

## Evolving Practice Patterns in Treatment of Major Retinal Diseases in Singapore

### Dear Editor,

Neovascular (“wet”) age-related macular degeneration (AMD), diabetic macular edema (DME) and retinal vein occlusion (RVO) are amongst the most common causes of blindness.<sup>1-3</sup>

Traditionally, these conditions were treated with thermal laser photocoagulation, however, the advent of anti-vascular endothelial growth factor (VEGF) has revolutionised the treatment of these diseases.<sup>1,4,5</sup> These anti-VEGF agents (ranibizumab and bevacizumab) aim to stop retinal angiogenesis and reduce macular oedema. Numerous trials have evaluated the efficacy of these treatments in western populations, however, there are no clear guidelines for anti-VEGF use in Asian countries where the pattern of retinal disease is different.

This study surveyed the current practice patterns of ophthalmologists in Singapore with regards to the use of anti-VEGF and established therapies for the management of 3 major retinal disease: AMD, DME and central retinal vein occlusion (CRVO).

### Materials and Methods

A questionnaire was sent to all accredited ophthalmologists in Singapore. The survey included 32 questions on anti-VEGF treatment, follow-up and investigations of AMD, polypoidal choroidal vasculopathy (PCV), DME and CRVO.

### Results

Seventy-seven responses (40%) were received. DME was considered ‘treatable’ by majority (81.0%), followed by CRVO (67.0%) and wet AMD (59.0%). Anti-VEGF monotherapy was the most common initial treatment for wet AMD, while combination therapy consisting of anti-VEGF and photodynamic therapy was the most common initial treatment for PCV. The estimated mean annual number of injections was 5.25 for ranibizumab and 5.75 for bevacizumab. Laser without anti-VEGF therapy was the most common treatment for DME (55%) and CRVO (46%).

### Discussion

In our survey, we found that most non-retinal specialists referred wet AMD cases to their retinal colleagues. This was

likely due to the growing complexity behind the diagnosis and treatment of AMD. In contrast, many non-retinal specialists prefer to continue treating DME and CRVO. Responses reflected an increased level of familiarity to DME and CRVO compared to AMD and the overall perception of the condition being ‘treatable’ was also rated as highest for DME, followed by CRVO, and wet AMD (Fig. 1).

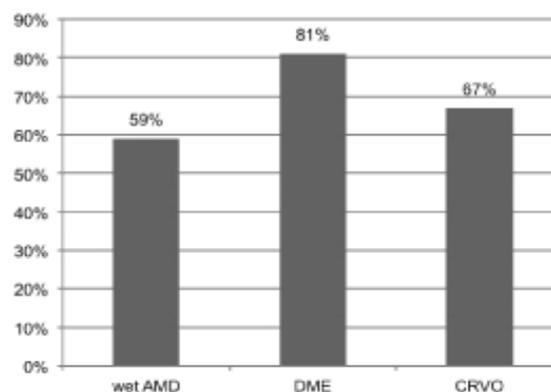


Fig. 1. Chart showing the percentage of responses indicating conditions perceived as ‘treatable’ by clinicians (n = 77).

Our survey demonstrated that despite the established superior visual outcome with anti-VEGF therapy,<sup>6</sup> laser monotherapy remains the most commonly used treatment for DME. We suspect that factors such as financial constraints, intensive follow-up, and visual outcome affect the choice of treatment modality. In such cases, clinicians must explain these factors carefully to patients, and together, agree at a preferred treatment regime. Our survey showed a similar spread of preferred treatment modalities in CRVO reflecting the multitude of opinions, and treatment options for treating this condition. In the case of AMD, majority of respondents indicated anti-VEGF monotherapy was their treatment of choice. Most respondents indicated they would initiate their treatment with 3-monthly injections and a pro re nata regime afterwards.

Overall, bevacizumab and ranibizumab use appeared to be divided roughly in a 7 to 3 ratio. Similar trends were noted in the American Preferences and Trends survey.<sup>7</sup> However, there remains a large variation in terms of monitoring and retreatment. The estimated number of retreatments within the first year was <6 in our survey (Fig. 2). This retreatment number suggested that the monthly dosing of anti-VEGF used in the pivotal MARINA, ANCHOR and CATT trials<sup>5,8,9</sup> was rarely adopted in practice. This was consistent with data described in the US Medicare analysis (2006 to 2008) showing the mean number of injections to be only 4.3 within the first year, and discontinuation rate of 53.6% within 1 year. The reasons for discontinuity were found to be multifactorial and avoidable, including lack of understanding and mismatch in expectations. Therefore, efforts to improve patient education are important to achieve optimal treatment outcome.

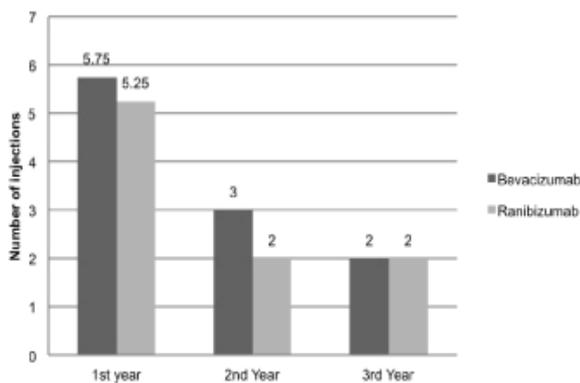


Fig. 2. Chart showing the estimated number of injections received by AMD patients up to year 3.

Responses regarding treatment of PCV reflected the unfamiliarity to this condition. In our survey, the proportion of PCV among wet AMD cases was estimated to be 30% to 50% consistent with most Asian populations.<sup>10</sup> The optimal treatment for PCV remains unclear, although the EVEREST trial reported superior angiographic (but not visual acuity) outcome with PDT and PDT combined with ranibizumab over ranibizumab monotherapy. Despite the sound rationale behind combining the vaso-occlusive effect of PDT with the anti-angiogenic effects of anti-VEGF therapy, potential deleterious effects such as damage to choroidal vasculature remains a concern. A recent consensus paper from Singapore recommends combination therapy as initial treatment for subfoveal PCV.<sup>11</sup> This highlights that for PCV, further research is needed to study the optimal treatment regime.

## Conclusion

In conclusion, our survey shows the trends and evolving practice patterns of clinicians in Singapore in the management of major retinal disease. Despite the myriad of recent randomised controlled trials which have demonstrated the safety and efficacy of these new treatments, the variation in current practice patterns likely reflects the lack of consensus for optimal strategies. In such an environment, frequent update of the latest information and audit of local data are important to ensure practice patterns evolve in the right direction. Particular attention should also be paid during the informed consent process to ensure that all relevant information has been explained to the patient before arriving at a consensus for the treatment regime.

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