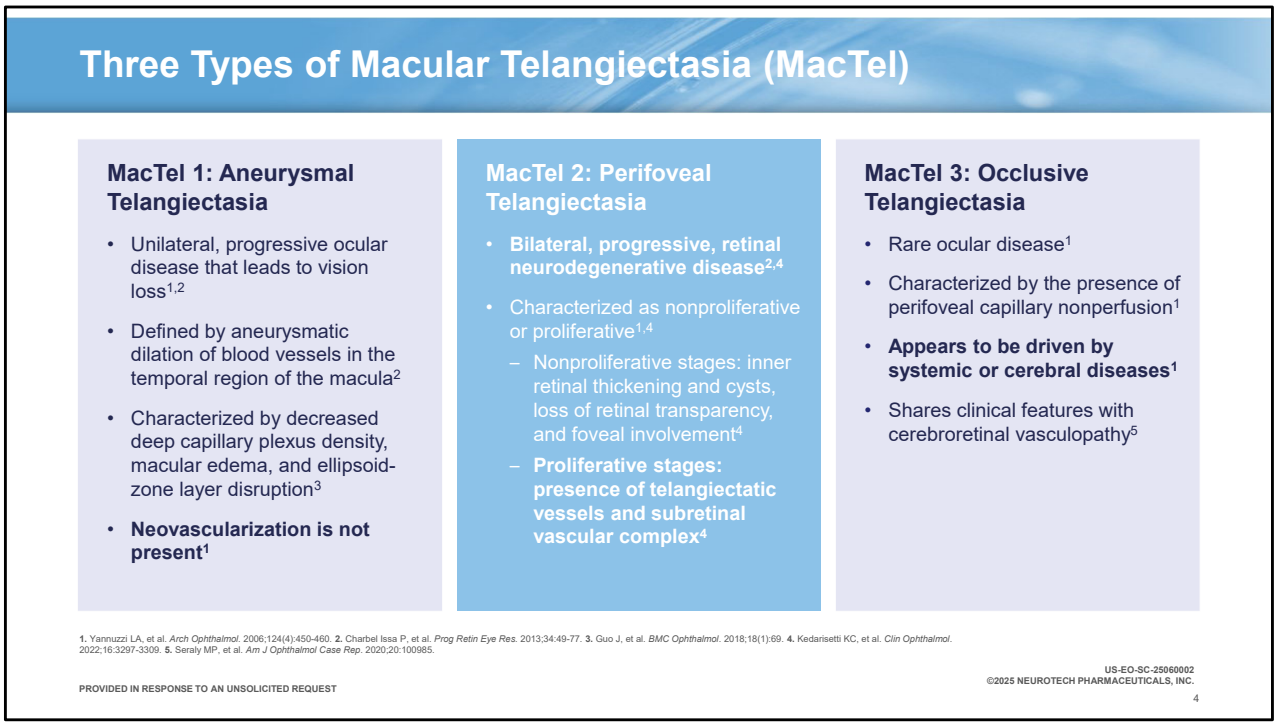
MacTel Disease State Awareness (DSA)

June 2025

PROVIDED IN RESPONSE TO AN UNSOLICITED REQUEST

Table of Contents

MacTel: Overview and Epidemiology



Speaker Notes:

- There are three different types of macular telangiectasia, or MacTel: aneurysmal, perifoveal, and occlusive.
- MacTel 1 is characterized by aneurysmatic dilation of blood vessels in the temporal region of the macula, decreased deep capillary plexus density, macular edema, ellipsoid-zone layer disruption, and no neovascularization; MacTel 1 is progressive and leads to vision loss
- The presence of microaneurysms and unilateral disease help to distinguish MacTel 1 from MacTel 2
- MacTel 3 is rare and appears to be driven by systemic or cerebral diseases
- MacTel 2, which is the focus of this slide deck, is a bilateral neurodegenerative retinal disease with nonproliferative and proliferative stages. Additional information on MacTel 2 follows.

MacTel 2: Neurodegenerative Retinal Disease Associated With Central Vision Impairment[1]

MacTel 2 is a **neurodegenerative retinal disease** that leads to **vision loss**; it may start in one eye, but it almost always affects **both eyes**[1]

Photoreceptor loss occurs in MacTel 2 and leads to central vision loss and functional impairment[1,2]

Patients experience substantial burden of illness due to loss of visual acuity, including visual field defects and **impaired reading and driving ability**[2-4]

No curative or disease-altering treatments currently exist[1,2]

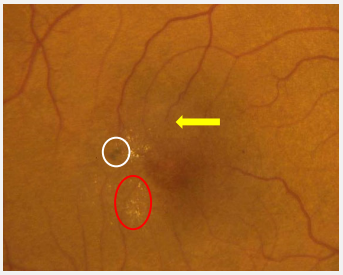
1. Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **3.** Heeren TFC, et al. *Retina*. 2014;34(5):916. **4.** Bronstad PM, et al. *JAMA Ophthalmol*. 2013;131(3):303-309.

Speaker Notes:

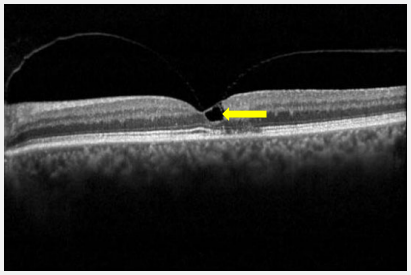
- MacTel is a bilateral, neurodegenerative retinal disease leading to vision loss involving retinal apoptosis
- MacTel causes photoreceptor loss which results in central vision loss and a loss of function
- Patients experience substantial burden of illness due to loss of visual acuity, including visual field defects and impaired reading and driving ability
- There are no curative/disease-altering treatments currently

MacTel 2 Results in Changes to the Retina[1,2]

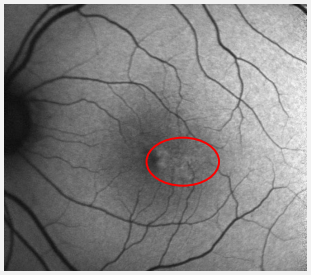
Microvascular Abnormalities (arrow), **Crystals** (red circle), **Pigment Hyperplasia** (white circle)



Cavitary Lesion on OCT (arrow)



Luteal Pigment Loss on AF (red circle)



These early changes seen in OCT and AF are often misdiagnosed as lamellar holes, vitreomacular traction, or cysts, contributing to the underdiagnosis of MacTel 2

AF, autofluorescence; OCT, optical coherence tomography. Images provided by Dr. Thomas Aaberg.
1. Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77.

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6

Speaker Notes:

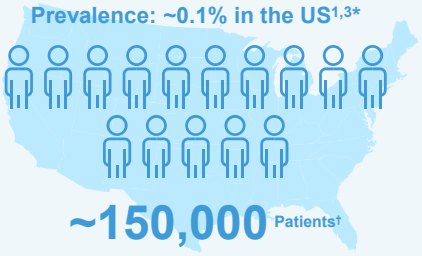
- Early retinal changes seen with optical coherence tomography and autofluorescence, like microvascular abnormalities, crystallization, pigment hyperplasia, cavitary lesions, and pigment loss, may be misdiagnosed, contributing to the underdiagnosis of MacTel 2.

MacTel 2 is Underdiagnosed, With an Estimated Prevalence of 0.1% in the US[1*]

Incidence: ~0.8/100,000 persons/year[2,3]

~2,700 new cases/year[†]

Prevalence: ~0.1% in the US[1,3*]



~150,000 Patients[†]

Patients are diagnosed in mid-late decades

Symptoms appear around age **40–50 years**[4]

Mean age of diagnosis is **57 years**[5]

Approximately **2% of MacTel patients are under age 40 years**[6]

Patient population may be underestimated

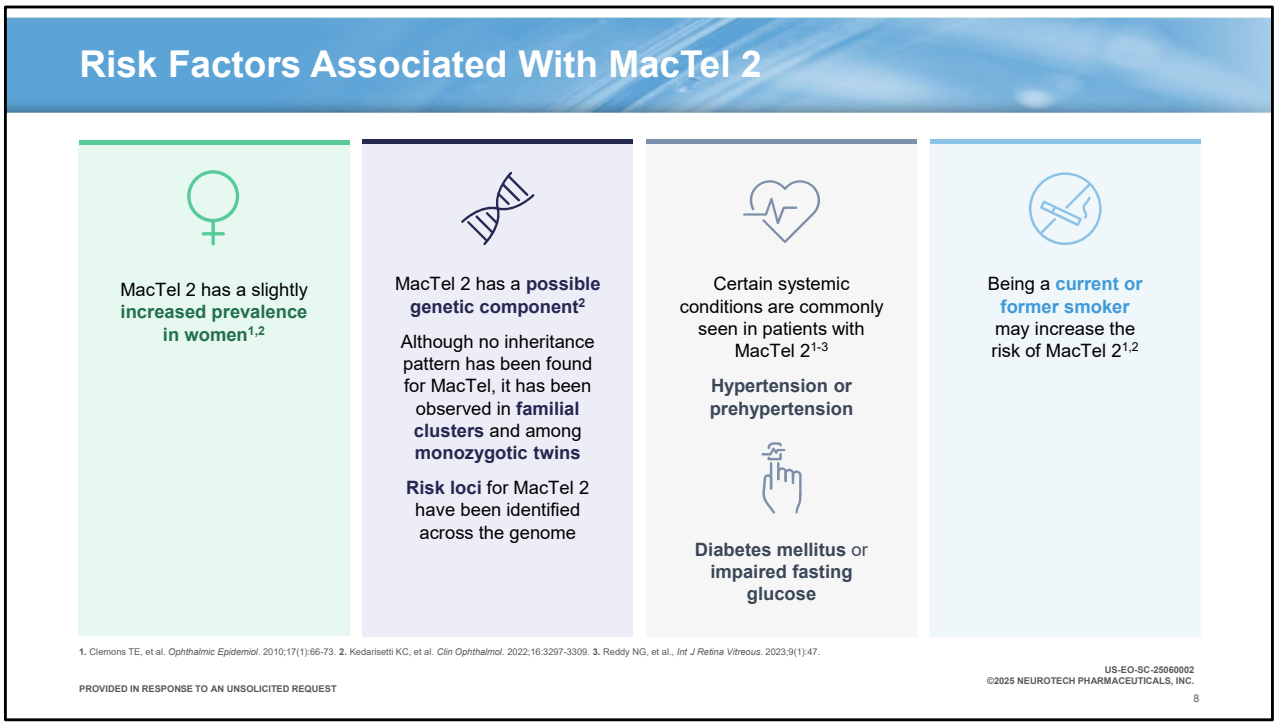
Underdiagnosis and misdiagnosis of MacTel contributes to the potentially **underestimated patient numbers**[4]

*Among patients aged 43–86 years; based on Beaver Dam, Wisconsin. †Calculation performed using the US 2020 population (331,449,281).[3]

1. Klein R, et al. *Am J Ophthalmol*. 2010;150(1):55-62.e2. **2.** Starr MR, et al. *Ophthalmic Surg Lasers Imaging Retina*. 2020;51(5):S35-S42. **3.** United States Census Bureau. "Populations and People." Accessed Jan 2024. **4.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **5.** Clemons TE, et al. *Ophthalmic Epidemiol*. 2010;17(1):66-73. **6.** Reddy NG, et al., *Int J Retina Vitreous*. 2023;9(1):47.

Speaker Notes:

- MacTel affects more than 100K Americans, with almost 3K newly diagnosed patients/year
- Patients experience symptoms in their 40s-50s, and are commonly diagnosed in their 50s-60s
- Patient population is likely underestimated due to underdiagnosis and lack of advanced imaging technology in population studies



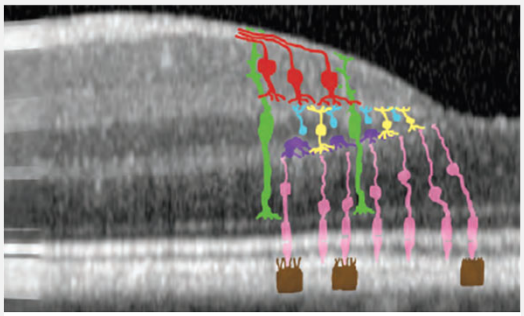
Speaker Notes:

- The risk of developing MacTel 2 may be increased in certain groups, including women, those with a genetic predisposition, those with hypertension or prehypertension, those with diabetes mellitus or impaired fasting glucose, and current or former smokers.

MacTel 2 Disease Diagnosis

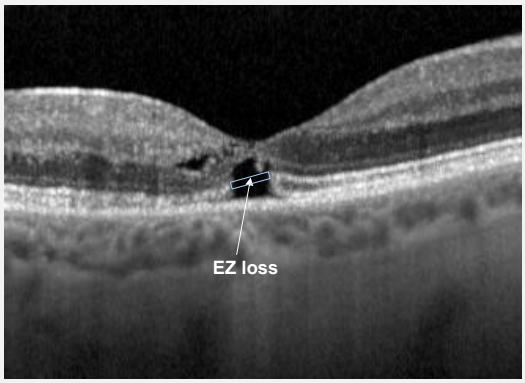
Photoreceptor Loss in MacTel 2 Leads to Functional Vision Loss[1]

Healthy retina OCT
(Cross-section through the fovea[2])



● Müller glial cell ● Ganglion cells ● Bipolar neurons ● Photoreceptors
● Horizontal neurons ● Amacrine neurons ● Retinal pigment epithelium

MacTel OCT



EZ, ellipsoid zone; OCT, optical coherence tomography. Image on left reprinted with permission from Neal Adams, M.D., under a license agreement. Image on right provided by Dr. Thomas Aaberg.
1. Heeren TFC, et al, *Ophthalmology*. 2020;127(11):1539-1548. **2.** Adams NA. *Atlas of OCT*. Franklin, MA, USA: Heidelberg Engineering; 2024.

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Speaker Notes:

- Photoreceptor loss in MacTel leads to impairment of visual function
- Loss of the ellipsoid zone is a marker for photoreceptor loss and of disease severity
- On optical coherence tomography (OCT), photoreceptor loss is reflected in ellipsoid zone (EZ) loss and can be used to measure EZ breaks

Size and Rate of Enlargement of EZ Loss in MacTel 2

In healthy eyes, the **mean area ± SD of superficial foveal avascular zone was 0.27 ± 0.101 mm^2** based on OCT-A[1]

In studies of MacTel 2, baseline **EZ loss area has been ~0.5–0.6 mm^2**, with a **rate of change of ~0.08 mm^2 per year**[2,3]

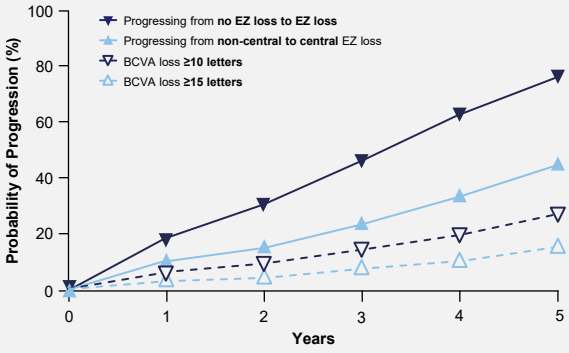
EZ, ellipsoid zone; OCT-A, optical coherence tomography angiography; SD, standard deviation.
1. Shahlaee A, et al. *Am J Ophthalmol*. 2016;161:50-55.e1. **2.** Heeren TFC, et al. *Retina*. 2018;38(Suppl 1):S20-S26. **3.** Neurotech data on file.

Speaker Notes:

- To put EZ area loss with MacTel 2 into context, the mean area of the superficial foveal avascular zone was 0.27 mm^2 in healthy eyes.
- With MacTel 2, EZ area loss has been shown to be approximately ~0.5 to 0.6 mm^2, with loss increasing by ~0.08 mm^2 each year.

Most MacTel 2 Patients Develop EZ Loss With a Subsequent Impact on Vision[1]

Based on findings from the MacTel Natural History Study (N=507)[1]



5

76% develop an EZ loss 5 years after diagnosis[1]

45% progress from non-central to central EZ loss 5 years after diagnosis[1]

Total EZ area loss results in significant BCVA loss[1,2]

BCVA, best corrected visual acuity; EZ, ellipsoid zone.
1. Peto T, et al. *Retina*. 2018;38(Suppl 1):S8-S13. **2.** Chew EY, et al. *Ophthalmol Sci*. 2023;3(2):100261.

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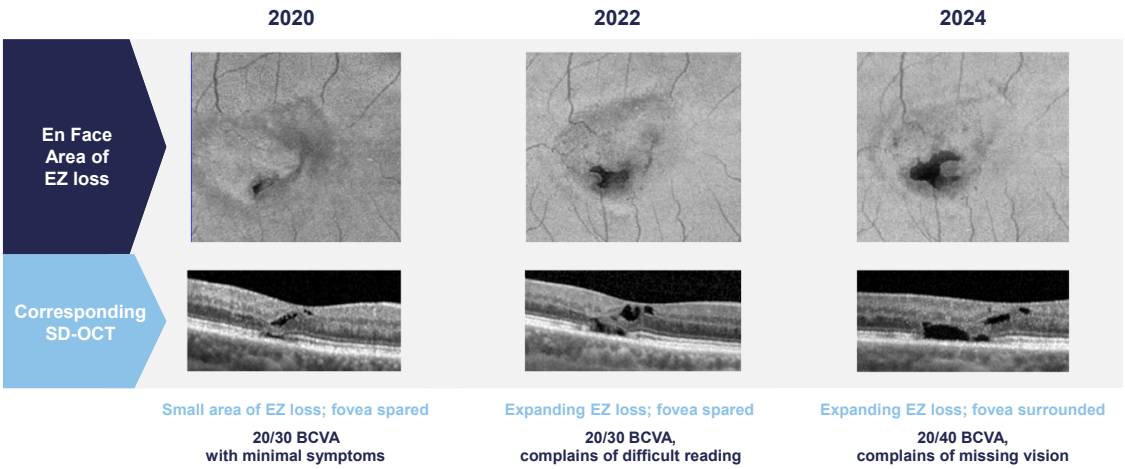
12

Speaker Notes:

- About three quarters of MacTel patients develop EZ breaks (includes both noncentral and central break) 5 years after diagnosis
- About half of patients progress from noncentral to central EZ loss 5 years after diagnosis

BCVA Over Time May Not Adequately Capture MacTel 2 Progression or Visual Function[1]



BCVA, best corrected visual acuity; EZ, ellipsoid zone; SD-OCT, spectral domain optical coherence tomography. Images provided by Dr. Thomas Aaberg.

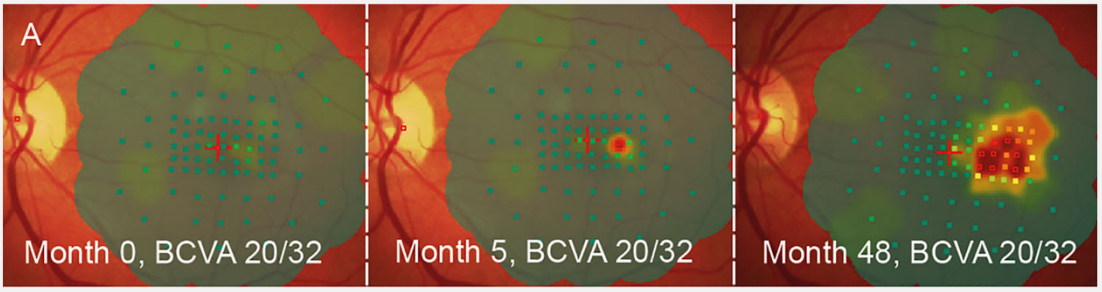
1. Pauleikhoff D, et al. *Acta Ophthalmol.* 2019;97(7):e998-e1005.

Speaker Notes:

- EZ loss is not always correlated with significantly decreased BCVA; however, affected patients may still experience substantial visual impairment

BCVA Often Does Not Reflect Disease Burden[1,2]

Progression of disease over 4 years[1]



These microperimetry images mapping areas of photoreceptor loss demonstrate the development and subsequent expansion of a scotoma in a MacTel patient, yet visual acuity remains stable[1-3]

1. Heeren TFC, et al. *Invest Ophthalmol Vis Sci*. 2015;56(6):3905-3912. **2.** Charbel Issa P, et al. *Invest Ophthalmol Vis Sci*. 2007;48:3788-3795. **3.** Heeren TFC, et al. *Ophthalmology*. 2020;127:1539-1548.

Speaker Notes:

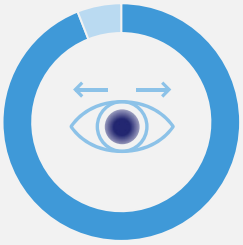
- Paracentral scotomas might go undiagnosed/unappreciated by an HCP, particularly in the setting of good visual acuity
- Microperimetry can reveal scotoma area increases in temporal region even when there is little effect on visual acuity
- Visual acuity (BCVA/Snellen visual acuity) is often a poor measure of MacTel patients' disability, because these patients can use eccentric fixation to "see around" the progressively worsening blind spot (or scotoma) which is developing in each eye
- Microperimetry is useful in understanding the patient experience since it can reveal scotoma changes independent from BCVA

Irreversible Vision Loss and Compromised Visual Function[1,2]

Patients with a scotoma have a mean BCVA of 20/63[3]

Scotomas, or visual field defects, force patients to compensate with small eye movements, resulting in delayed reactions and other impairments not reflected in visual acuity[4]

47%
Patients with absolute scotomas[1]

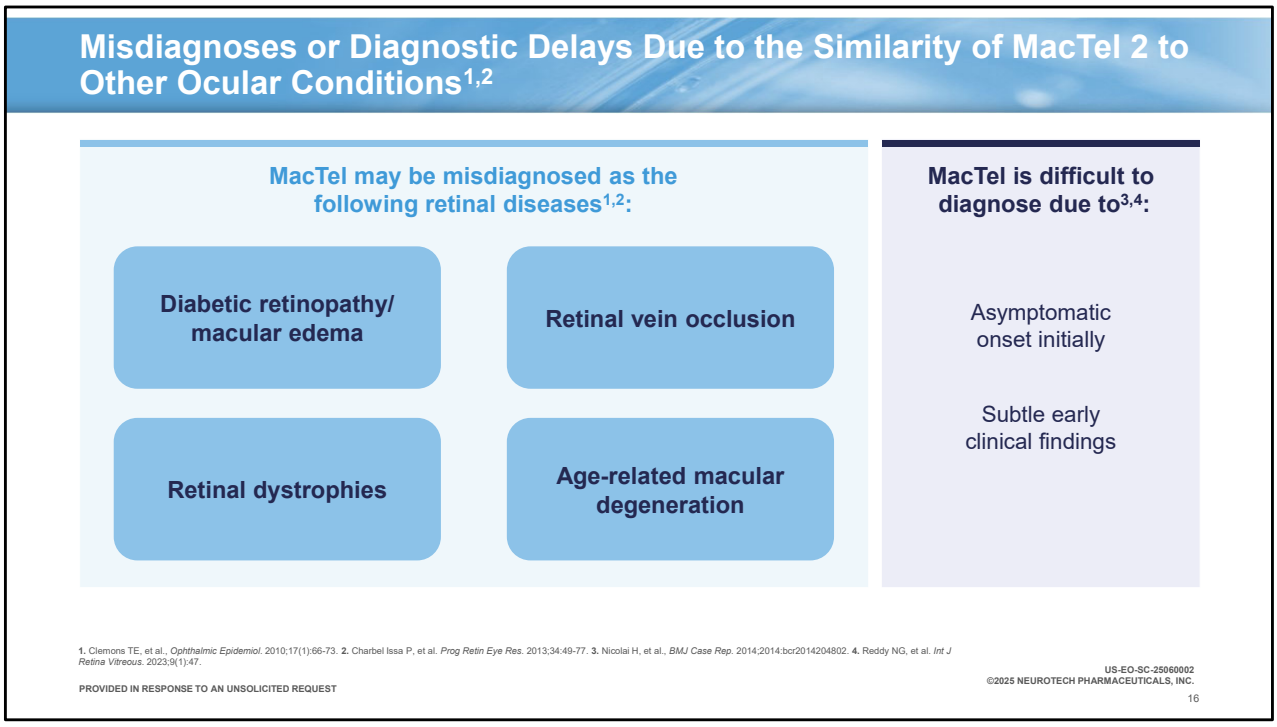


94%
Patients with scotomas that expanded within 5 years[5]*

*Those with an initial scotoma had an average growth rate of 1.3 new test points with an absolute scotoma per year.[4]
BCVA, best correlated visual acuity.
1. Vujosevic S, et al. *Retina*. 2018;38(Suppl 1):S14-S19. **2.** Dalkara D, et al. *Hum Gene Ther*. 2016;27(2):134-147. **3.** Finger RP, et al. *Invest Ophthalmol Vis Sci*. 2009;50(3):1366-1370. **4.** Bronstad PM, et al. *JAMA Ophthalmol*. 2013;131(3):303-309. **5.** Heeren TFC, et al. *Invest Ophthalmol Vis Sci*. 2015;56(6):3905-3912.

Speaker Notes:

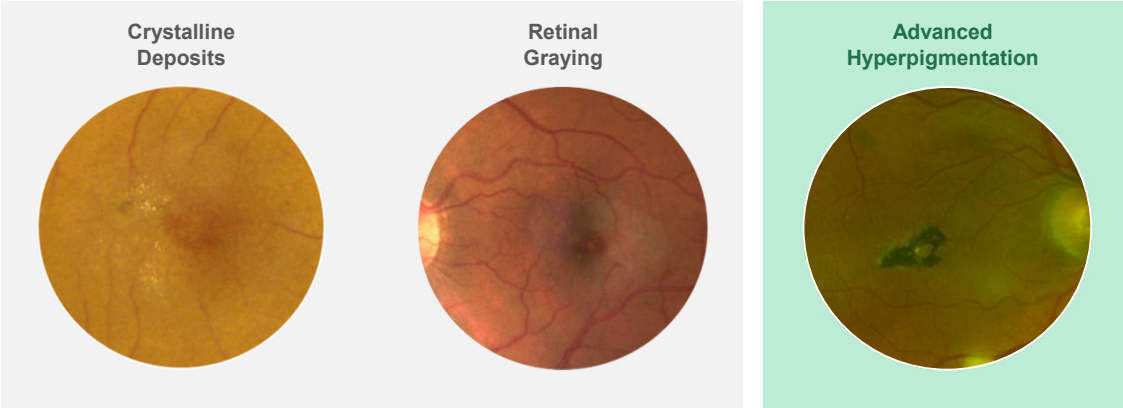
- MacTel patients face BCVA loss and scotomas, which impair visual function
- More than a third of patients have BCVA worse than 20/50; though letter loss is gradual (1 letter per year), significant decreases may occur due to scotomas or neovascular membrane development
- Close to half of patients had absolute scotomas, while almost all patients with initial scotomas had them grow into larger scotomas after 5 years
- Scotomas force patients to compensate with small eye movements, leading to delayed reaction times



Speaker Notes:

- In addition to the potential for misdiagnoses, early-stage disease is often asymptomatic, with subtle clinical effects that can delay MacTel diagnosis until patients seek outpatient attention in later stages following symptom manifestation
- MacTel often progresses slowly, with minimal effects on Snellen visual acuity in early-stage disease
- Accurate diagnosis is often delayed possibly due to low awareness among clinicians and patients, and potential for misdiagnosis as other conditions

Fundus Changes Can Be Subtle in Early MacTel 2[1]



Images provided by Dr. Thomas Aaberg.
1. Charbel Issa P, et al. *Prog Retin Eye Res.* 2013;34:49-77.

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17

Speaker Notes:

- If MacTel is suspected, the fundus photos can be used to evaluate and document the macular changes
- Fundoscopic/fundus photo examination can be utilized to detect MacTel clinical features, although this technique may miss some early-stage disease

OCT and OCT-A Can Aid in Making a MacTel 2 Diagnosis and Monitoring for Neovascularization[1,2]

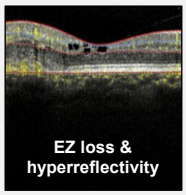
Common OCT findings[1,2]:

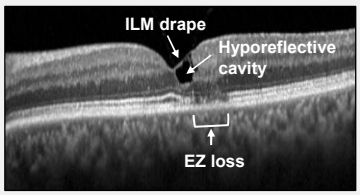
Disruption/loss of EZ

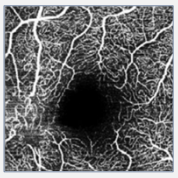
Hyporeflective cavities in the inner and outer neurosensory retina

ILM drape

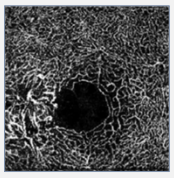
OCT-A shows retinal and choroidal vasculature in high resolution without the need for intravenous dye[1,3]



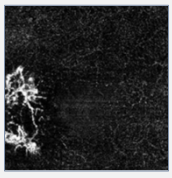




Telangiectasia in SVP



Telangiectasia in DVP



Neovascularization in AVZ

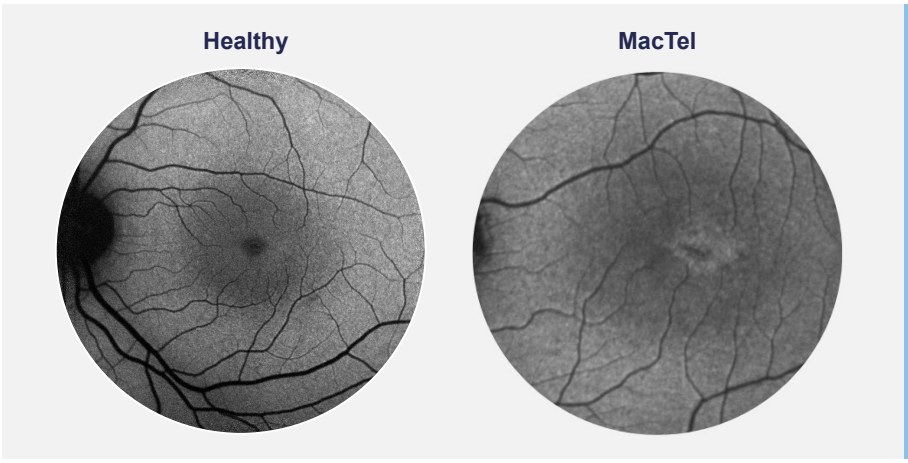
AVZ, avascular zone; DVP, deep vascular plexus; EZ, ellipsoid zone; ILM, internal limiting membrane; OCT, optical coherence tomography; OCT-A, optical coherence tomography angiography; SVP, superficial vascular plexus. Images provided by Dr. Thomas Aaberg.

1. Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **3.** AAO What is Macular Telangiectasia? 2023 Available: https://www.aao.org/eye-health/diseases/macular-telangiectasia#:~:text=Published%20Sep.,vision%20for%20activities%20like%20reading. Accessed Nov 2024.

Speaker Notes:

- OCT is especially useful for detecting retinal changes associated with early disease (eg, right angle blood vessels)
- OCT and OCT-A may also be used to diagnose MacTel and detect neovacsularization

FAF Can Detect the Earliest Stages of MacTel 2[1-3]



Macular pigment loss in eyes with MacTel is associated with increased auto-fluorescence[2]

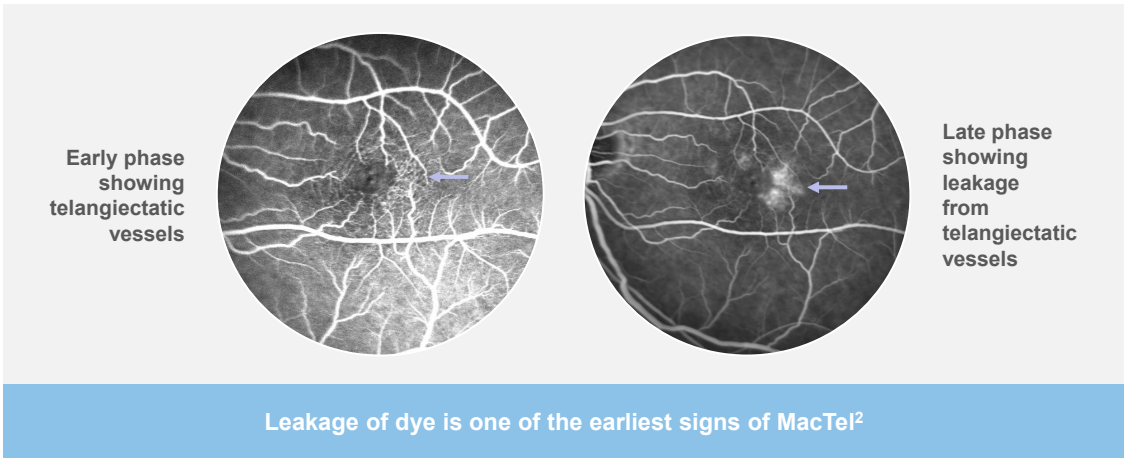
FAF, fundus autofluorescence. Images provided by Dr. Thomas Aaberg.
1. Gillies MC, et al. *Ophthalmology*. 2009;116(12):2422-2429. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **3.** Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309.

19

Speaker Notes:

- In the healthy macula, macular pigment strongly absorbs blue light, resulting in decreased autofluorescence; in MacTel, increased autofluorescence is associated with loss of macular pigment
- Fundus autoflourescence (FAF) can detect the earliest stages of MacTel and measure macular pigment optical density

FA Has Been Considered the Gold Standard for MacTel 2 Diagnosis[1]



Leakage of dye is one of the earliest signs of MacTel[2]

FA, fluorescein angiography. Images provided by Dr. Thomas Aaberg.
1. Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **2.** Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309.

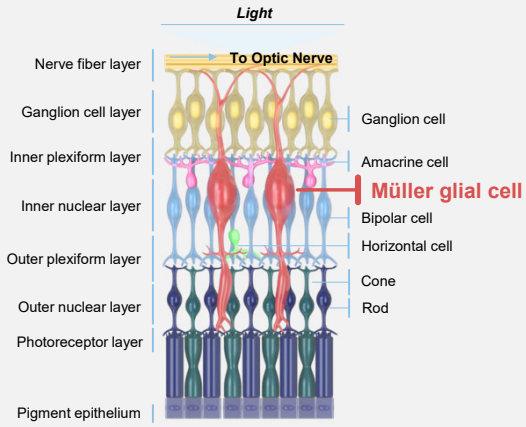
Speaker Notes:

- Fluorescein angiography can also be employed to confirm a MacTel diagnosis by revealing telangiectatic vessels
- One characteristic that may help distinguish MacTel 2 from other diseases is the lack of angiographic leakage or pooling of fluorescein dye into hyporeflective cavities
- Fluorescein angiography may not be necessary with OCTA

Pathogenesis

Irreversible Vision Impairment With Müller Glial Cell Dysfunction[1]

- Müller glial cells are the most common glial cell type in the human retina, providing structural and neurotrophic support[2]
- In MacTel, Müller glial cells experience apoptosis, which results in **retinal neurodegenerative effects**[1,3]
- Müller glial cell dysfunction and apoptosis lead to **macular photoreceptor and ganglion cell loss**, causing **impaired central and sharp vision** in affected patients[1,4,5]



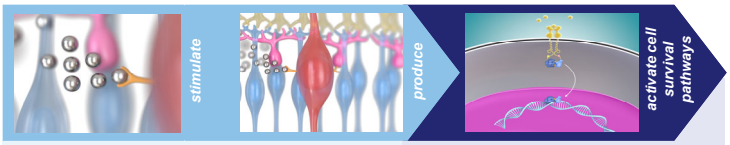
1. Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309 **2.** Kobat SG, Turgut B. *Beyoglu Eye J*. 2020;5(2):59-63. **3.** Powner MB, et al. *Ophthalmology*. 2013;120(11):2344-2352. **4.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **5.** Muller S, et al. *Ophthalmologica* 2019;241(3):121-129.

22

Speaker Notes:

- Müller glial cells provide structural and neuroprotective support to protect photoreceptors and ganglion cells
- In MacTel 2, dysfunction of Müller glial cells is central to neurodegeneration and leads to neuronal damage, including photoreceptor apoptosis, and vasculopathy
    - Vasculopathy of Müller glial cells includes telangiectasis, blood-retina barrier breakdown, and intraretinal neovascularization
    - Deep retinal neovascularization may be caused by due to long-term upregulation of vascular endothelial growth factor-A and downregulation of pigment epithelium-derived factor

CNTF Is Key to Protecting Retinal Neurons[1,2]



CNTF
(ciliary neurotrophic factor)

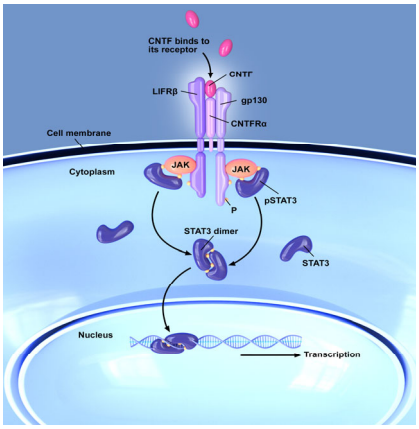
Müller glial cell

- CNTF binds to CNTF receptors on Müller glial cells, activating the JAK-STAT pathway[1,3]
  - Prompts production of growth factors and neuroprotective factors, including CNTF[1]

Neuroprotective factors, including CNTF

- Neuroprotective factors provide structural/ neuroprotective support by activating cell survival pathways[3,4]
- Müller glial cell dysfunction and apoptosis impede production and effectiveness of neuroprotective factors[3]

Enabling macular photoreceptor protection[1,2]



CNTF, ciliary neurotrophic factor; JAK-STAT, Janus kinase/signal transducers and activators of transcription.
1. Bringmann A, et al. *Prog Retin Eye Res*. 2009;28(6):423-451. **2.** Wen R, et al. *Prog Retin Eye Res*. 2012;31(2):136-151. **3.** Rhee KD, et al. *Proc Natl Acad Sci U S A*. 2013;110(47):E4520-E4529. **4.** Cayouette M, et al. *J Neurosci*. 1998;18(22):9282-9293.

Speaker Notes:

- Müller glial cell production of CNTF is key for protecting retinal neurons
- CNTF is specifically responsible for promoting photoreceptor cell survival
- MacTel causes Müller glial cell dysfunction and apoptosis, which in turn disrupts the neuroprotective effects of CNTF

Preclinical Data: Ocular Delivery of CNTF Can Significantly Slow Progression of Retinal Degeneration[1-8]

Authors	Publication Date	Study Subjects	Key Findings
Cayouette et al.	1998	Mouse	Demonstrated that intraocular adenovirus-mediated gene transfer of CNTF reduces photoreceptor loss in homozygous *rds* mouse[1]
Peterson et al.	2000	Rat	Showed that, in rat retinas, CNTF-mediated changes in Müller cell function yield a secondary neuroprotective signaling to photoreceptors and suggested that the impact of CNTF on the JAK-STAT pathway influences neuronal survival[2]
Liang et al.	2001	Mouse and Rat	Found that intravitreal administration of CNTF enables broad and long-term histological photoreceptor protection in mice and rats for 8.5–9.0 months and 6.0 months, respectively[3]
Sieving et al.	2006	Human	Showed improved acuities of 10–15 letters for n=3 of 7 patients who received CNTF delivered via encapsulated cells implanted into the vitreous[4]
Kassen et al.	2009	Zebrafish	Demonstrated that CNTF has neuroprotective effects on photoreceptors in retinas of adult zebrafish[5]
Talcott et al.	2011	Human	Showed improved photoreceptor survival vs contralateral eyes which experienced progressive photoreceptor death[6,*]
Zhang et al.	2011	Human	Demonstrated CNTF delivery via intraocular encapsulated cell technology led to improved BCVA loss of <15 letters in the high dose group (96.3%) vs low dose (83.3%) and sham (75%)[7]
Rhee et al.	2013	Mouse	Found that low levels of CNTF intravitreally injected in mouse retinas stimulate Müller glial cells and promote photoreceptor neuroprotection[8]

*Included n=2 patients with retinitis pigmentosa and n=1 with Usher syndrome type 2.[6]
CNTF, ciliary neurotrophic factor; JAK-STAT, Janus kinase/signal transducers and activators of transcription.
1. Cayouette M, et al. *J Neurosci*. 1998;18(22):9282-9293. **2.** Peterson WM, et al. *J Neurosci*. 2000;20(11):4081-4090. **3.** Liang FQ, et al. *Mol Ther*. 2001;4(5):461-472. **4.** Sieving PA, et al. *Proc Natl Acad Sci U S A*. 2006;103(10):3896-3901. **5.** Kassen SC, et al. *Exp Eye Res*. 2009;88(6):1051-1064. **6.** Talcott KE, et al. *Invest Ophthalmol Vis Sci*. 2011;52(5):2219-2226. **7.** Zhang K, et al. *Proc Natl Acad Sci U S A*. 2011;108(15):6241-6245. **8.** Rhee KD, et al. *Proc Natl Acad Sci U S A*. 2013;110(47):E4520-E4529.

Speaker Notes:

- There is broad availability of preclinical/clinical evidence that indicates ocular CNTF delivery can significantly slow retinal degeneration progression

Impact on Patients

Vision Impairments Significantly Impact Daily Life[1-6]

Reduction in reading capability[3,5]

- **Decreases by 50 WPM** on average for MacTel patients from the healthy average of 190 WPM
- **Struggle reading numbers:** paying bills, dialing phone numbers, seeing prices correctly when shopping
- **Difficulties with daily tasks:** reading medication bottles, computer usage, reading and following recipes

I can't read books anymore. I literally pick up a book to read it and I have to move my head around and I go through the first few pages and really bad eye starts burning. I just have to put books down, so I had to give up reading.

– MacTel Patient[5]

Limitations on driving[1,2,4,5]

- **Slower reaction** to road hazards (eg, road hazards suddenly appearing)
- Only able to drive short distances/daylight hours due to **difficulty navigating roads and reading road signs**
- **Difficulty judging distance** and perceiving straight lines

*The first symptoms I was having where I knew something was wrong….was with **driving**. Every linear line is bent in my vision…I constantly see other cars in my lane so I can't pass vehicles anymore because I can't discern where the vehicles are at. And if they are white, silver, or grey I can't see them at all.*

– MacTel Patient[5]

WPM, words per minute.

1. Hearen TFC, et al. *Ophthalmology*. 2020;127(11):1539-1548. **2.** Lee , et al. AAO. "Driving Restrictions per State." 2023; **3.** Finger RP, et al. *Invest Ophthalmol Vis Sci*. 2009;50(3):1366-137033. **4.** Bronstad PM, et al. *JAMA Ophthalmol*. 2013;131(3):303-309. **5.** Neurotech data on file. **6.** Charbel Issa P, et al. *Doc Ophthalmol*. 2009;119(2):133-140.

Speaker Notes:

- With a lack of approved treatments and a high degree of disease subtlety, the impact of MacTel on patients' daily life may be difficult for HCPs to detect
- Patients often emphasize that MacTel makes reading and driving significantly more difficult
- MacTel literature has shown that patients experience significant disease impact on their ability to read and drive
- Visual impairment from MacTel can make common tasks such as paying bills, shopping, and driving more difficult

Distorted Vision With MacTel 2

Patients with **nonproliferative MacTel** often experience **metamorphopsia**[1]

- Present in 83% of MacTel eyes without neo-vascularization

1. Charbel Issa P, et al. *Doc Ophthalmol*. 2009;119(2):133-140.

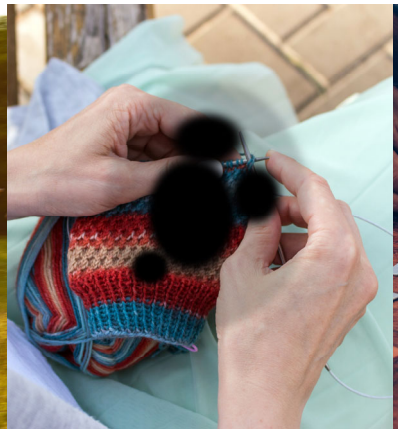
PROVIDED IN RESPONSE TO AN UNSOLICITED REQUEST

27

Speaker Notes:

- Patients with MacTel 2 frequently have visual distortion, including metamorphopsia, even when the disease does not impact visual acuity
- Metamorphopsia has been found to be common in early, nonproliferative stages of MacTel 2
- Metamorphopsia can interfere with reading ability, and therefore, vision-related quality of life

Visual Symptoms Have Significant Impact on Daily Life[1]



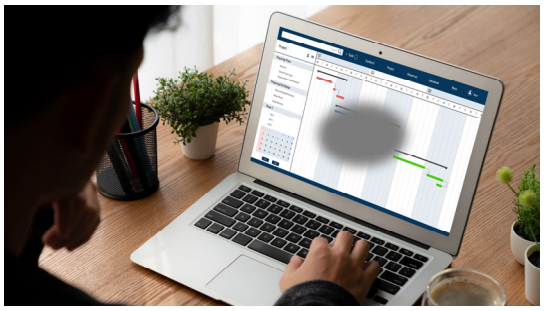
1. Neurotech data on file.

PROVIDED IN RESPONSE TO AN UNSOLICITED REQUEST

Speaker Notes:

- Visual symptoms of MacTel 2 can significantly impact daily life
- Patients often have profound scotomas, or blind spots; absolute scotomas are present in about half of eyes in patients with MacTel 2

MacTel 2 Affects Productivity Leading to Socioeconomic Burdens[1]



MacTel can cause economic burden during prime earning years[2,3]

Employment disruption and reduced wages[1,2]

- Substantial productivity loss for affected patients
- Need to find an accommodating job for their vision symptoms
- Fear of potential job loss
- Feelings of uncertainty about financial stability

Caregiver burden[1]

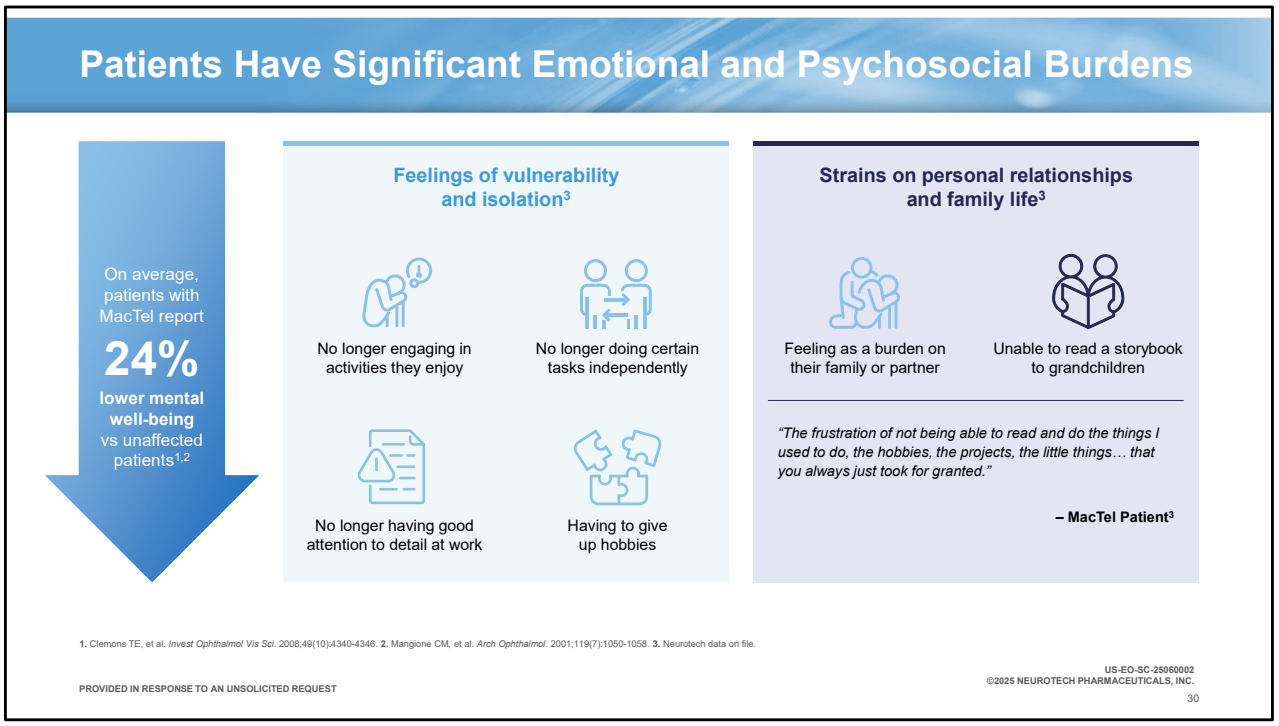
- Economic cost due to time spent on in-home care and transportation to appointments

1. Rein DB, et al. *Ophthalmology*. 2022;129(4):369-378. 2. Neurotech data on file. 3. Heeren TFC, et al. *Retina*. 2014;34(5):916-919.

PROVIDED IN RESPONSE TO AN UNSOLICITED REQUEST

Speaker Notes:

- MacTel and vision loss generally have significant impacts on the overall economy and individual productivity
- MacTel can cause an economic burden on a patient during their prime earning years: vision loss results in employment disruption, caregiver burden, and medical costs



Speaker Notes:

- MacTel patients report lower mental well-being vs unaffected individuals
- Vision loss from MacTel can make patients feel vulnerable, isolated, and put strain on their relationships

MacTel 2 Key Takeaways

Photoreceptor loss in MacTel leads to functional vision loss[1,2]

Most MacTel patients develop **ellipsoid zone loss** with a subsequent impact on vision[3]

BCVA often does not reflect disease burden; patients may develop a scotoma, but visual acuity remains stable[1,4,5]

MacTel may be **misdiagnosed** as other retinal diseases, leading to diagnostic delays[6]

There are currently **no approved disease-modifying treatments** for MacTel, and patients therefore continue to decline[2]

Dysfunction in Müller glial cells and apoptosis leads to vision impairment[1,7,8]

Ocular delivery of CNTF may significantly **slow progression** of retinal degeneration[8,9]

Visual symptoms have a significant **impact on daily life,** including work productivity[10]

Patients with MacTel experience significant **emotional and psychosocial burdens**[11-13]

CNTF, ciliary neurotrophic factor; BCVA, best corrected visual acuity.

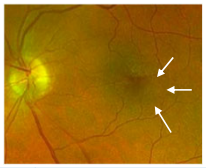
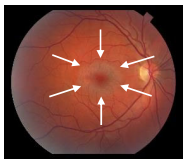
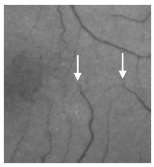
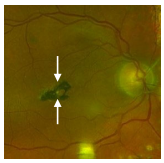
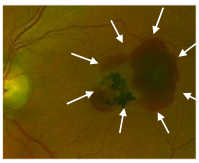
1. Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **3.** Peto T, et al. *Retina*. 2018;38(Suppl 1):S8-S13. **4.** Heeren TFC, et al. *Invest Ophthalmol Vis Sci*. 2015;56(6):3905-3912. **5.** Charbel Issa P, et al. *Invest Ophthalmol Vis Sci*. 2007;48:3788-3795. **6.** Clemons TE, et al. *Ophthalmic Epidemiol*. 2010;17(1):66-73. **7.** Powner MB, et al. *Ophthalmology*. 2013;120(11):2344-2352. **8.** Shen W, et al. *J Neurosci*. 2012;32(45):15715-15727. **9.** Tao W, et al. *Invest Ophthalmol Vis Sci*. 2002;43(10):3292-3298. **10.** Rein DB, et al. *Ophthalmology*. 2022;129(4):369-378. **11.** Clemons TE, et al. *Invest Ophthalmol Vis Sci*. 2008;49(10):4340-4346. **12.** Lamoureux EL, et al. *Invest Ophthalmol Vis Sci*. 2011;52(5):2520-2524. **13.** Neurotech data on file.

Appendix

Different ophthalmologic imaging findings can be observed across the spectrum of MacTel 2 disease severity[1,2*]

Nonproliferative disease
(exudative telangiectasia and foveal atrophy)[2]

Proliferative disease
(subretinal neovascularization)[2]

	Occult telangiectatic vessels	Loss of retinal transparency	Right-angled blood vessels	Retinal pigment clumps	Subretinal neovascularization
					
DFE	**Faint graying and depigmentation; mostly normal**[3]	**Slight graying and loss of transparency of the parafoveolar retina**[3]	**Dilated and blunted right-angle venules; perifoveal telangiectasia**[3]	**Dark pigmented plaque**[3]	**SNV, fibrovascular proliferation in the parafoveal area**[2,4,5]
FA	**Occult vascular abnormalities** are barely detectable[4]	**Mild telangiectatic** and **microaneurysmal changes adjacent to the fovea** with **mild late leakage**[3]		**Ischemia** and marked late **leakage in** the **temporal perifovea**[3]	
OCT	Subtle **hyperreflective middle retinal layer**[3,6]	**Hyporeflective inner retinal cavities**[6]	**Central EZ collapse** and **photoreceptor loss**[3]	Retinal **hyperreflective deposits** and **cysts**[3]	**SNV**, foveal **contour irregularities**[4,6]

*MacTel five-stage classification first defined by Gass and Blodi in 1993[5]; in 2022, Chew et al. introduced a 7-stage classification system using OCT HR, pigment, and EZ loss as an alternative to the Gass-Blodi five-stage system.[7]
DFE, dilated fundus exam ; EZ, ellipsoid zone; FA, fluorescein angiography, OCT, optical coherence tomography; SNV, subretinal neovascularization. Images provided by Dr. Thomas Aaberg.
1. Charbel Issa P, et al. *Prog Retin Eye Res.* 2013;34:49-77. **2.** Kedarisetti KC, et al. *Clin Ophthalmol.* 2022;16:3297-3309. **3.** Chin EK, et al. *Invest Ophthalmol Vis Sci.* 2013;54(7):4459-4470. **4.** Yannuzzi , et al. *Arch Ophthalmol.* 2006;124(4):450-460. **5.** Gass JD, Blodi BA. *Ophthalmology.* 1993;100(10):1536-1546. **6.** Venkatesh R, et al. *Int J Retina Vitreous.* 2022;8(1):26. **7.** Chew EY, et al. *Ophthalmol Sci.* 2023;3(2):100261.

33

Speaker Notes:

- Various clinical features are defined in early (nonproliferative) and late-stage (proliferative) MacTel via fundoscopy, fluorescein angiography, and optical coherence tomography
- These clinical features can be used to assist in diagnosing patients who are in early- and late-stage disease