CME Monograph

Targeting Anterior Uveitis:

A Focus on Iontophoresis and Other Advanced Technologies

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ACTIVITY DESCRIPTION

Anterior uveitis is the most common form of uveitis. It can be associated with significant morbidity, including permanent loss of vision, as a result of complications that can develop without appropriate treatment. Topical corticosteroid treatment to control inflammation is the mainstay for management of anterior uveitis, but there are limitations associated with its use. This educational activity reviews the challenges accompanying topical corticosteroid therapy and presents information on emerging therapeutics, with a focus on corticosteroid delivery by iontophoresis as a novel approach.

TARGET AUDIENCE

This educational activity is intended for ophthalmologists, including ophthalmology fellows.

LEARNING OBJECTIVES

Upon completion of this activity, participants will be better able to:

- Describe the mechanism of action of iontophoresis and other advanced drug-delivery technologies
- Review the safety and efficacy data on dexamethasone treatment via iontophoresis for the treatment of anterior uveitis
- Use dexamethasone treatment via iontophoresis in appropriate patient scenarios

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Targeting Anterior Uveitis:
A Focus on Iontophoresis and Other Advanced Technologies

Anterior uveitis has an estimated annual incidence of 26.6 to 102.7 of every 100,000 adults in the United States and accounts for up to 90% of uveitis cases seen in community practices in Western countries.[1,2] Affected patients can experience pain, photophobia, and decreased vision. Furthermore, they are at risk for permanent loss of vision from complications that can develop without appropriate treatment.

Topical corticosteroid treatment to control inflammation is the mainstay for management of anterior uveitis, but there are limitations associated with its use. This activity reviews the challenges accompanying topical corticosteroid therapy and presents information on emerging therapeutics, with a focus on corticosteroid delivery by iontophoresis as a novel approach.

ANTERIOR UVEITIS: CURRENT MANAGEMENT

Dr Sheppard: Anterior uveitis, which involves inflammation of the iris and is often accompanied by ciliary body inflammation (iridocyclitis), accounts for up to 90% of uveitis cases in Western countries and has an estimated prevalence of 1 in 4500 people.[1,3-6] There are numerous identifiable etiologies for anterior uveitis, but they can be broadly divided into infectious and noninfectious causes. A detailed history, physical examination, review of systems, and careful ocular examination are essential for identifying underlying causes, which will direct a targeted treatment plan.

Elimination of all inflammation is the treatment goal for every case. Treatment for infectious uveitis requires pathogen-directed antimicrobial agents, with or without corticosteroids. Topical corticosteroid treatment is the standard for anti-inflammatory treatment of noninfectious anterior uveitis as well.

There are a number of topical corticosteroid products from which to choose. Difluprednate emulsion, 0.05%, is my preferred agent. In 2 phase 3 studies, difluprednate administered 4 times daily was found to be noninferior to prednisolone acetate suspension, 1%, used 8 times daily for clearing anterior chamber cells (ACCs).[7,8] The rate of study discontinuation due to lack of efficacy was also lower in the difluprednate group.[9]

What is your current approach for treating anterior uveitis?

Dr Silverstein: I also use difluprednate, along with a cycloplegic agent, and both oral and topical treatment with a nonsteroidal anti-inflammatory drug. I typically use 1% atropine as the cycloplegic agent for all uveitis cases. Depending on the uveitis etiology and severity of the inflammation, I might also prescribe high-dose oral prednisone and start systemic immunomodulatory treatment.

Dr Fein: Although difluprednate is also my corticosteroid of choice, I sometimes start with topical prednisolone because of cost and insurance issues, and I use a cycloplegic in patients who have significant pain and/or photophobia. After ruling out infectious etiologies, I would also add high-dose oral prednisone if there is posterior segment inflammation.

Dr Korenfeld: I believe nonsteroidal anti-inflammatory drug treatment is helpful if cystoid macular edema is present. I also like to give a sub-Tenon corticosteroid injection to provide a depot effect, especially if I think systemic corticosteroid therapy might be needed, but the patient has medical comorbidities that might be affected by the side effects of systemic corticosteroids.

Dr Sheppard: Because bioavailability is limited with topical administration, corticosteroid treatment for anterior uveitis can require frequent dosing, and a prolonged course of treatment can also be necessary.[10] Patient nonadherence, difficulties with drop administration, tearing, blepharospasm, and irritation can reduce medication absorption, thereby compromising treatment efficacy. In addition, intensive and ongoing therapy puts patients at risk for corticosteroid-related side effects, including intraocular pressure (IOP) elevation and cataract development, along with preservative-related corneal toxicity.

Several treatments are being developed for anterior uveitis, with the aim of minimizing side effects or improving drug delivery compared with those of conventional corticosteroid therapy **(see Sidebar: Innovative Treatments for Anterior Uveitis)**. In this discussion, we are focusing on transscleral iontophoresis. This approach to ocular corticosteroid delivery is provided as an in-office procedure and is less invasive than an injection. It might overcome the toxicity, compliance, and administration issues associated with topical administration. Compared with topical administration, iontophoretic corticosteroid treatment improves intraocular drug delivery and appears to have a low risk of causing IOP elevation.[10]

OCULAR IONTOPHORESIS

Intraocular penetration of a topically administered medication through the intact barriers of the cornea and sclera depends on passive diffusion, which is a slow process driven by a concentration gradient **(Figure 1)**.[11] Intraocular accumulation of most systemically administered medications also relies on passive diffusion of the compound through blood vessel walls, although some substances, such as ascorbic acid, enter the eye from the systemic circulation through an active transport mechanism in the ciliary processes.

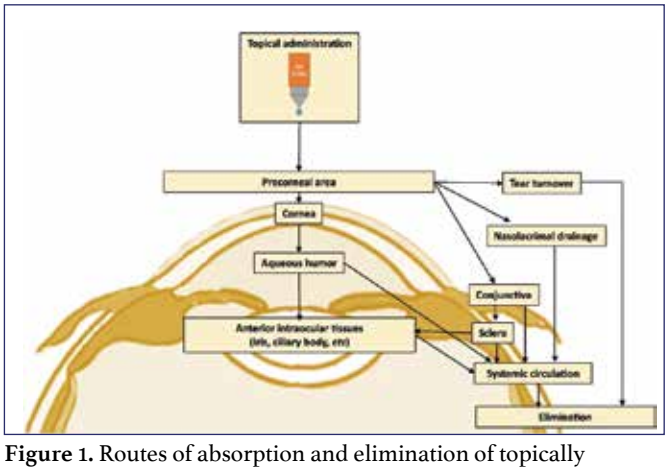

Figure 1. Routes of absorption and elimination of topically administered agents

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Innovative Treatments for Anterior Uveitis

Reproxalap (formerly ADX-102 and NS2) is being developed as a topical treatment for uveitis, allergic conjunctivitis, and dry eye disease. It is an aldehyde "trap" that rapidly binds free aldehydes, which are potent intracellular proinflammatory compounds.[1,2] The drug-aldehyde dimer is transported intracellularly, where it is quickly metabolized. In a phase 2 clinical trial, reproxalap showed promising activity as a treatment for noninfectious anterior uveitis, and it was not associated with intraocular pressure (IOP) elevation.[1,2] Phase 3 studies investigating reproxalap for the treatment of uveitis and allergic conjunctivitis are ongoing,[3,4] and a phase 2 study is investigating reproxalap in patients with dry eye disease.[5]

CLS-TA is a triamcinolone acetonide formulation delivered into the suprachoroidal space using a proprietary microinjector system. It is being developed as a treatment for macular edema associated with noninfectious uveitis, including anterior uveitis, as well as for retinal vein occlusion and diabetic macular edema. Topline results from a phase 3 study of CLS-TA for noninfectious uveitis showed the percentage of patients with a ≥ 15 ETDRS (Early Treatment Diabetic Retinopathy Study) letter gain from baseline to week 24 was significantly higher in the CLS-TA arm than in the control arm receiving a sham injection (46.9% vs 15.6%; $P < .001$).[6] Elevated IOP occurred in 11.5% of patients receiving CLS-TA. There were no serious treatment-related adverse events.

In addition to transscleral iontophoresis, noninvasive transscleral delivery of dexamethasone is being developed as a treatment for anterior uveitis, using a system for diffusion-based passive delivery of the active compound. The technology involves a scleral lens-type applicator (Visulex-P) to deliver dexamethasone sodium phosphate (DSP). This system was evaluated in a phase 1/2 study that randomized 44 patients with noninfectious anterior uveitis to receive (1) prednisolone acetate, 1%, up to 6 drops daily; (2) DSP, 8%, weekly; or (3) DSP, 15%, weekly.[7] Rates of resolution of anterior chamber cells were similar in the 3 treatment arms at follow-up visits on study days 8, 15, and 29. The investigational treatments were well tolerated and associated with slight IOP elevation only at the first follow-up visit on day 8.

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Iontophoresis, which means "ions that are being carried," uses an electric current to promote drug penetration to its target. It is based on the electrical principle that ions with like charges repel each other. Iontophoresis has a long history of use in dentistry, dermatology, and rheumatology for improving drug delivery.[12] It was not developed commercially until the 1980s, when it was introduced to treat hyperhidrosis.[13] At approximately the same time, iontophoresis began to be used for the delivery of anti-inflammatory drugs into joint spaces to avoid trauma caused by intra-articular injections.[12] Iontophoresis was first evaluated for ocular drug delivery more than a century ago[14] and has been or is currently being studied for delivery of a variety of medications to treat several ocular diseases, including dry eye disease,[15] keratoconus,[16] anterior uveitis,[10] and age-related macular degeneration.[17]

With iontophoretic delivery, application of an electric current to an aqueous drug solution using a cathodic or anodic electrode hydrolyzes the water molecules into hydroxide or hydronium ions, respectively. An opposite-charged electrode is placed at a distal site to complete the electrical circuit, and the ions generated by hydrolysis drive the like-charged drug molecule into tissues **(Figure 2)**.[14]

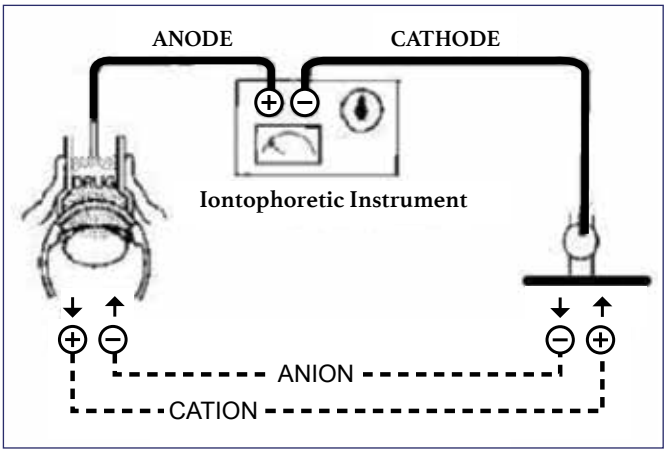

Figure 2. Ocular iontophoresis of a positively charged drug uses an anodic electrode to generate positively charged hydronium ions

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Iontophoretic drug delivery is affected by properties of the barrier tissue (ie, mucous membrane or not, lipophilicity/hydrophilicity, charges, and thickness); the ion being delivered (ie, charge density in the pH of the delivery setting, concentration, molecular size, and molar potency); and the applied electric current (level and duration).[12,18] Proof-of-concept studies show that with modulation of these parameters, a wide array of therapeutics, including small molecules, biologics, and nanoparticles, can be preferentially delivered into the anterior or posterior tissues of the eye to reach therapeutically meaningful concentrations.[19,20]

Preclinical studies conducted in rabbits showed that with iontophoresis, concentrations of corticosteroids (methylprednisolone and dexamethasone) in anterior and posterior segment tissues and fluids exceeded those achieved after intravenous or topical administration.[19-21] The results of these studies also showed a dose-response relationship between the intraocular levels of the corticosteroids and the applied current, duration of iontophoresis, and drug concentration. Ocular iontophoresis resulted in

negligible systemic corticosteroid levels and was not associated with any clinical or histological evidence of toxicity.

A variety of active pharmaceutical ingredients are being developed for ocular iontophoresis, but only a 40-mg/mL dexamethasone phosphate solution formulated for iontophoresis (EGP-437) has advanced to a confirmatory phase 3 clinical trial.[22]

Iontophoretic delivery of EGP-437 is performed with a proprietary system that comprises an annular ocular applicator, an external battery, and an anodic electrode that is placed on the forehead **(Figure 3)**.[23] The ocular applicator features a foam annulus that serves as a reservoir for the dexamethasone phosphate solution. This annulus makes contact with the perilimbal conjunctiva. The applicator houses the cathodic electrode that transfers current from the battery to the drug reservoir, resulting in the creation of hydroxyl ions.

Figure 3. Ocular applicator of a transscleral iontophoresis system

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A phase 1/2 study of EGP-437 treatment for noninfectious anterior uveitis evaluated 4 electric current dose levels: 1.6, 4.8, 10.0, and 14.0 mA-min.[10] It enrolled 40 patients with an ACC score ≥ 1.5 who received a single iontophoretic treatment (4-minute application) and were followed to day 28.

An ACC score of 0, analyzed as the primary efficacy end point, was achieved by 47.5% and 60.0% of patients on days 14 and 28, respectively.[10] At both visits, the highest response rates were achieved in the 2 lower-dose groups **(Table 1)**, presumably because the higher current levels drove the dexamethasone deeper into the eye, rendering it less effective for treating inflammation in the anterior segment.

Table 1. Percentage of Patients Achieving an Anterior Chamber Score of 0[10]

Dose Group*, mA-min	Percentage of Patients	
	Day 14	Day 28
1.6	80	80
4.8	60	60
10.0	20	50
14.0	30	50
Total	47.5	60

* n = 10 in each dose group

pressure remained relatively stable and in the normal range in most patients. The most commonly reported adverse events were conjunctival hyperemia (16%), punctate keratitis (11%), conjunctival edema (10%), eyelid edema (6%), and eye pain (6%). There were no serious adverse events or nonocular systemic corticosteroid-mediated effects.

Two phase 3 studies investigating EGP-437 for the treatment of noninfectious anterior uveitis have been recently completed, and results have yet to be published. The initial phase 3 study included 193 patients with an ACC score ≥ 1 who were randomized to receive EGP-437 delivered for 3 minutes on days 0 and 7 or a 14-day tapering regimen of prednisolone acetate, 1% (8 times daily for 1 week, then 6 times daily for 1 week).[24] The primary efficacy end point was the percentage of patients with an ACC score of 0 at day 14.

Enrollment in a confirmatory phase 3 study was completed in April 2018.[22] In this study, patients were randomized to receive EGP-437 or a tapering regimen of topical prednisolone acetate, 1%. The primary outcome measure was the proportion of patients with an ACC count of 0 at day 14.

IONTOPHORESIS IN THE CLINICAL SETTING: PRACTICAL AND SAFETY CONSIDERATIONS

Dr Sheppard: EGP-437 iontophoresis is a procedure that is very easy to learn and perform. It can be done by a technician, an optometrist, or a physician assistant instead of by an ophthalmologist. The setup is simple and straightforward. There is no need for a speculum. The applicator is placed by the doctor or technician after anesthetizing the eye with topical anesthetic. I find it is helpful to have the patient look at me directly when I am placing the applicator. Because it can be difficult for patients to keep both eyes open, I put a drop of anesthetic in the fellow eye as well. The applicator is held in place throughout the procedure while another assistant manages the control unit. The treatment takes just 3 minutes, and it is very well tolerated. Removing the sticky electrode from the forehead might be the worst part of the procedure for patients.

What is known about the half-life of dexamethasone phosphate in the eye after iontophoretic delivery?

Dr Korenfeld: With iontophoresis, the drug is delivered not only into the relatively dynamic aqueous humor, but also into tissues, where it reaches higher levels than those after topical administration and is eliminated more slowly than from the aqueous humor.[19]

Dr Sheppard: Does the application of electric current with iontophoresis create any particular safety concerns?

Dr Korenfeld: Ocular iontophoresis is performed using a weak current that is applied for a short time at just a few sessions. It does not seem to pose any safety issues. Some patients report a mild tingling sensation that is localized around the forehead electrode, but it is not a feeling of discomfort. Patients with implanted electronics, such as pacemakers or defibrillators, were excluded from participating in the clinical trials, which seems prudent, because the electrical discharge from the iontophoresis device could potentially interfere with the proper functioning of these types of devices.

Dr Sheppard: Some patients treated with EGP-437 developed punctate keratopathy. This event was mild and resolved by the first posttreatment day. Was the event associated with exposure to the electric current?

Dr Korenfeld: I think that the punctate keratopathy developed as a result of the ocular surface being exposed while the eye is kept open for 3 minutes during the treatment. Instilling a drop of an artificial tear to keep the cornea hydrated during the treatment might prevent punctate keratopathy.

Dr Sheppard: Topical dexamethasone and prednisolone are known to cause clinically significant IOP elevation.[25] Intraocular pressure has been minimally affected in patients treated with EGP-437 delivered via iontophoresis.[10]

The reason for the relative safety of iontophoretic dexamethasone administration is not fully understood, but considering the available data, would you use this delivery system in a patient who is a known steroid responder?

Dr Fein: I think the experience is very encouraging. I would consider using iontophoresis to deliver dexamethasone in a patient who is a known steroid responder or even in a patient with mild glaucoma, assuming I can rely on the person to return for IOP monitoring.

Dr Korenfeld: Because I think that iontophoresis delivers a more potent treatment than anything else we have available to target inflammation in anterior uveitis, I would prefer to use it on any patient, even if it meant prescribing another medication for the short term to control steroid-induced IOP elevation.

CASE 1: ACUTE ENDOGENOUS NONINFECTIOUS ANTERIOR UVEITIS

From the Files of John Sheppard, MD, MMSc, FACS

Case History

A 25-year-old white man presents with a 2-day history of severe pain, redness, photophobia, and blurred vision in his right eye. He has ankylosing spondylitis and is positive for human leukocyte antigen B27 (HLA-B27). The patient has a history of 2 previous ipsilateral uveitic flares, hepatitis, and acute gastroenteritis. Visual acuity is 20/80 OD and 20/20 OS. Intraocular pressure is 12 mm Hg OD and 18 mm Hg OS. **Figure 4** shows photographs from the slit-lamp examination.

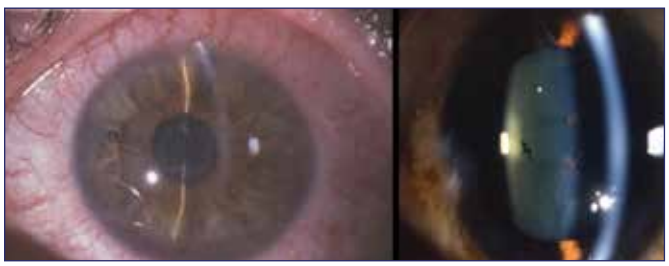

Figure 4. Slit-lamp examination images of the patient in Case 1
Images courtesy of John Sheppard, MD, MMSc, FACS

Discussion

Dr Sheppard: The inflammation in eyes with HLA-B27+ anterior uveitis can be severe and difficult to control. The uveitis is often associated with systemic inflammatory disease that mandates patient referral to a rheumatologist.[26] Treatment for the uveitis can require intensive corticosteroid therapy, with administration that is topical, oral, or by periocular injection.

I think iontophoretic delivery of dexamethasone would be useful for managing this type of anterior uveitis. Where would you position it in your treatment algorithm for anterior uveitis?

Although EGP-437 was used as standalone corticosteroid treatment in clinical trials, I can imagine using it as induction therapy and for a steroid-sparing benefit. I would probably do the iontophoretic treatment and start patients on topical difluprednate, but I would prescribe difluprednate to be used just twice daily, for example, instead of 4 times daily, which is my current standard.

Dr Korenfeld: I also think that iontophoretic corticosteroid delivery could be used as induction therapy. I would use it as a substitute for a corticosteroid injection, and I would also follow it with topical corticosteroid treatment.

CASE 2: POSTERIOR SEGMENT UVEITIS

From the Files of Jordana G. Fein, MD, MS

Case History

A 45-year-old man presents with a 2- to 3-week history of cloudy vision in his left eye. He reports seeing "black hairs floating by" and occasional erythema. He denies any pain or tearing. He has borderline hypertension. Topical medication includes an over-the-counter vasoconstrictor, as needed. He has no allergies, history of surgery or trauma, or remarkable social history. Findings on examination are as follows:

- Visual acuity: 20/80 (pinhole: 20/25) OD; count fingers at 2 feet (pinhole: no improvement) OS
- Pupils 5 ≥ 3 reactive and no afferent pupillary defect OD; 5 ≥ 4.5, minimal reaction, and presence of relative afferent pupillary defect OS
- Extraocular movement: Full, with no pain
- Visual field: Full OD; peripherally constricted OS
- Intraocular pressure: 16 mm Hg OD; 14 mm Hg OS
- Anterior segment: Normal OD; trace conjunctival injection, inferior keratic precipitates, and 2 to 3+ cells without hypopyon OS
- Posterior segment: Clear media, normal fundus examination results, and optic nerve margins and vessels OD; retinal whitening in the periphery but hazy media is obscuring visualization OS

The acute onset and unilateral presentation of the uveitis in this patient suggested an infectious process. The differential diagnosis would include toxoplasmosis, syphilis, tuberculosis, Lyme disease, viral infections, and sarcoid. Laboratory testing confirmed a syphilitic etiology.

The patient was admitted to the hospital to begin intravenous treatment with aqueous crystalline penicillin G and discharged with a peripherally inserted central catheter to complete the intravenous treatment. Concurrently, he was diagnosed as being positive for human immunodeficiency virus. At 1 week after starting penicillin, the vitritis in his left eye was improved, the retinitis had resolved, and visual acuity had improved to 20/250 (pinhole: 20/80 +1). The patient was then started on oral prednisone and continued on intravenous antibiotics.

Discussion

Dr Sheppard: Syphilitic uveitis is treated with penicillin, according to guidelines for the treatment of neurosyphilis.[27] Once the antibiotic is started, corticosteroid therapy is an important adjunct to control the inflammation and prevent damage to anterior and posterior segment tissues.[28]

What are your thoughts about using iontophoresis to deliver the corticosteroid in this setting?

Dr Korenfeld: I think it would be a good option. With proper selection of the treatment parameters, iontophoresis can deliver high

levels of dexamethasone into posterior segment tissues and fluids.[19,20] For a patient such as this who is immunocompromised, I would much rather use iontophoresis to administer a corticosteroid than violate the globe by giving an intraocular injection.

Dr Fein: I also feel that the iontophoretic treatment has a safety advantage for this patient, and might have been an adjuvant therapy were it available at the time. Data from a pilot phase 1b/2a study investigating EGP-437 for the treatment of macular edema provide clinical evidence supporting its efficacy for controlling inflammation in the posterior segment.[29] The study enrolled 25 patients with macular edema associated with retinal vein occlusion, diabetic retinopathy, or postsurgical cystoid macular edema.[29,30] Iontophoresis with EGP-437 was performed on days 0, 4, and 9 at 14.0 mA-min (3.5 mA). The primary outcome was reduction in mean central subfield thickness on days 4, 9, 14, and 21. As a control, patients with no improvement at day 14 were given the dexamethasone intravitreal implant and reevaluated at day 21 or 28.[30]

Data were reported from 19 patients, and the interim results indicate that noninvasive treatment with iontophoresis can deliver dexamethasone to the posterior segment.[30] Responses were better in pseudophakic eyes than in phakic eyes. There were no serious treatment-related adverse events. There were also no IOP elevations, perhaps because the higher electric current level delivers the dexamethasone into the posterior segment and avoids the anterior segment.

Dr Korenfeld: One possible explanation for the better response rate in the pseudophakic eyes might be that the intraocular lens acted as a platform for prolonged release of the corticosteroid.

Dr Silverstein: The current used in the macular edema study was higher than that used in the anterior uveitis studies.[10,29] Did the higher current seem to cause problems with comfort?

Dr Sheppard: I have not gotten any feedback on that issue. According to my observations during the dose-ranging phase 2 anterior uveitis study, some patients experienced greater discomfort, and I suspect they were in the higher current group. Nevertheless, the patients found the treatment tolerable.

TAKE-HOME POINTS

Topical corticosteroid treatment is the cornerstone of therapy for anterior uveitis, but it has limitations relating to intraocular penetration, patient compliance, and side effects.

Iontophoretic corticosteroid delivery shows promise as an alternative method for addressing some of the challenges of topical treatment:

- Preclinical studies show that high corticosteroid concentrations are attained in anterior and posterior segment tissues and fluids
- Clinical trials show that EGP-437, a dexamethasone phosphate formulation for ocular iontophoresis, cleared ACCs after just 1 or 2 treatments, was noninferior to intensive treatment with topical prednisolone acetate, and had minimal to no adverse effect on IOP

Other modalities under investigation for the treatment of anterior uveitis include a novel aldehyde trap compound, suprachoroidal triamcinolone acetonide, and a diffusion-based dexamethasone delivery system.

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1. Transscleral iontophoresis increases intraocular delivery of a compound by:
   A. Altering epithelial tight junctions
   B. Changing the compound's charge
   C. Electrorepulsion
   D. Increasing active transport

2. Which of the following is NOT a reason for interest in ocular iontophoresis as an alternative to topical administration for corticosteroid treatment?
   A. Avoids preservative-related ocular surface toxicity
   B. Improves bioavailability
   C. Has a lower cost
   D. Overcomes compliance issues

3. What is the anti-inflammatory mechanism of action of reproxalap?
   A. Binds free aldehydes
   B. Binds to intercellular adhesion molecule-1
   C. Prevents release of proinflammatory cytokines by immune cells
   D. It has the same mechanism of action as corticosteroids but has a unique route of delivery

4. Top-line results from a phase 3 study evaluating CLS-TA (triamcinolone acetonide delivered into the suprachoroidal space) for the treatment of noninfectious uveitis showed the investigational agent:
   A. Caused no IOP elevations
   B. Failed to meet its primary end point
   C. Was associated with a significantly higher percentage of patients gaining ≥ 15 ETDRS letters at week 24 compared with the control group
   D. Was associated with a significantly higher percentage of patients achieving an ACC score of 0 by day 7 compared with the control group

5. The efficacy of iontophoretic drug delivery is affected by properties of the:
   A. Electrical current density
   B. Barrier tissue
   C. Ion being delivered
   D. All the above

6. In a phase 1/2 study evaluating EGP-437 for the treatment of noninfectious anterior uveitis, the treatment response rate was higher in groups treated with:
   A. Higher electric current dose levels
   B. Higher concentration of dexamethasone phosphate
   C. Lower electric current dose levels
   D. Topical difluprednate

7. In a phase 1/2 study of noninfectious uveitis, 47.5% and 60.0% of patients receiving EGP-437 at days 14 and 28, respectively, had which of the following responses?
   A. Increased IOP
   B. Decreased IOP
   C. ACC score of 0
   D. No change in ACC score

8. Which was the most commonly reported adverse event in the phase 1/2 study evaluating EGP-437 for the treatment of noninfectious anterior uveitis?
   A. Conjunctival hyperemia
   B. Eye pain
   C. Eye burning
   D. Eyelid bruising

9. Which uveitic anatomic location might be appropriately treated with iontophoretic delivery of EGP-437?
   A. Choroid
   B. Iris
   C. Optic nerve
   D. Pars plana

10. In a phase 1/2 study, the rate of resolution of ACCs at serial follow-up visits in eyes treated with a system for passive delivery of dexamethasone using a topical scleral lens-type applicator (Visulex-P) was:
    A. Dose related, depending on the concentration of dexamethasone used
    B. Dose related, depending on the electric current used
    C. Higher than that of the control group treated with topical prednisolone acetate
    D. Similar to that of the control group treated with topical prednisolone acetate