RAPID Program Fact Sheet

November 9, 2020

Overview

Launched in 2015, the RAPID program[i] is a government-run initiative in Alberta that provides patients living with certain eye conditions access to ongoing treatment with anti-VEGF therapies. It does so at no cost to the patient.

The program offsets its expenses by incentivizing retina specialists to use a cheaper anti-VEGF, Avastin (bevacizumab), which was originally designed as a cancer treatment. Since Avastin was never submitted for regulatory approval as a treatment for eye diseases, when it is administered in this way it is used "off label"—that is, it is used in a way the manufacturer did not intend. Policymakers behind RAPID justify this by pointing to certain studies that have shown that Avastin works similarly to Lucentis (ranibizumab) and Eylea (aflibercept)[ii], the brand name therapies that cost significantly more. They are also supported by a therapeutic review conducted by the Canadian Agency for Drugs and Technologies in Health (CADTH) in 2016, which listed Avastin as the preferred anti-VEGF for initial use in the eye.[iii]

RAPID: Structure and Controversy

In Canada, many patients living with macular edema, particularly wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME), have benefited from anti-VEGF therapies. The treatments contain an antibody that moderates the development of blood vessels that would otherwise grow uncontrollably with these diseases, leading to severe vision loss or blindness—The FBC website has more information on AMD and treatment options.[iv] Today, approximately 100,000 Canadians are treated with anti-VEGF therapies, many of them seniors and a significant number living in long-term care homes.

Before the widespread use of anti-VEGF to treat these diseases, it was not uncommon for patients to undergo forms of laser surgery that would destroy abnormal blood vessel growth, but this could also damage the surrounding, healthy tissue, often leaving patients with blind spots in their vision. Anti-VEGF therapies dramatically advanced the standard of care by precisely targeting a molecule responsible for blood vessel development, avoiding the kind of damage that could result from laser therapy.

The trade-off is that anti-VEGF drugs need to be administered frequently, typically every one-to-three months, and must be injected directly into the eye. They also carry a price tag that varies dramatically depending on the drug being used. To curtail these costs and also guarantee access to the drugs themselves, some provinces have developed publicly-funded plans that guide physicians in the use of anti-VEGF. And some of these plans, including the RAPID program in Alberta, incentivize physicians to use the less expensive therapy—in this case, Avastin.

Forms of anti-VEGF and other treatments

The commonly used anti-VEGF therapies are Lucentis, Eylea, and Avastin. Lucentis requires monthly injections into the eye, while each Eylea injection is designed to last two months (after an initial set of monthly injections). In addition to VEGF, Eylea also blocks the action of placental growth factor (PIGF), which causes the growth of new blood vessels. Both of these drugs are widely reimbursed across most jurisdictions and prevent vision loss by blocking the action of VEGF. Avastin was designed as a cancer

treatment but is commonly used "off-label."[v] Ophthalmologists, eye specialists, and researchers continue to discuss the pros and cons of these different treatments.

At the same time, the treatment landscape for macular diseases continues to evolve. For instance, CADTH recently recommended that provinces fund a new anti-VEGF therapy called Beovu (brolucizumab)[vi], which requires fewer injections per year than the other therapies. And there are other developments in this space as well: for instance, though not covered by most provinces, time-release implants such as Ozurdex have shown effectiveness for treating certain patients, particularly those experiencing inflammation alongside irregular blood vessel growth and in some situations may be considered for patients who are non-responders to anti-VEGF therapies.[vii]

Forms of anti-VEGF and other treatments

The RAPID program enlists a specialized group of physicians called retina specialists to administer anti-VEGF to Albertans living with the relevant eye conditions. General physicians and ophthalmologists are not eligible to be a part of the initiative. By being involved in the program, retina specialists are given significantly higher reimbursement rates if they adhere to an 80/20 ratio of injecting Avastin. In other words, they are financially incentivized to inject Avastin 80% of the time.

In the eyes of some policy and health experts, this is problematic, since some patients have been shown to respond to certain anti-VEGF treatments more optimally than others.[viii] There is also evidence that slowing down the frequency of injections over time may be beneficial, an approach call "treat-and-extend,"[ix] which is included on the labels of the Health Canada-approved anti-VEGFs. Some worry that RAPID's reimbursement structure may lead specialists to inject more often than needed. At the same time, others are concerned about an overall lack of transparency and public reporting. Only limited data has been released by health authorities in Alberta, so patients and patient groups are left with little to tell them about the safety and effectiveness of RAPID.

To complicate matters, in 2019 a group of eye specialists in British Columbia alerted their provincial government to a potential spike in glaucoma cases among those being treated with anti-VEGF. Similar to Alberta, B.C. has a program that prioritizes the use of Avastin, and some members of the medical community expressed concern that its off-label use in the eye could be linked to the rise in glaucoma. It is possible that this is related to the way that the drug is repackaged by the province, who receives it from the manufacturer in quantities that are appropriate for its intended use—this practice is called "vial splitting" and has attracted some controversy over the last several years. Health authorities in B.C. continue to analyze the potential link, but have taken the position that a higher rate of glaucoma is not grounds to discontinue the use of Avastin. According to B.C.'s Health Minister, doing so would compromise their initiative and block access to these sight-saving drugs for those who rely on public coverage.[x]

Whether patients are being treated as part of a public program such as RAPID or not, it is important that they know the drug they are being treated with and speak regularly and openly with their specialist.

Recommendations

1. Treatment and outcome data from the RAPID program should be regularly collected, reviewed and published to inform treatment decision making and improve health outcomes.

2. Taking into account available data, achieving the best patient outcomes should drive treatment choice.
3. The most cost-effective treatment option can be considered as a first option for treatment-naïve patients if this will not compromise a patient's vision. Both clinical data and patient's life circumstances should be taken into account when making this decision.
4. Using the best available data and taking into account clinical and contextual circumstances, treatment switching should be considered for patients who are considered non-responders to current treatment.
5. Treatment frequency should be informed by the most recent evidence and guidelines, taking into account patient preference, circumstances and quality of life.
6. Engage patients in decision making over any changes in treatment option or frequency. The discussion should be informed by clear and sufficient information and support.
7. Support patients' understanding of the risks of changes to their treatment regimen if this could negatively impact their eye health outcomes or quality of life.

References

[i] RAPID is an acronym for "Retina Anti-Vascular Endothelial Growth Factor Program for Intraocular Disease."

[ii] Scott, I. U., VanVeldhuisen, P. C., Ip, M. S., *et al*. Effect of bevacizumab vs aflibercept on visual acuity among patients with macular edema due to central retinal vein occlusion: The score2 randomized clinical trial. *JAMA*, 2017. 317(20):2072-2087. doi:10.1001/jama.2017.4568. https://pubmed.ncbi.nlm.nih.gov/28492910/.

[iii] https://www.cadth.ca/sites/default/files/pdf/TR0009_anti-vegf-in-brief-e.pdf

[iv] https://www.fightingblindness.ca/eye-diseases-pathways/age-related-macular-degeneration/

[v] The product monograph for Avastin includes the following language under Warnings and Precautions: "AVASTIN is not formulated and has not been authorized for intravitreal use. Local and systemic adverse events have been reported in the post-market setting with unauthorized intravitreal use."

[vi] https://cadth.ca/sites/default/files/cdr/complete/SR0632%20Beovu%20-%20CDEC%20Final%20Recommendation%20%E2%80%93%20May%2025%2C%202020_for%20posting.pdf

[vii] Busch, C., Fraser-Bell, S., Iglicki, M., *et al.* Real-world outcomes of non-responding diabetic macular edema treated with continued anti-VEGF therapy versus early switch to dexamethasone implant: 2-year results. *Acta Diabetologica*, 2019. 56:1341-1350. doi: 10.1007/s00592-019-01416-4.

[viii] Amoaku W. M., Chakravarthy, U., Gale, R., *et al*. Defining response to anti-VEGF therapies in neovascular AMD. *Eye* 2015. 29:721-731. https://doi.org/10.1038/eye.2015.48. https://www.nature.com/articles/eye201548

[ix] Abedi, F., Wickremasinghe, S., Islam, A.F.M., *et al*. Anti-VEGF treatment in neovascular age-related macular degeneration: a treat-and-extend protocol over 2 years. *Retina*, 2014. 34(8):1531-1538. doi: 10.1097/IAE.0000000000000134. https://journals.lww.com/retinajournal/Abstract/2014/08000/ANTI_VEGF_TREATMENT_IN_NEOVASCULAR_AGE_RELATED.4.aspx.

[x] https://news.gov.bc.ca/releases/2019HLTH0078-001060