LESS INFLAMMATION WITH NEW MANUFACTURING PROCESS FOR ABICIPAR PEGOL

With the use of a new manufacturing process, the incidence of intraocular inflammation was reduced in the open-label 28-week MAPLE study of abicipar pegol (Allergan/Molecular Partners) compared with the rate in two previous phase 3 trials, according to the manufacturers.

In 123 patients with wet age-related macular degeneration (AMD) in the MAPLE trial, the incidence of intraocular inflammation (IOI) was 8.9% with the new manufacturing process for abicipar, the companies announced in a joint press release. The incidence of severe IOI was 1.6%, with one reported case of iritis and one reported case of uveitis. There were no reported cases of endophthalmitis or retinal vasculitis in the study. In the CEDAR and SEQUOIA phase 3 randomized controlled studies, IOI rates of greater than 15% were reported, while the IOI rates for the comparator, monthly 0.5 mg ranibizumab (Lucentis, Genentech), were less than 1%.

In CEDAR, injections of abicipar 2.0 mg were given at a fixed interval of 8 weeks after three initial monthly doses. In the two phase 3 trials, in which patients were randomly assigned to abicipar at fixed intervals of 8 or 12 weeks or to ranibizumab, results in both abicipar arms were noninferior to ranibizumab for the primary endpoint, the proportion of patients with stable vision at week 52. Overall treatment-emergent adverse events were similar among the three treatment arms in the phase 3 trials

Abicipar is a designed ankyrin repeat protein, or DARPin. Allergan expects to file a biologics license application for abicipar with the US FDA in the first half of 2019, according to the press release. Additional data from the MAPLE study will be presented at a scientific conference later in 2019, the companies said.

FARICIMAB SHOWED BENEFIT OVER RANIBIZUMAB IN PHASE 2 STUDY IN DME; FURTHER TRIALS PLANNED IN DME, AMD

In a phase 2 randomized clinical trial, faricimab (Genentech/Roche) met its primary endpoint, demonstrating statistically superior visual acuity gains compared with ranibizumab at week 24 in treatment-naïve patients with diabetic macular edema (DME), according to an article in press in *Ophthalmology*.[1] The phase 2 BOULEVARD study (NCT02699450) was designed to compare the safety and efficacy of faricimab, a bispecific antibody targeting angiopoietin-2 (Ang-2) and VEGF-A, with ranibizumab in patients with DME. The top-line results of this study were announced in February 2018.

The trial enrolled 229 patients aged 18 years or greater with center-involving DME. Those who were treatment-naïve (n = 168) were randomly assigned 1:1:1 to intravitreal 6.0 mg faricimab, 1.5 mg faricimab, or 0.3 mg ranibizumab. Those previously treated with anti-VEGF therapy (n = 61) were randomly assigned 1:1 to 6.0 mg faricimab or 0.3 mg ranibizumab. Patients were dosed monthly for 20 weeks, followed by an observation period up to week 36 to assess durability of effect.

In treatment-naïve patients, mean improvement in ETDRS visual acuity was 13.9 letters with 6.0 mg faricimab, 11.7 letters with 1.5 mg faricimab, and 10.3 letters with 0.3 mg ranibizumab. The 6.0 mg faricimab dose demonstrated a statistically significant gain over ranibizumab (P = .03). In both patient populations, faricimab resulted in dose-dependent reductions in central subfield thickness on OCT, improvements in diabetic retinopathy severity score, and longer time to retreatment during the observation period compared with ranibizumab. There were no new or unexpected safety signals.

In a company statement, Genentech noted that two phase 3 trials, YOSEMITE (NCT03622580) and RHINE

(NCT03622593), were initiated last year to confirm the visual acuity and durability results of the phase 2 BOULEVARD study.

The company also announced that, in collaboration with Roche, it is initiating two global phase 3 trials investigating faricimab in the treatment of wet AMD. These identically designed multicenter randomized phase 3 trials, TENAYA (NCT03823287) and LUCERNE (NCT03823300), will evaluate the efficacy, safety, and durability of faricimab compared with aflibercept (Eylea, Regeneron) for the treatment of wet AMD.

In top-line results of the phase 2 STAIRWAY trial announced in October 2018, patients receiving faricimab either every 16 weeks or every 12 weeks experienced sustained vision gains comparable to patients who received ranibizumab dosed every 4 weeks. These results demonstrated the potential for extended durability with faricimab, according to Genentech.

1. Sahni J, Patel SS, Dugel PU, et al. Simultaneous inhibition of angiopoietin-2 and VEGF-A with faricimab in diabetic macular edema: BOULEVARD phase 2 randomized trial [article in press]. *Ophthalmology*. https://www.aaojournal.org/article/S0161-6420(18)33358-X/fulltext.

GENE THERAPY ACQUISITIONS ANNOUNCED

Acquisitions of two ocular gene therapy companies were announced in the first quarter of 2019. The biotechnology company Biogen announced that it plans to acquire Nightstar Therapeutics, and the pharmaceutical giant Roche announced that it will acquire Spark Therapeutics.

Spark, the developer of Luxturna (voretigene neparvovec), announced in February that it had entered into a definitive merger agreement for Roche to fully acquire it at a price of $114.50 per share in an all-cash transaction. This corresponds to a valuation of approximately $4.8 billion, the company said. Under the merger agreement, Roche will commence a tender offer to acquire all outstanding shares of Spark's common stock, and Spark will file a recommendation statement with a unanimous recommendation from its board that Spark shareholders tender their shares to Roche. Closing of the transaction is expected in the second quarter of 2019.

Biogen announced in March that it had entered into an agreement to acquire Nightstar, a gene therapy company focused on adeno-associated virus (AAV) treatments for inherited retinal disorders. Nightstar has two AAV-based therapies in clinical trials, including the phase 3 STAR trial in patients with choroideremia with results expected in the second half of this year. Under the terms of the agreement, Biogen will pay $25.50 in cash for each share of Nightstar, a total transaction value of approximately $800 million on a fully diluted basis. Biogen said it expects to complete the acquisition by mid-year 2019. ■

NEWS BRIEFS

> DOSING RESUMED IN PHASE 3 TRIALS IN GEOGRAPHIC ATROPHY AFTER SUSPENSION LAST YEAR

Enrollment and dosing have resumed in two phase 3 trials of APL-2 in patients with geographic atrophy (GA) in AMD, according to the manufacturer and sponsor of the trials, Apellis Pharmaceuticals. Enrollment in the DERBY and OAKS trials had been voluntarily paused in October because of "cases of noninfectious inflammation in patients treated from a single manufacturing lot of APL-2 intravitreal investigational material," according to Apellis.

After an investigation, the company said it believes that the likely source of inflammation was an impurity in the active pharmaceutical ingredient that was introduced during scale-up of the manufacturing process. The manufacturing process has now been modified to eliminate the impurity, and a sufficient supply of APL-2 has been produced using the modified manufacturing process to conduct the rest of the phase 3 GA program, the company said.

Dosing was restarted with the agreement of the independent safety monitoring committee for the trials, according to Apellis. Full enrollment in both trials is expected to be completed by the first quarter of 2020, the company said.

> ARKANSAS ODs SECURE EXPANDED SCOPE OF PRACTICE

A bill signed into law on March 27 by Arkansas Gov. Asa Hutchinson amends that state's optometric scope of practice act to permit optometrists to perform new procedures, including selective laser trabeculoplasty and Nd:YAG laser capsulotomy, certain injections (excluding intravenous and intraocular injections), lid lesion removal, and chalazion incision and curettage. The bill was supported by the Arkansas Optometric Association and the American Optometric Association's Future Practice Initiative.[1]

The scope of practice law still prohibits optometrists from performing cataract surgery and radial keratotomy and from selling prescription drugs. With passage of the law, Arkansas became the fourth state to permit laser procedures for ODs.

1. Arkansas secures expanded scope of practice. American Optometric Association. March 28, 2019. www.aoa.org/news/advocacy/arkansas-secures-expanded-scope-of-practice. Accessed March 29, 2019.