A LOOK AT IMPLANTS FOR DIABETIC EYE DISEASE

A review of approved and emerging implant-based treatments for diabetic retinopathy and diabetic macular edema.

By Matthew Pfannenstiel, MD, and Leanne Clevenger, MD

Diabetic eye disease (DED) continues to be a leading cause of vision impairment among working-age adults worldwide, and the burden of diabetic retinopathy (DR) and diabetic macular edema (DME) on patients and health care systems is expected to increase substantially. Conventional treatments—including focal/grid laser photocoagulation, intravitreal anti-VEGF agents, and corticosteroids—have significantly improved visual outcomes over the past 2 decades. However, many patients experience incomplete responses, require frequent injections, or struggle with adherence due to treatment burden or access limitations.[1-3]

Implantable drug-delivery platforms have emerged as an important evolution in the management of DED. By enabling sustained intraocular therapeutic exposure, implants are designed to reduce treatment frequency, improve durability of response, and better match the chronic, relapsing nature of DED. Early corticosteroid implants have now been followed by refillable anti-VEGF reservoirs and investigational gene-based and biomaterial-driven approaches, reshaping long-term treatment strategies. Here, we summarize currently approved implants, emerging technologies, and future directions in sustained therapy for DED (Table).

APPROVED IMPLANT OPTIONS

Several intravitreal implants are currently available for the treatment of DME, primarily using corticosteroid or anti-VEGF delivery to target inflammatory and vascular permeability pathways known to contribute to DME. These devices differ in biodegradability, duration of drug release, and suitability for specific patient populations.[1,4]

Intravitreal Corticosteroid Implants

Corticosteroids exert beneficial effects in DME by inhibiting inflammatory cytokines, stabilizing the blood-retinal barrier, and downregulating VEGF expression.[1] The dexamethasone intravitreal implant 0.7 mg (Ozurdex, Abbvie) is a biodegradable polymer-based implant that delivers sustained corticosteroid exposure for approximately 3 to 4 months. Multiple randomized and real-world studies have demonstrated significant improvements in BCVA and reductions in central retinal thickness in patients with DME, including those previously treated with anti-VEGF agents.[5-7]

The dexamethasone implant has shown utility in pseudophakic eyes, vitrectomized eyes, and patients with inflammatory-predominant DME or suboptimal anti-VEGF response (Figure).[1,6] Adverse effects such as IOP elevation and cataract progression are well characterized and generally manageable with appropriate monitoring.[5-7]

TABLE. COMPARISON OF IMPLANT-BASED THERAPIES FOR DIABETIC EYE DISEASE

Name (Manufacturer)	Delivery Method	Treatment Duration	FDA Approval Status
Dexamethasone intravitreal implant 0.7 mg (Ozurdex, Abbvie)	Office-based intravitreal injection of biodegradable implant	Approximately 3 to 4 months	FDA approved for DME
Fluocinolone acetonide intravitreal implant 0.19 mg (Iluvian, ANI Pharmaceuticals)	Office-based intravitreal injection of non-biodegradable implant	Up to 36 months	FDA approved for DME in previously steroid-treated patients without clinically significant IOP rise
Port delivery system with ranibizumab (Susvimo, Genentech/Roche)	Surgically implanted refillable ocular reservoir with office-based refill-exchange	Continuous delivery; refill approximately every 6 months for DME and every 9 months for DR	FDA approved for DME and DR in previously anti-VEGF-responsive patients
OTX-TKI (Axpaxli, Ocular Therapeutix)	Axitinib hydrogel administered by intravitreal injection	Intended for injections 1 to 2 times per year	Investigational
EYP-1901 (Duravyu, EyePoint)	Bioerodible vorolanib intravitreal insert administered by intravitreal injection	Designed for sustained release for approximately 6 to 9 months	Investigational
Surabgene lomparvovec (sura-vec/ ABBV-RGX-314, Abbvie/Regenxbio)	Suprachoroidal AAV8 gene therapy administered as a single in-office injection	Intended as a one-time treatment with multi-year expression/ durability	Investigational
4D-150 (4D Molecular Therapeutics)	Single intravitreal AAV gene therapy injection	Intended for multi-year sustained expression after one administration	Investigational

Abbreviations: AAV, adeno associated viral; DME, diabetic macular edema; DR, diabetic retinopathy

The fluocinolone acetonide intravitreal implant 0.19 mg (Iluvien, ANI Pharmaceuticals) represents a longer-acting, non-biodegradable corticosteroid platform approved for chronic DME insufficiently responsive to other treatments. This implant delivers low-dose fluocinolone acetonide continuously for up to 36 months. The pivotal FAME trials demonstrated sustained visual improvement and edema control over 3 years, with durable anatomic benefits and meaningful reductions in treatment burden.[8]

Long-term real-world studies, including the PALADIN study, have confirmed sustained efficacy and a favorable safety profile in carefully selected patients who have demonstrated steroid tolerance.[9] Cataract formation and IOP elevation remain common, underscoring the importance of patient selection and pre-implant steroid challenge.[8,9]

Intravitreal Reservoir

The port delivery system (PDS) with ranibizumab (Susvimo, Genentech/Roche) is a refillable, surgically implanted reservoir that continuously releases ranibizumab into the vitreous cavity and is periodically refilled via a minimally invasive office-based procedure.

Clinical studies of the PDS have demonstrated the feasibility of extended anti-VEGF delivery with reduced treatment frequency in retinal disease, supporting the broader concept of durable refillable intraocular biologic therapy. However, disease-specific evidence in DME is still evolving, and safety considerations such as conjunctival complications, implant-related adverse events, and endophthalmitis remain important for patient counseling and long-term monitoring.[10,11]

KEY TAKEAWAYS

- Currently approved implants for diabetic eye disease include the dexamethasone intravitreal implant 0.7 mg (Ozurdex, Abbvie), fluocinolone acetonide intravitreal implant 0.19 mg (Iluvien, ANI Pharmaceuticals), and port delivery system with ranibizumab (Susvimo, Genentech/Roche).
- Several biodegradable polymer implants, sustained-release intraocular delivery systems, and combination antiinflammatory strategies remain under investigation.
- Surabgene lomparvovec (sura-vec/ABBV-RGX-314, Abbvie/Regenxbio) and 4D-150 (4D Molecular Therapeutics) are both in phase 2 for diabetic macular edema.

INVESTIGATIONAL IMPLANTS

The future of implant therapy for DED is increasingly focused on long-term disease modification and novel biologic approaches to address both the vascular and neurodegenerative aspects of DED.[4,12] Hydrogel-based systems and nanotechnology-enabled platforms are being explored to improve drug stability, prolong release, and enhance tissue targeting in retinal disease.[12,13,16] Additional innovation is occurring in platforms designed for controlled release, improved ocular bioavailability, and multimodal treatment delivery. As these technologies mature, cost-effectiveness analyses and real-world durability studies will be critical to define their role alongside established treatment paradigms.[12,13,16]

Tyrosine Kinase Inhibitors

Sustained-release tyrosine kinase inhibitor (TKI) implants are an investigational strategy for DR and DME. Unlike extracellular anti-VEGF agents, TKIs act intracellularly to inhibit VEGF receptor signaling and may also affect related angiogenic and inflammatory pathways implicated in vascular leakage and neovascularization.

OTX-TKI (Axpaxli, Ocular Therapeutix), an axitinib-containing bioresorbable hydrogel implant, is being evaluated in phase 3 for nonproliferative DR, with dosing strategies that include single or repeat administration at 24 weeks.

EYP-1901 (Duravyu, EyePoint), a bioerodible intravitreal insert containing vorolanib, is under investigation in two phase 3 trials for the treatment of DME. These platforms are intended to reduce injection burden while maintaining durable suppression of VEGF-driven permeability and disease progression.[19-21]

For more on TKIs, see *The Potential of Tyrosine Kinase Inhibitors.*

Gene Therapy

Gene-based delivery systems represent a rapidly evolving investigational category. These treatments typically use viral vectors to promote sustained intraocular expression of therapeutic proteins after a single administration. Contemporary reviews highlight the promise of ocular gene therapy while also emphasizing manufacturing, durability, and inflammatory safety challenges that must be addressed before broader clinical adoption.[14,15]

IMPLANTABLE DRUG DELIVERY SYSTEMS REPRESENT A TRANSFORMATIVE ADVANCE IN THE MANAGEMENT OF DR AND DME.

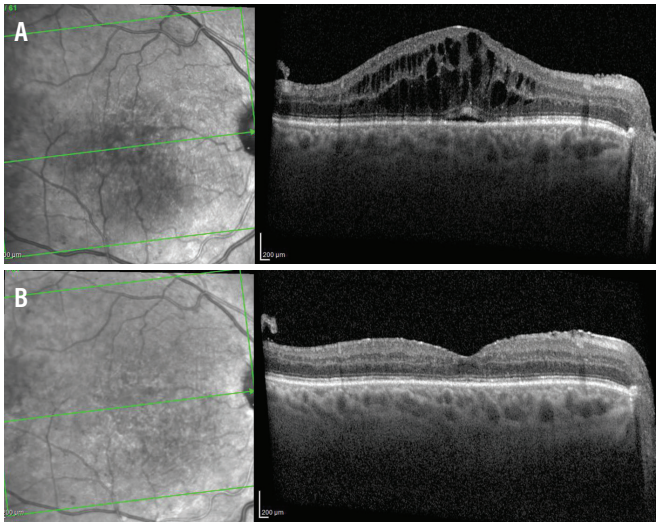

Figure. This patient with DME was not responding well to anti-VEGF therapy (A), necessitating the addition of a dexamethasone implant (B).

In DED, most clinical gene therapy strategies have focused on sustained intraocular suppression of VEGF signaling. Adeno-associated viral (AAV) vectors are the predominant platform used, as they can drive prolonged retinal expression after a single administration. These gene therapies largely target VEGF-A directly through viral-mediated expression of anti-VEGF proteins; however, newer therapies are also investigating inhibition of VEGF-C, placental growth factor, and other mediators of vascular permeability and inflammation. Routes of delivery vary by platform and include intravitreal, suprachoroidal, and subretinal administration, each with tradeoffs in transduction efficiency, procedural complexity, and inflammatory risk.[14-16]

Surabgene lomparvovec (sura-vec/ABBV-RGX-314, Abbvie/Regenxbio) is an AAV8-based therapy encoding an anti-VEGF antibody fragment administered suprachoroidally for DME.[17] Early data from the phase 2 ALTITUDE trial have been encouraging.[17]

Early data from the phase 2 SPECTRA trail of 4D-150 (4D Molecular Therapeutics) is also promising.[18] This intravitreal gene therapy is designed to potentially provide multi-year expression of an aflibercept-like anti-VEGF moiety and an inhibitory RNA molecule that blocks intracellular expression of VEGF-C.

ADVANTAGES, LIMITATIONS, AND PATIENT SELECTION

Implant-based therapies offer several advantages over intravitreal injections, including reduced treatment burden, improved adherence potential, and more consistent

BEYOND SUSTAINED DELIVERY: CAN WE MEASURE WHAT'S LEFT?

A noninvasive method for measuring residual drug could lead to pharmacologically guided care.

By Gennady Landa, MD, and Gennady Friedman, PhD

When managing diabetic eye disease, refillable anti-VEGF reservoirs and sustained-release corticosteroid implants can reduce injection frequency and treatment burden while maintaining therapeutic exposure.[1-3] Yet one clinically important question remains unanswered at follow-up visits: How much active drug is left inside the implant?

Currently, retina specialists rely on predetermined retreatment schedules and indirect evidence of declining therapeutic effect, such as recurrent fluid on OCT, worsening visual acuity, or disease progression. This reactive approach may expose some patients to recurrence before retreatment, while subjecting others to retreatment procedures or supplemental therapy despite adequate remaining drug. It can also make it difficult to distinguish drug depletion from other causes of suboptimal response.

A newly developed proprietary technology platform, developed through a collaboration between the Department of Ophthalmology at the Icahn School of Medicine at Mount Sinai and the College of Engineering and Computing at Drexel University, may offer another approach. The concept incorporates engineered magnetic nanoparticles confined within the implant matrix and uses an external reader to obtain a noninvasive signal associated with the amount of drug remaining. In principle, the measurement could be performed during a routine office visit and provide quantitative information to complement OCT, visual acuity, and clinical examination. A low residual drug measurement could favor retreatment, whereas an adequate measurement with disease activity may prompt consideration of an alternative mechanism or adjunctive therapy.

While this is a promising concept, many hurdles to clinical translation remain, including validation of measurement accuracy, signal stability over time, biocompatibility, nanoparticle confinement, compatibility with implant manufacturing, and performance across different therapeutic agents, implant materials, geometries, positions, and tissue overgrowth or fibrosis. Finally, prospective studies must show the benefits of real-time monitoring.

For retina specialists managing diabetic eye disease, the ability to measure what remains inside an implant could represent the next step toward precision dosing and more proactive disease control. ■

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AI disclosure: ChatGPT 5.6 (OpenAI) was used to assist with language editing and manuscript formatting. All content was reviewed, verified, and revised by the authors.

pharmacokinetics.[3,12] These benefits are particularly relevant for patients with limited access to care, poor injection tolerance, or chronic/persistent edema requiring frequent retreatment.

However, implants are not without risk. Surgical implantation, device-specific complications, steroid-related adverse events, and higher upfront costs must all be weighed against expected benefits.[1,4] Thoughtful patient selection remains paramount: Corticosteroid implants may be best suited for pseudophakic patients, those with inflammatory DME phenotypes, or eyes refractory to anti-VEGF therapy while anti-VEGF implants may offer broader applicability across different disease stages.[6,8,10]

UPDATING THE PARADIGM

Implantable drug delivery systems represent a transformative advance in the management of DR and DME. With multiple approved corticosteroid implants and expanding anti-VEGF and investigational platforms, retina specialists

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now have unprecedented opportunities to individualize therapy and reduce treatment burden. Careful patient selection, vigilant monitoring, and continued evaluation of long-term outcomes remain essential as emerging technologies further reshape the therapeutic landscape of DED.[3,4,6] ■

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AI disclosure: Microsoft Copilot (version 148.0.3967.70) was used to assist with drafting and editing of the article. The authors reviewed the entire contents of this article and confirmed its accuracy.
Disclosure of off-label/investigational use: OTX-TKI, EYP-1901, surabgene lomparvovec, and 4D-150 are investigational therapies that are not currently FDA approved.