A primer on latest treatment options for AMD

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WET AGE-RELATED MACULAR DEGENERATION

The current treatments for wet age-related macular degeneration (wAMD) inhibit a molecule called vascular endothelial growth factor (VEGF). This molecule leads to abnormal blood vessel growth and instability. Currently available anti-VEGF drugs—Avastin (Genentech), Eylea (Regeneron), Lucentis (Genentech)—are remarkably safe and very effective for wAMD. However, with current treatments, most patients need frequent injections indefinitely. More recently, a new anti-VEGF agent, Beovu (Novartis), was FDA-approved for wAMD with suggestion of longer duration of action and reduced need for injections; however, safety concerns related to inflammation have limited widespread use of this agent. Fortunately, several clinical trials are underway to evaluate new therapies that target other pathways and/or are formulated to produce a more longer-lasting effect and, in turn, reduce treatment burden. Here, we summarize several such therapies under investigation, primarily focusing on late-stage trials (Phases 2 & 3).

PORT DELIVERY SYSTEM (GENENTECH): This treatment consists of a small refillable device that is implanted into the wall of the eye during a surgical procedure. The small implant stores and continuously releases anti-VEGF medication into the eye by diffusion, taking the place of frequent injections. The device can be refilled in the office. Current studies have evaluated refills every 6 months, and some early studies showed that patients could go on average about 15 months without needing a refill. The Port Delivery System has completed a Phase 3 clinical trial and we expect the data will be filed with the FDA soon.

FARICIMAB (GENENTECH): Faricimab inhibits two pathways leading to abnormal blood vessel growth and leakage: It binds and inactivates a molecule called angioptietin-2 (Ang-2) in addition to the VEGF molecule that current medications inhibit. By binding both molecules, faricimab may lead to improved outcomes and longer treatment duration. In current trials, the medication is being given up to every 4 months after a series of monthly doses. Phase 3 trials are ongoing, and we expect data in 2021.

CONBERCEPT (CHENGDU KANGHONG): Conbercept is an engineered anti-VEGF that has been widely used in China since its approval there in 2013. It has been reported that conbercept may be a more potent medication because of its ability to address multiple targets, potentially resulting in a longer-lasting treatment (~3 months). Phase 3 trials in the U.S. are ongoing.

KSI-301 (KODIAK SCIENCES): KSI-301 is a specially formulated anti-VEGF drug called an antibody polymer conjugate. The medication is expected to stick around the eye for a longer time and deliver a greater dose of medication with one injection. Patients in the ongoing trials are receiving treatment with the medication every 3 to 5 months, and some have gone up to 6 months before needing retreatment with an injection. A larger trial comparing KSI-301 to currently available medications is ongoing, and we expect to get data in 2021.

SUNITINIB (GRAYBUG): Sunitinib is a specially formulated depot medication that slowly dissolves over time in the eye. The medication acts in a slightly different way to inhibit VEGF. Because it is a depot, the medication releases over time, allowing for the possibility of extended treatment effect. In recent trials, 90% of patients were able to go 3 months without needing re-treatment, and 70% of patients were able to go to 6 months without needing retreatment. The medication is currently in a Phase 2 clinical trial.

AKST4290 (ALKAHEST): AKST4290 is a small molecule inhibiting the immunomodulators playing a role in inflammation and neovascularization; two processes important in wAMD. This medication is unique from the others in that it is administered by mouth. Two small trials showed initial benefit of AKST4290 therapy in terms of vision stabilization and improvement. A larger Phase 2 trial evaluating this medication is underway.