires the shortest interval.

As such, the physician may risk over-treating one eye, but avoids under-treating the fellow eye, thus minimizing the risk of avoidable vision loss.

At present, several countries reimburse only partially, or not at all, for bilateral injection procedures. This means that physicians have no choice but to treat at separate visits, which increases the burden on clinics, healthcare systems and patients, by preventing efficiencies from same-day procedures. In order to enable payors to make informed choices about whether or not to reimburse treatment, the body of clinical data supporting the safety and efficacy of bilateral anti-VEGF therapy must be further developed.