

RETINA TODAY

Guidance for the Clinical Management of Myopic Choroidal Neovascularisation: The Earlier, the Better

An interview discussion with
Kyoko Ohno-Matsui, MD, PhD;
Nicolas Leveziel, MD, PhD;
and Timothy Lai, MD, FRCS, FRCOphth

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A video series titled "The Importance of Early Diagnosis and Intervention in Myopic CNV" to accompany this supplement is available for viewing at EyeTube.net/series/novartis-lucentis/what-is-myopic-cnv.

Myopic choroidal neovascularisation (myopic CNV) is a common vision-threatening complication of myopia and pathological myopia. In 2013, a panel of renowned experts in medical retina worked together on a consensus of recommendations for the optimal clinical management of patients with myopic CNV.¹ The "Myopic choroidal neovascularisation: current concept and update on clinical management" review paper summarises the latest myopic CNV literature in the context of clinical experience and provides valuable practical guidance and treatment recommendations to physicians.¹

Retina Today: Why is this paper "Myopic choroidal neovascularisation: current concepts and update on clinical management,"¹ important for physicians treating myopic CNV?

Kyoko Ohno-Matsui, MD, PhD: There has been significant advancement in our understanding of the epidemiology, pathogenesis, and natural history of myopic CNV in recent years. This review paper attempts to summarise all of these important developments. It is authored by a number of leading myopic CNV experts from both Europe and Asia.¹

The guidance comes at an opportune time, as recent clinical trials have demonstrated the favourable efficacy and safety profiles of anti-VEGF agents in myopic CNV. These agents have now changed the way we manage our

patients with myopic CNV.

As a co-author of this clinical management update, I believe we have critically summarized the latest myopic CNV literature. This, combined with our own extensive clinical experience, has resulted in credible diagnosis and treatment recommendations that are current, informative and practical.

WHAT IS MYOPIC CNV?

Retina Today: What is the current definition of myopic CNV?

Dr. Ohno-Matsui: Myopic CNV is commonly referred to as subretinal neovascularisation in pathological myopia. The scar phase of myopic CNV is known as Fuchs' spot or Forster-Fuchs' retinal spot.

TABLE 1. CO-EXISTING PATHOLOGIES AND DIFFERENTIAL DIAGNOSES FOR MYOPIC CHOROIDAL NEOVASCULARISATION.¹

Other co-existing degenerative changes associated with myopia	Differential diagnosis for CNV
Myopic traction maculopathy	Neovascular AMD (nAMD)
Macular hole	Myopic macular haemorrhage due to lacquer cracks
Retinal tear or detachment	Punctate inner choroidopathy (typically co-exists with myopia)
Dome-shaped macula	Multifocal choroiditis
Staphyloma	Idiopathic CNV (in a myope, this is considered myopic CNV)
Atrophic changes (patchy atrophy, tessellated changes, and diffuse atrophy) AMD, age-related macular degeneration; CNV, choroidal neovascularisation Adapted from <i>British Journal of Ophthalmology</i> . Reprinted with permission.	

Historically, it was thought that myopic CNV only occurred in eyes with pathological myopia, but we now know that it can occur at any degree of myopia or in eyes without typical myopic degenerative fundus changes.¹

It is important that we have a generally recognizable definition of myopic CNV, as this will help us differentiate myopic CNV from other pathologies such as neovascular age-related macular degeneration (nAMD), multifocal choroiditis, punctate inner choroidopathy, myopic traction maculopathy, or lamellar macular hole. Therefore, in everyday clinical practice, myopic CNV can be differentially diagnosed using the refractive status of the eye and excluding any of these other CNV-related disorders (Table 1).¹

Retina Today: Why is it important to diagnose and treat myopic CNV early?

Dr. Ohno-Matsui: Without treatment, many patients with myopic CNV lose vision. In a 10-year follow-up study, it was shown that if myopic CNV was left untreated, visual acuity deteriorated to less than 20/200 vision in 5 years in approximately 9 out of 10 patients.² In our clinic, we have observed that untreated myopic CNV often leads to scarring within 1 year, and that CNV-related atrophy develops around the scar tissue. This CNV-related atrophy tends to enlarge over time and can only be prevented if the CNV disappears completely after treatment.

Untreated myopic CNV often leads to scarring within 1 year, and CNV-related atrophy develops around the scar tissue.

—Kyoko Ohno-Matsui, MD, PhD

Timothy Lai, MD, FRCS, FRCOphth: In my clinical experience, I believe it is important to diagnose and treat myopic CNV early before it progresses to atrophy or scar formation, as there are limited treatment results once atrophy or scar has formed. There are many co-existing pathologies for pathologic myopia. These can include, for example, myopic traction maculopathy, or myopic foveoschisis, epiretinal membrane, vitreomacular traction, and macular hole. It is imperative that these be identified, as they require different therapies than myopic CNV.¹ There are also conditions that may mimic myopic CNV, such as CNV due to nAMD or punctate inner choroidopathy. Both of these should be managed differently than myopic CNV.¹ It is also important for the physician to identify whether a retinal haemorrhage is due to lacquer cracks rather than myopic CNV to avoid unnecessary treatment.¹

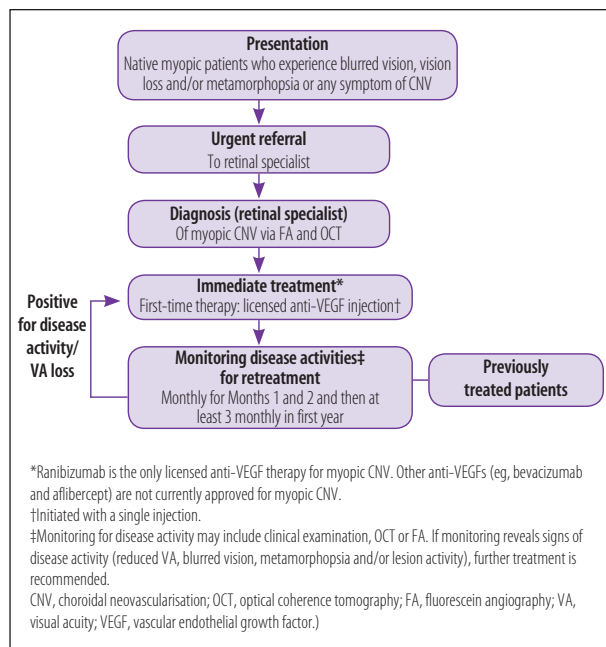


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Figure 1. Treatment algorithm for myopic choroidal neovascularisation.

Retina Today: What are the clinical differences between nAMD and myopic CNV?

Dr. Ohno-Matsui: That is a good question, and one that deserves attention. Even though anti-VEGFs are used to treat both nAMD and myopic CNV, these diseases are managed differently in terms of monitoring and treatment.^{1,3,4} In my opinion, the differential diagnosis may not be too difficult, as there are a number of recognisable differences between these 2 conditions.

First, evidence shows that as a patient's degree of myopia increases, their likelihood of AMD decreases, and that even patients with mild myopia have a lower-than-normal chance of developing AMD.⁵ Second, myopic CNV is a type 2 CNV, which in almost all cases, is located between the neurosensory retina and the retinal pigment epithelium (RPE), and which never features pigment epithelial detachment (PED). In nAMD, most cases of CNV are type 1, which are located in the sub-RPE space and which can feature PEDs.⁶

Furthermore, myopic CNV lesions look different from those of nAMD, especially in younger patients.¹ Most of us are familiar with nAMD lesion characteristics, but myopic CNV typically features "small, classic" lesions found near the fovea, which cause an initial rapid decrease in vision. Metamorphopsia and central scotoma may or may not be present.⁶ When viewed using slit-lamp biomicroscopy, myopic CNV appears as a subretinal greyish membrane surrounded by hyper-pigmented borders. If retinal haemorrhages are present, they are usually small in number and confined to a small area.⁶

EARLY DIAGNOSIS PATIENT CASE STUDY

By Timothy Lai, MD, FRCS, FRCOphth

A female patient presented with high myopia of around -12 dioptres, but with very good visual acuity of 20/25 (Figure 2). She complained of slight metamorphopsia that had first appeared the day before her initial presentation. During the initial examination, a very small macular haemorrhage was observed. Fluorescein angiography was performed to confirm the diagnosis of myopic CNV (Figure 3). A spectral domain OCT assessment indicated a small CNV lesion with minimal fluid at the fovea (Figure 4).

Immediate intravitreal injection of Lucentis was administered. The patient was followed-up a week later and an improvement in vision was observed. An OCT was also performed at this time that showed the CNV lesion had started to regress. Over the following 3-month period, the patient remained symptom-free and routine monitoring with OCT revealed complete regression and no recurrence of the CNV (Figures 5 and 6).

In this particular case, over a long period of follow-up, only a single injection was required to treat the patient successfully and restore her 20/20 vision. Had the patient

presented later, it is my view that she might have required additional injections before this outcome was achieved.

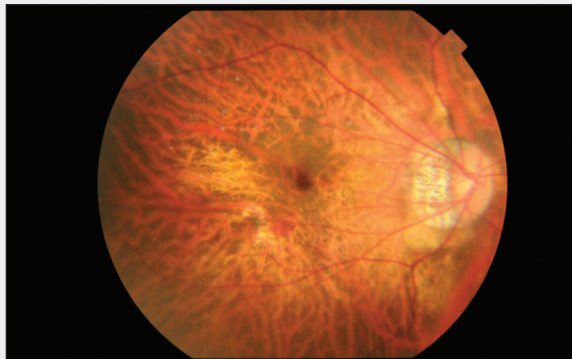


Figure 2. At baseline, patient presented with 20/25 vision, and discovered a small macular haemorrhage on colour photography.

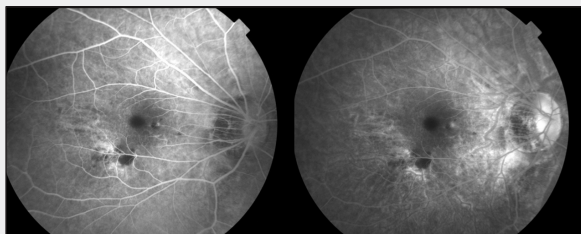


Figure 3. Fluorescein angiography at baseline shows both early and late phases of myopic choroidal neovascularization.

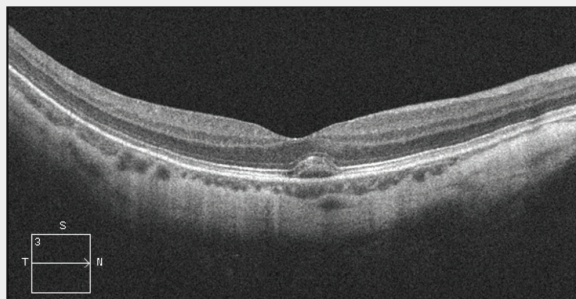
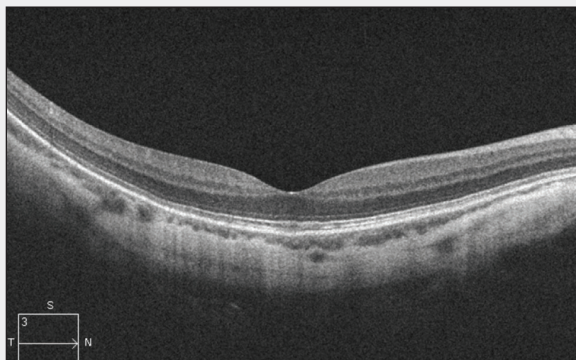
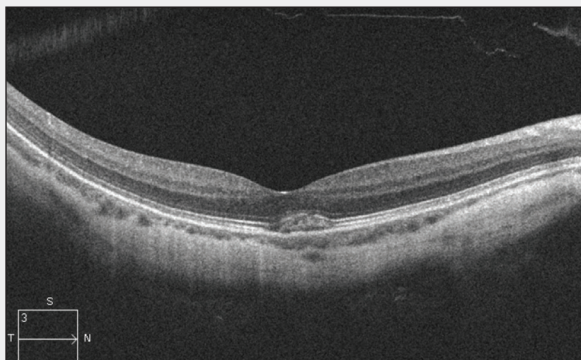


Figure 4. Spectral-domain optical coherence tomography at baseline; patient was 20/25 but with a small macular haemorrhage.



Figures 5 and 6. At week 1 and month 1 after initial treatment with intravitreal Lucentis, patient's vision improves and the haemorrhage completely resolves.

Retina Today: Why does the treatment algorithm contained in the review paper advocate urgent referral?

Dr. Lai: The review paper's treatment algorithm (Figure 1)

advocates urgent referral to physicians who have expertise in managing myopic CNV, because this allows prompt diagnosis and appropriate treatment.¹ We now have an effective, licensed therapy for myopic CNV, Lucentis (ranibizumab,

Images courtesy of T. Lai, MD.

IMMEDIATE TREATMENT PATIENT CASE STUDY

By Nicolas Leveziel, MD, PhD

A 50-year-old woman experienced recent metamorphopsia and near visual acuity decrease. Her visual acuity at the first examination was 20/50 for her involved right eye and 20/25 for her fellow eye. Fluorescein angiography showed an extrafoveal hyperfluorescent lesion, surrounded by a hypofluorescent ring on early frames (Figure 7). On late frames, a leakage of the dye was revealed by a disappearance of the previous hypofluorescent ring. On spectral domain OCT scans, the neovascular complex appeared as a hyperreflective pre-epithelial lesion associated to intraretinal cysts (Figure 8a).

After 1 intravitreal injection of ranibizumab, the visual acuity increased to 20/25 and the situation remained stable functionally and morphologically for long-term follow-up, ie, more than 12 months (Figure 8b).

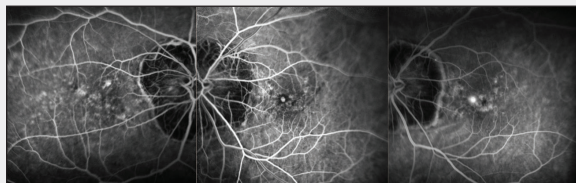


Figure 7. Extrafoveal hyperfluorescent lesion.

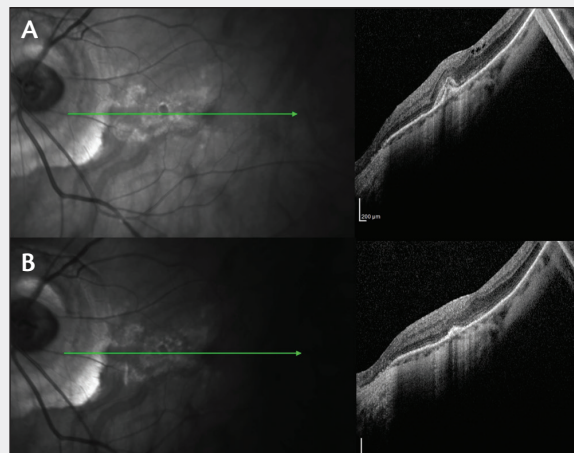


Figure 8a. Neovascular complex appeared as a hyperreflective pre-epithelial lesion associated with intraretinal cysts.

Figure 8b. After one intravitreal injection of Lucentis, patient's visual acuity improved from 20/50 to 20/25 and remained stable during the long-term follow-up.

Image courtesy of N. Leveziel, MD, PhD.

It is important to diagnose and treat myopic CNV early, before it progresses to atrophy or scar formation.

—Timothy Lai, MD, FRCS, FRCOphth

Novartis Pharma AG). A subgroup analysis of the large RADIANCE study showed that patients with larger CNV or worse visual acuity at baseline tended to require more injections than smaller lesion sizes or better visual acuity at baseline, although they still achieved similar visual gains.^{7,8}

This is also reflected in my own experience—if Lucentis treatment is administered early enough, fewer injections are required to achieve excellent visual acuity outcomes. The simple message is that if patients are referred and treated earlier, their treatment burden may be reduced.^{7,8}

Retina Today: What are some of the common challenges physicians face when trying to ensure early referral of myopic CNV patients?

Dr. Lai: The biggest challenge for physicians is ensuring

the diagnosis is correct. The patients I see with pathological myopia often have extensive retinal scarring and retinal atrophy is frequently present in their macula. I find that this makes the differential diagnosis of myopic CNV more difficult, particularly if those patients are elderly and have vision loss. In these cases, I use both the patient's visual acuity and subjective symptoms, such as metamorphopsia or scotomas, to confirm my diagnosis. I also closely examine their fundus images and perform additional spectral domain OCT and fluorescein angiography as appropriate.

TREATING MYOPIC CNV: CURRENT STANDARD OF CARE

Retina Today: Why is immediate treatment with a licensed anti-VEGF as the first line treatment emphasized in the algorithm?

Nicolas Leveziel, MD, PhD: As mentioned by Dr. Ohno-Matsui, it is important because if a patient with myopic CNV is treated too late, a fibrotic lesion will develop after 3 months, and the lesion will then progressively be surrounded by atrophy leading to the poor long-term visual acuity outcomes associated with this condition.¹ This is why it is important to treat the patient as soon as possible.

Lucentis is recommended as the first-line treatment

because it is the only treatment to date that shows superior efficacy in a large study when compared with verteporfin photodynamic therapy (vPDT), which was the previous standard of care.⁴

RADIANCE was a large, double-masked, randomized controlled study that included 277 myopic CNV patients from diverse ethnic populations (including European and Asian countries).⁴ Patients in the vPDT arm who could be switched to Lucentis at month 3 did not achieve the same visual acuity gains at the end of the study as those treated initially with Lucentis.⁴ The study not only demonstrated the superior efficacy of Lucentis compared with vPDT at month 3 in terms of vision gain, Lucentis further showed a significant improvement in visual acuity of 14.4 letters at month 12, with a median of 2 injections.⁴ The ocular and

symptoms (such as metamorphopsia), or signs of myopic CNV disease activity on FA or OCT (meaning, intraretinal or subretinal fluid or active leakage).¹

We also recommended patients should be educated to return to the retina specialist for recurrence of metamorphopsia or if the patient notices a decline in vision.¹ After the first year, the ophthalmologist will decide the appropriate frequency of follow-up visits needed on a case-by-case basis, again with the request that patients should return for evaluation if they notice metamorphopsia or any drop in vision.¹

TREATING MYOPIC CNV: OTHER TREATMENT OPTIONS

Retina Today: There are other treatment options available for myopic CNV. What is the evidence to support those treatments?

Dr. Leveziel: Prior to Anti-VEGF therapies, the most common treatment options for myopic CNV included laser photocoagulation and vPDT. Unfortunately, these treatment options only maintain visual acuity, but do not improve long-term vision.^{6,10,11}

As we briefly mentioned earlier, vPDT was the previous standard of care for myopic CNV. Although the results from the VIP study showed significantly higher efficacy for vPDT vs placebo at 1 year in terms of the percentage of patients with less than 8-letter loss, unfortunately after 2 years there was no significant difference vs placebo.¹⁰ Another limitation to this treatment may be long-term chorioretinal atrophy, which can contribute to vision loss.¹ For this reason, I rarely used vPDT for the treatment of myopic CNV.

Laser photocoagulation is another treatment option, but it is only suitable in the treatment of extrafoveal myopic CNV.^{6,11} In my experience, extrafoveal myopic CNV accounts for 10% to 12% of cases, and laser photocoagulation is destructive to the retina.

Retina Today: What about other anti-VEGF treatments for myopic CNV? What is the evidence to support those treatments?

Dr. Leveziel: Although Lucentis is currently the only licensed anti-VEGF treatment for myopic CNV in Europe, our paper did discuss 2 other treatments that are not licensed in Europe: aflibercept and bevacizumab.¹

Aflibercept was investigated in a double-masked, sham-controlled trial that showed its efficacy in improving visual acuity in East-Asian patients with myopic CNV.¹² To date, the results have not been published in a peer-reviewed journal.

Bevacizumab is not indicated for ocular use.¹³ Further, if it is compounded for intravitreal use, this may raise concerns about its safety and the potential risk of infection associated to compounding.^{1,14,15} ■

Lucentis is recommended as the first-line treatment for myopic CNV.

—Nicolas Leveziel, MD, PhD

nonocular safety profiles were consistent with those reported in other indications and no new safety signals were identified in patients treated with Lucentis.⁴

Consequently, these results led to the regulatory approval of Lucentis for myopic CNV in July 2013, and Lucentis is currently the only anti-VEGF treatment licensed for the treatment of myopic CNV in Europe.⁹

Retina Today: How are treatment, monitoring, and re-treatment of myopic CNV with anti-VEGFs different from nAMD?

Dr. Leveziel: Patients with myopic CNV require far fewer injections than patients with nAMD.^{1,4} In the majority of myopic CNV cases, patients will only need 1 or 2 injections in the first year.⁴ Patients with myopic CNV generally do not need to be monitored as frequently as patients with nAMD.^{1,3,9}

In our review paper based on current evidences, we recommended monthly monitoring for the first 2 months after the first Lucentis intravitreal injection for myopic CNV, with clinical evaluation and appropriate imaging.¹ If there is no disease activity after the first 2 months, monitoring schedules can be revised to every quarter for the rest of the first year.¹ It should be noted that we defined “disease activity” as any drop in vision, new or persistent visual

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DISCLAIMER: The answers provided are based on the physicians' own experiences of anti-VEGF treatments in their respective countries of residence. Labels may vary in other countries and the discussions may not reflect local practice or may not be representative for all patients.

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