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. 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.

Retina Today: Why is this paper “Myopic choroidal neovascularisation: current concepts and update on clinical management,” 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.

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>
<thead>
<tr>
<th>TABLE 1. CO-EXISTING PATHOLOGIES AND DIFFERENTIAL DIAGNOSES FOR MYOPIC CHOROIDAL NEO-VASCULARISATION.¹</th>
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<tbody>
<tr>
<td>Other co-existing degenerative changes associated with myopia</td>
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<tr>
<td>Myopic traction maculopathy</td>
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<tr>
<td>Macular hole</td>
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<td>Retinal tear or detachment</td>
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<td>Dome-shaped macula</td>
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<td>Staphyloma</td>
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<tr>
<td>Atrophic changes (patchy atrophy, tessellated changes, and diffuse atrophy)</td>
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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.\(^1\)

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.\(^3,4\) 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.\(^6\)
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**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.

**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,

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**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.
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 super-
ior efficacy in a large study when compared with verte-
porfin 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.6 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
nonocular safety profiles were consistent with those report-
ed in other indications and no new safety signals were iden-
tified in patients treated with Lucentis.4

Consequently, these results led to the regulatory approv-
al 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, moni-
toring schedules can be revised to every quarter for the rest
of the first year.1 It should be noted that we defined “dis-
ease activity” as any drop in vision, new or persistent visual
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 metamor-
phopsia or if the patient notices a decline in vision.1 After
the first year, the ophthalmologist will decide the appro-
friate frequency of follow-up visits needed on a case-by-case basis,
again with the request that patients should return for evalu-
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TREATING MYOPIC CNV:
OTHER TREATMENT OPTIONS

Retina Today: There are other treatment options avail-
able 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. 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 myo-
pic CNV.6,11 In my experience, extrafoveal myopic CNV
accounts for 10% to 12% of cases, and laser photocoagula-
tion 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 con-
cerns about its safety and the potential risk of infection
associated to compounding.1,14,15

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Timothy Lai, MD, FRCS, FRCOphth, the department of ophthalmology and visual sciences, The Chinese University of Hong Kong.

Nicolas Leveziel, MD, PhD, the department of ophthalmology, Faculté de Médecine de Poitiers, in Poitiers, France.

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.
