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Gene Therapy, the Future of Eye Care?

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ReachMD Moderator:
On this episode, we'll hear from Drs Courtney Crawford and Raj Maturi. We caught up with them at the 2025 American Academy of Ophthalmology annual meeting in Orlando, Florida, where they shared their perspectives on how ocular gene therapy fits into the future of eye care, early insights on routes of administration, and tips for discussing gene therapy with patients.

Dr. Crawford is a board-certified retina specialist and founder of Star Retina in Burleson, Texas. He previously served for 10 years as a physician in the U.S. Army, where he attained the rank of Lieutenant Colonel.

And Dr. Maturi is a board-certified retina specialist at the Midwest Eye Institute and founder of Retina Partners Midwest in Carmel, Indiana, where he focuses on macula, retina, and vitreous care.

To kick things off, we asked Dr. Maturi how he identifies patients who might benefit from ocular gene therapy.

Dr. Maturi:
Even my patients who manage to keep up with treatments, often find the frequency of injections and visits disruptive to their daily lives. Many of them talk about not being able to sleep the night before, for example. This burden can take a toll on them, their caregivers, and even the healthcare system.[1] So these are the kind of signals that tell me more about a durable approach that could potentially help them.

We see this impact in the data, as well. As highlighted in Weng's 2023 review, a large US study of 50,000 eyes with neovascular AMD, they found that over 1/3 of the patients received fewer injections than the 8 to 12 per year regimen used in pivotal trials associated with optimal vision outcomes. Another study cited in the same review showed that by year 7, 90% of patients had discontinued treatments.[1]

But I don't think of gene therapy only as an option for patients with treatment fatigue; I see it as something we could consider much earlier in the disease course, as long as we confirm that the active neovascular membrane is responding to anti-VEGF treatment.[2]

For me, recognizing a patient who may benefit from gene therapy isn't about waiting until we have exhausted other options. The first thing is that they have to respond to anti-VEGF treatment given intravitreally.[2] And if they are, why not consider an option with the potential to preserve vision and reduce treatment burden by decreasing the frequency of visits and giving them more independence right from the start.[1]

Dr. Crawford:
I would start considering gene therapy right at the time of diagnosis. That first clinical visit really sets the framework for the journey a patient will take with macular degeneration.

The reality is, in 2025, we have more options than ever before. But to me, gene therapy represents where medicine is heading—towards more personalized and durable treatment approaches.

While no single therapy is 'the best' for everyone, I ask patients what they're looking for. Are they comfortable coming in every two to three months? Would they prefer something that stretches to every six months? Or are they interested in gene therapy, knowing that it still requires monitoring but offers another path in our growing menu of treatment options for wet AMD?

ReachMD Moderator:
With that background in mind, Dr Maturi, what's your approach to helping patients better understand gene therapy when considering a clinical trial?

Dr. Maturi:
When I explain gene therapy to patients, I describe it as a way of giving cells new genetic instructions so they can produce a protein, to correct a faulty process, or to correct a process on how a gene is behaving to treat their eye disease.[3]

These transgenes—or in other words, the therapeutic genetic sequence—is typically delivered to the eye by adeno-associated viruses, or an AAV. And they're favored in retinal gene therapy because they've been extensively studied and used in the first approved gene therapy for the eye.[2,4,5]

One of the first questions patients often ask is, "Will this change my DNA?" And I explain that with AAVs, the risk is low. The transgene is delivered into the cell, but it stays episomal, meaning it stays separate from the patient's DNA. This is an important point to highlight because this means it helps limit the potential for interfering with the patient's nuclear genome.[2]

The second advantage is tropism, the AAV's affinity for retinal cells. Certain serotypes, like AAV8, have shown strong transduction efficiency into photoreceptors and the retinal pigment epithelium.[4,5]

And finally, AAVs are not known to replicate or cause disease in humans.[2] Combined with the fact that the eye is small, self-contained, and immune privileged, this contributes to an encouraging safety profile for ocular gene therapy as it continues to be evaluated in large pivotal studies.[2,5] Unlike most other organs, we can also monitor the effects in real time with noninvasive imaging, such as OCT, so both the patient and physician can see how the retina is responding to the treatment.[2]

ReachMD Moderator:
So, Dr. Maturi, what are some key considerations when it comes to the administration route for gene therapy?

Dr. Maturi:
There are several factors that we should keep in mind. Certain administration routes may be better suited depending on the patient, the disease, and the product. The three main delivery methods are subretinal, intravitreal, and suprachoroidal.[2]

The subretinal approach is the one we're most familiar with after the approval of the first gene therapy for a rare ocular disease in 2017.[6] This method requires surgical intervention in the operating room, where the vector is delivered into the subretinal space after a vitrectomy. The resulting transduction is largely confined to the area of the bleb, so you're targeting a very defined region of the retina.[2]

One advantage with this approach is that exposure to the vitreous and anterior segment is minimal, which lowers the risk of inflammation or an immune response.[2] From a surgical standpoint, the technique is similar to procedures we already perform, like submacular hemorrhage treatment.

Intravitreal delivery is a less invasive option. It's performed in the office, much like an anti-VEGF injection, so it's familiar to both patients and the retina specialists. The downside is that the vitreous and the anterior segments are more broadly exposed to the vector, which increases the chance of inflammation or immune response. That said, its accessibility and ease of administration make it an attractive option for some common retinal diseases.[2]

The third and more recently established option is suprachoroidal delivery, which is already used in a commercially approved, non-gene therapy product. The injection is also performed in the office and given anteriorly—similar to an intravitreal injection—but then it diffuses posteriorly toward the retina. Again, the advantage here is that the vector stays compartmentalized toward the back of the eye, limiting exposure to the vitreous and anterior segment.[2]

I do tell patients that, compared to an intravitreal injection, this method can cause more discomfort or a sense of pressure during the procedure itself. For many physicians, it's still relatively new, but it's a feasible approach that builds on our familiarity with in-office procedures.[2]

So overall, the route we choose really comes down to balancing precision, safety, patient tolerance, and again what's most practical for both the patient and the treating physician.

ReachMD Moderator:
Dr. Crawford, how do you evaluate whether a patient is a surgical candidate for a subretinal gene therapy trial?

Dr. Crawford:
Well, in my opinion, if you're healthy enough to have cataract surgery, then you're healthy enough to receive subretinal gene therapy. In fact, in the study arms we've done so far, all of the patients have undergone cataract surgery.

That said, candidacy can be a bit more nuanced, especially in patients with significant peripheral retinal pathology. For example, if someone has lattice degeneration, peripheral retinal holes, or very high myopia, elevating the retina during the procedure could make those conditions worse. In those cases, I might treat the pathology ahead of time, or I may decide the patient isn't the best candidate for subretinal gene therapy.

And from a recovery standpoint, there's not much more required beyond the typical post-op care for a standard vitrectomy. There's no complicated positioning afterwards. Patients just need to stay upright for about 24 hours to let the medicine settle.

ReachMD Moderator:
Now Dr. Maturi, how do you evaluate whether a patient is a surgical candidate for a subretinal gene therapy trial?

Dr. Maturi:
That's a good question. I think a major consideration is making sure the patient can safely undergo surgery.

In my experience, it means that these are patients who are not taking anticoagulants that can't be paused for about ten days or so. They should also be able to maintain the required surgical positioning and follow postop instructions—for example, sitting upright when advised.

In general, my patients have been pseudophakic for subretinal delivery, consistent with the populations studied in earlier clinical trials. And finally, we also want the patient to have healthy conjunctiva without any evidence of infection to lower the risk of complications with surgery.

ReachMD Moderator:
Dr. Maturi, how do you walk patients through the subretinal delivery process?

Dr. Maturi:
The way I usually explain it to them is that we make three tiny incisions in the eye. And that these incisions are thinner than pencil lead. These incisions allow us to perform a vitrectomy, which is removal of the gel in the back of the eye.[2,7] By the time most patients are over the age of 50, this gel is already mostly broken down, so removing it can actually help reduce or even eliminate floaters that they already have.

Once removal of this gel is done, we create a very small opening in the retina, called a retinotomy, and then place the treatment underneath the retina. When we inject this treatment, it creates a small pocket called a bleb.[2,7] The body absorbs that bleb over time, and that's how the drug is released into the localized tissue.

Now, I tell patients that some changes in retinal cells can occur after treatment, which may affect the visual function in those cells. But I reassure them that we've learned to minimize the risk of complications by adjusting where we deliver the treatment to help protect central vision.[2,7]

ReachMD Moderator:
Dr. Crawford, what surgical insights would you share with clinicians who are beginning to perform subretinal gene therapy procedures?

Dr. Crawford:
Well, I think of it as a really elegant procedure. It's something that most retina specialists are already comfortable with because it uses techniques that are part of our daily armamentarium.

When I'm talking to a colleague who's new to the procedure, I usually start by emphasizing that visualization is the key to success.

For surgical setup, it's important to think carefully about the type of viewing system you use. I personally find that a wide-angle view is especially helpful, which is why I prefer a non-contact approach.

I've also found, that especially early on, vitrectomy is easier in pseudophakic patients—it makes the procedure more straightforward. A thorough vitrectomy with good peripheral vitreous shaving is essential. And just as important is making sure the hyaloid is fully elevated because even a small amount of hyaloid left behind can prevent you from creating a proper subretinal bleb.[2,7]

Now, positioning of the surgeon is another key part for bleb placement. Some of us are right-handed, so for right-handed surgeon working on the right eye, it's straightforward to target the inferior-nasal quadrant—around positions 4 to 6 o'clock—which is where you want to create your bleb and deliver therapy.

But if you're working on a left eye and you're a right-handed surgeon who typically sits at the head of the bed, you can't get perpendicular to the retina surface. So what I do now is sit temporal for left eyes, which makes it much easier to get perpendicular and reliably form a bleb on the first attempt.

Finally, with instrumentation, it's worth giving thought to the size and type of cannula or syringe you're using. Different options are available, and it's important to choose the setup that lets you work both safely and comfortably.

ReachMD Announcer:
That was Drs Courtney Crawford and Raj Maturi sharing their perspectives on gene therapy and how they approach patient conversations in retinal disease management at the 2025 American Academy of Ophthalmology annual meeting.

This program was brought to you by AbbVie Inc. and REGENXBIO Inc.

If you missed any part of this discussion, visit Industry Features on ReachMD.com where you can Be Part of the Knowledge.

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