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“The efficacy of ranibizumab for maintaining and even improving vision in patients with exudative CNV has surpassed our greatest expectations. Nevertheless, clinicians might still wonder whether there are any scenarios where existing therapies may still be preferred,” observed Dr Brown, vitreoretinal consultant, the Methodist Hospital, Houston, Texas.

The subgroup analyses were designed to explore where PDT may be a better alternative. However, the outcomes were consistently numerically superior and in most cases statistically significantly better in the ranibizumab groups compared with those undergoing PDT, he said.

Comparative trial

ANCHOR (Anti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularisation in AMD) enrolled patients who were at least 50 years old with a Snellen equivalent VA of 20/40 to 20/320 and lesions that were at least 50% classic and 5,400 microns or less in greatest linear dimension. A total of 423 patients were randomised to treatment with ranibizumab 0.3 or 0.5mg or PDT. Ranibizumab was administered as a monthly intravitreal injection. Patients in the PDT group received a treatment at baseline and then as needed based on quarterly fluorescein angiography. Ranibizumab patients were administered sham PDT at baseline and subsequently as needed while the PDT group was given sham intravitreal injections.

Data from follow-up at one year demonstrated statistically significant differences favouring both ranibizumab 0.3mg and 0.5mg compared with PDT in the primary efficacy endpoint analysis of proportion of eyes losing less than 15 letters of ETDRSVA (94% and 96% vs. 64%). Lucentis was also superior in multiple secondary efficacy analyses, including the proportion of eyes with a vision gain of 15 or more letters (36% and 40% vs. 6%) and mean letter change from baseline VA (+8.5 and +11.3 vs. -9.5).

The results presented by Dr Brown compared outcomes in subgroups that divided patients in each treatment arm into quartiles according to age (50 to 64 years, 65 to 74 years, 75 to 84 years, and 85+ years), entry VA (20/63 or better, 20/80 to 20/100, 20/125 to 20/200, and 20/250 or worse), and lesion size (<1, >1 to 2, >2 to 4, and >4 disc areas) as well as based on the absence or presence of occult CNV. Three endpoints were analysed for each subgroup, including the ANCHOR primary efficacy endpoint and the secondary efficacy endpoints of proportions of patients with a vision gain of 15 or more letters in VA and mean VA change from baseline.

ranibizumab more effective across all age groups

In the age subgroup analyses, 88% of the youngest PDT patients experienced less than a 15-letter loss in VA. However, 100% of the youngest ranibizumab patients achieved that primary efficacy criterion, and the results for the older quartiles were also consistently superior in the ranibizumab groups.

Results of the analysis of the proportion of patients who gained 15 or more letters of VA showed that the oldest patients (85 years and older) in all treatment groups had the least chance of achieving that benefit. Nevertheless, almost one in five of the oldest ranibizumab patients demonstrated such a significant gain in vision, and both doses of ranibizumab consistently outperformed PDT in all age subgroups.

Considering mean change in VA from baseline to 12 months, patients of all ages treated with ranibizumab benefited with a mean improvement. While the gains in the oldest quartile for both ranibizumab doses were less than in the three younger groups, there was a mean loss of vision in all PDT subgroups that ranged from 1.5 to 10.2 letters.

For the entry VA subgroup analyses, primary efficacy outcomes in the ranibizumab groups were again consistently excellent, with 92% to 100% of patients in all ranibizumab subgroups losing less than 15 letters of vision. In the PDT arm, 93% of patients who entered the study with the worst level of vision avoided a loss of 15 or more letters, but the results deteriorated across the subgroups as entry vision improved so that only 44% of the patients who had 20/63 or better vision at baseline were able to maintain vision within 15 letters of their entry level.

“These data for the PDT group demonstrate the floor effect that is often discussed in AMD studies and which refers to a low likelihood of significant worsening among those who already have very poor vision,” Dr Brown noted.

A ceiling effect (i.e., a low likelihood of significant vision improvement in AMD patients who come into a trial with relatively good vision) was more evident in the ranibizumab groups in the analyses considering the proportions of patients with VA gains of 15 or more letters as patients in the best VA quartile in each dosage group were less likely than those in the middle two quartiles to enjoy such a significant improvement in vision. However, between 18% and 54% of patients in all ranibizumab VA subgroups gained 15 or more letters of vision compared with only 3% to 9% of PDT patients.

Greater average gain in visual acuity

Similarly, all ranibizumab VA subgroups benefited with a mean gain in VA that ranged from 6.6 to 13.6 letters. In contrast, there was a mean gain of 0.3 letters in the PDT patients with 20/250 or worse vision at baseline, but losses ranging from 6.6 to 18.6 letters in the remaining PDT VA subgroups.

“The subgroup results showed that the PDT patients who started the study with relatively better vision had the most to lose,” Dr Brown said.

In the subgroup analyses of lesion size, between 90% and 100% of ranibizumab patients across all subgroups maintained VA within 15 letters of baseline compared with between 58% and 71% of the PDT patients.

“It was in the lesion size analysis where I thought PDT might have a chance of demonstrating some advantage. However, the results might be explained in part by the fact that the average lesion size in this study was small, less than two disc areas. Furthermore, in the PDT group, it was the patients with larger lesions who seemed to have the better primary efficacy endpoint outcomes, which was counterintuitive,” Dr Brown said.

In contrast, both PDT and ranibizumab seemed to perform better in patients with the smallest lesions in analyses of the proportion of patients gaining 15 or more letters of VA. A similar pattern was observed in the ranibizumab groups in the analyses of mean change in VA, although all subgroups exhibited a mean vision gain that ranged from one to three lines. Mean vision losses ranging from 1.5 to 2.5 lines were observed across all quartiles in the PDT group, and the greatest loss occurred among patients with the smallest lesions.

“These data confirmed our hypothesis that the lesion sizes drove the data in the PDT group and that eyes with no occult component would do better with PDT. However, even among the latter eyes, the results were far superior with ranibizumab.”

The absence or presence of occult CNV at baseline on treatment outcomes had no influence on positive responses to ranibizumab. In the PDT group, patients with 100% classic lesions fared better than their counterparts with some occult component in all of the primary and secondary efficacy analyses.

“These data confirmed our hypothesis that the classic lesions drove the data in the PDT group and that eyes with no occult component would do better with PDT. However, even among the latter eyes, the results were far superior with ranibizumab,” Dr Brown said.

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