



What's hot in ophthalmic development?

Pharmaceutical and medical device companies continue to face increasing pressures with getting drugs and devices to market.

Significant competition at earlier stages of a drug or device's life span, more rigorous Food and Drug Administration (FDA) requirements, rising development costs and failure rates in clinical trials have resulted in a basic shift in the strategic planning of clinical drug/device development. Now more than ever, pharmaceutical and medical device companies must identify and pursue the most promising ideas while curtailing the unproductive ones at the earliest stage possible. Avoiding wasting money, shortening of time frames and the distribution of resources to the best candidates are critical to effective drug/ device development. Additionally, the industry is faced with several challenges, including remaining profitable, to carry out innovative discovery research, to bring new medicines and devices more quickly to the marketplace and to ensure that the regulatory review process is both rapid and efficient.

Ocular Surgery News provides brief descriptions of types and trials of drugs and devices that appear promising. These drugs and devices are proceeding through the regulatory process necessary to obtain FDA approval.

Refractec Viewpoint

A new technique called conductive keratoplasty (CK) is under investigation to correct farsightedness using the Refractec Viewpoint CK System from Refractec Inc. (Irvine, Calif.). The technique uses a high-frequency, low-power energy source to deliver electrical energy to the periphery of the cornea. The treatment spots are placed in a circular pattern to reshape the tissue. This steepens the cornea's optical surface to better focus light and treat farsightedness. By adjusting the pattern of the treatment spots, it is possible to treat various levels of farsightedness.

"It is extraordinarily easy to use," Peter Hersh, MD, told *Ocular Surgery News*. "Procedure wise, it is easy to apply, it is well tolerated by the patient, patients are comfortable, and we do these procedures more quickly than we do laser in situ keratomileusis."

According to Dr. Hersh, patients' vision tends to stabilize during the first postoperative month, and the refraction seems to stabilize after 3 months.

The Refractec system can treat up to a maximum of 4 D of hyperopia. In a phase 3 trial, 54 patients underwent conductive keratoplasty with the Refractec system. At 6 months postoperatively, 56% of the patients were 20/20 or better, and 89% were 20/40 or better. The expanded phase 3 trials allow the enrollment of an additional 346 eyes.

"It seems that [refractive] stability is achieved between 3 and 6 months," Dr. Hersh said. "The average change in re-refraction stability was 0.128 D between the 3- to 6-month examinations. This kind of stability seems very encouraging."

Rescula

Rescula (unoprostone isopropyl) from CIBA Vision (Duluth, Ga.) is a prostaglandin derivative, which rapidly lowers intraocular pressure (IOP) with few side effects, according to the company. Aqueous humor drainage is facilitated, whereas production of aqueous humor remains unchanged. Clinical studies with Rescula revealed equal or stronger IOP reducing activity, as compared with timolol, and is better than pilocarpine and epinephrine, according to several studies. It shows no affinity for pigmented ocular tissues and has not caused the iris color changes seen in latanoprost (Xalatan, Pharmacia & Upjohn) Additionally, according to studies, Rescula does not cause mydriasis, miosis or reduced ocular tissue blood flow and has no effect on accommodation.

Rescula is metabolized by corneal estrases, producing an active metabolite. Like other prostaglandins, it lowers IOP without causing an initial temporary pressure spike. However, it shows little or no activity in prostaglandin-sensitive tissues.

Additionally, Rescula can be safely and effectively combined with other anti-glaucoma drugs. By increasing aqueous and uveoscleral outflow, Rescula can supplement the action of aqueous inflow suppressing agents.

In a study of human eyes that had received unoprostone isopropyl, color Doppler imaging revealed an increase in blood flow velocity in the central renal artery and the posterior ciliary artery.

Selecta 7000

Coherent Medical Group (Santa Clara, Calif.) has developed the Selecta 7000 for selective laser trabeculotherapy (SLT), a pressure-lowering procedure for glaucoma. The system is a q-switched, frequency-doubled Nd:YAG laser with a 400 μm spot size and 3 nanosecond pulse. This unique combination of parameters allows the laser to generate very low fluence levels (W/cm^2). Since the energy delivered is below the thermal relaxation time for cells of the trabecular meshwork, SLT does not create the same photocoagulative damage associated with argon laser trabeculoplasty (ALT). This technique involves no discernable tissue damage.

The system selectively treats portions of the trabecular meshwork by fracturing melanin particles in certain trabecular meshwork cells through a process called photothermolysis. This benign use of laser light works on a cellular level to stimulate lower IOP while preserving the structural integrity of the eye.

According to investigators, SLT appears to offer pressure-lowering effects substantially equivalent to those of ALT through a safer, less traumatic procedure. Pressure tends to drop more rapidly than with ALT and can occur as early as the first day postoperatively. SLT has full regulatory release worldwide, with the exception of the United States, and it has been in full clinical use for over 2 years in Japan and Europe.

According to Karim Damji, MD, of Ottawa, Ontario, Canada, where the Selecta 7000 is approved for use, the pressure lowering affects of the argon laser and the Selecta 7000 are equivalent based on a randomized, controlled study. However, the Selecta 7000 uses less energy, does not alter the architecture of the eye as much as the argon laser, it is easier to use, and there is less pain involved, he said.

SLT lowers IOP by gently irradiating the eye's trabecular meshwork, permitting it to filter fluid more efficiently. SLT is much less traumatic to the eye than ALT, Dr. Damji said. ALT may damage the trabecular meshwork (drainage system) in the eye and is generally performed only twice on each eye during the patient's lifetime, he added. SLT works at a cellular level and has the potential to be repeatable. Limited clinical data to date indicates SLT can lower IOP in patients who already have exhausted their ALT treatment options.

Visudyne therapy

Recommended for approval by an FDA Advisory Panel, Visudyne (verteporfin for injection: QLT PhotoTherapeutics, Vancouver, British Columbia; CIBA Vision) is expected to launch in early 2000 for use in predominantly classic subfoveal choroidal neovascularization (CNV) for the treatment of age-related macular degeneration (AMD).

The results of the study report that Visudyne therapy reduces the risk of vision loss, compared with placebo, during the first year of the study in patients with the wet form of AMD. Visudyne therapy showed beneficial effects in the total study population. Additionally, results demonstrated that a subgroup of patients whose lesions were characterized by a specific, more aggressive, disease pattern experienced a large, clinically relevant benefit.

H. Andrew Strong, PhD, senior director of clinical research for QLT, reported the early study results in 142 eyes with CNV in the open label, non-randomized study. One-hundred twenty-eight of the eyes had AMD. Dr. Strong said that patients gained an average of one line of visual acuity 1 week postoperatively. But between 4 weeks and 12 weeks, the leakage returned.

According to Dr. Strong, researchers eventually chose to retreat patients at 3 months, which is when the recurring leakage returned to baseline levels. Retirements at shorter intervals did not improve results.

Phase 3 trials of Visudyne, known as the Treatment of AMD with Photodynamic Therapy Study (TAP), were randomized, placebo-controlled and double masked. At the start of the study, researchers believed that baseline visual acuity could impact outcomes, according to Neil Bressler, MD, of the Wilmer Eye Institute and chair of the TAP Study Advisory Group.

The TAP study showed that for predominantly classic lesions, the indication for which treatment was proposed, 33% of Visudyne-treated eyes and 61% of placebo-treated eyes lost 3 or more lines of visual acuity. Results differed by an average of 2 lines in favor of Visudyne at 12-month examinations. While Visudyne was intended to reduce the risk of vision loss, 16% of patients experienced an improvement in vision of one or more lines in the overall study population.

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