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A conversation with Mathew MacCumber, MD, PhD, an ophthalmologist at Rush University Medical Center who serves as the protocol co-chair for this trial

Clinical Trial Profile: A Randomized Trial Comparing Immediate vs. Deferred Surgery for Symptomatic Epiretinal Membranes

Mathew MacCumber, MD, PhD is an ophthalmologist specializing in vitreoretinal surgery at Rush University Medical Center. He is a professor and research director in the Department of Ophthalmology at Rush. His many areas of expertise include eye injuries and trauma, inflammatory eye disease and retinal disorders. He researches the management of epiretinal membranes, age-related macular degeneration and diabetic retinopathy, and he has a particular interest in ocular pharmacology and drug development.

Q: What is the main problem this study is evaluating?

A: In middle age, about one-third of adults develop a condition called epiretinal membrane (ERM), which is a thin sheet of fibrous tissue that forms on top of the retina. As a result, it can cause visual distortion and blurring. People generally need 20/50 vision to read newsprint. When a person's vision gets to that point or worse, most retinal specialists recommend surgery.

We perform a common operative procedure, a vitrectomy, which has a high overall success rate in helping patients improve their vision, making it safer for them to drive, allowing them to read and so forth. However, we know that in some cases the patient's vision does not improve and sometimes worsens.

There's been a push by some retina specialists to operate earlier. If an ERM causes a distortion in a patient's retina that results in having distorted vision, even if his or her visual acuity is 20/25 or even 20/20, this is still not a functional eye. We don't know how successful it is to operate earlier on patients. A patient's vision can improve, but if you're already starting at 20/25, how good will it get? We also don't know very well the predictors of which eyes would respond well to surgery and which wouldn't.

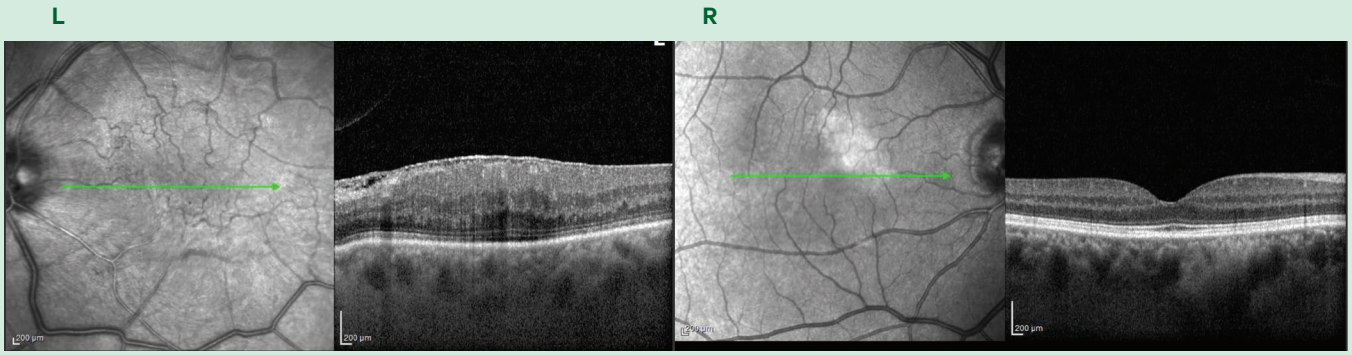

Figure. Two optical coherence tomography (OCT) scans of the retinas of a 70-year old man. He has a normal retina of the right eye (labeled R) and a left eye with a symptomatic epiretinal membrane (labeled L).

Q: What is the main objective this clinical trial is set up to evaluate?

A: This protocol will investigate whether it's better to operate early when a patient's vision is 20/25 to 20/40, or if it's okay to wait until it drops further and then operate. We'll compare visual acuity and other visual outcomes at 36 months between eyes randomized to immediate versus deferred surgery if the vision worsens.

Between these two groups, we'll compare changes in metamorphopsia — distorted vision; reading speed, which is a functional outcome; and optical coherence tomography outcomes (see Figure). We'll also look at complication rates. Within the deferred surgery group, we want to determine the rate and time of the progression of ERM and the need for a vitrectomy. How many eyes that don't have surgery will deteriorate and need a vitrectomy?

It's unknown whether delaying surgery, which allows the foveal architecture to remain compromised and potentially deteriorate, results in worse visual acuity outcomes than when surgery was performed earlier. We don't know how many eyes would maintain good vision if we operated sooner. There's a need to better understand the predictors of this progression. That data isn't well known, and that is what we're particularly interested in.

Q: Are there any secondary outcome measures you are interested in?

A: The other objectives we are exploring include measuring the associations between participant factors such as race, ethnicity, age and retinal anatomy with visual outcomes. We want to assess how often cataract surgery is needed after a vitrectomy for symptomatic ERM. We will also collect natural history data for deferred surgery eyes and assess that as well.

Q: How is the study funded?

A: The three-year, $2 million study is funded largely by the National Eye Institute through the National Institutes of Health.

Q: In addition to the data you'll gather, how will this trial be an improvement over previous studies that have evaluated ERM?

A: Since this is a prospective randomized trial, it is far superior to practically all other ERM studies because most prior studies were done retrospectively. Previous studies usually did not have any randomization, and none of them had the careful refraction and vision measurements that we are using. We're also using the most valid vision measurement tools from the beginning to the end of the study. The good news is that Sotrovimab, another monoclonal antibody,

does have efficacy against the Omicron variant and will be available soon; it was developed from the serum of someone who recovered from SARS1. The challenge with Sotrovimab is that it needs to be administered through an IV, which requires more training and monitoring for reactions after infusion. The benefit of the other monoclonals that worked was that patients could receive them subcutaneously at home, which is a tremendous benefit.

Q: Who would be an ideal candidate to participate in this trial?

A: We Patients who are age 50 and older, who have at least one eye with symptomatic ERM and who have had a change in vision or experienced a distortion in their vision within the previous 24 months are ideal candidates. Their ERM has to involve the central 3mm of the macula, and there must be a distortion of the foveal center.

Patients have to understand that they will be randomized; either they'll have surgery within one month of their enrollment or they will be observed and will receive surgery only if their vision or symptoms worsen.

Q: How are you and Rush involved in the trial?

A: Rush University Medical Center and Rush Oak Park Hospital are enrollment sites for the trial. Right now, we have 36 of our 50 targeted centers on board. We begin enrollment in January.

I've been helping to lead the development of this trial for the past several years. As protocol co-chair, I will review patients who are enrolled to make sure that they qualify, and I will also be the lead author with my co-chair, Darrell Baskin, MD, who is a vitreoretinal surgeon at Retinal Consultants of San Antonio.

More information on this clinical trial can be found at https://clinicaltrials.gov/ct2/show/NCT05145491.

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