CATT AND IVAN RESULTS

New RCT data show similar functional outcomes with all regimens, but prompts further study of possible safety difference

by Cheryl Guttman in Fort Lauderdale

A special session held during the 2012 annual meeting of the Association for Research in Vision and Ophthalmology featured investigators reporting outcomes from two years of follow-up in the Comparison of Age-related Macular Degeneration Treatments Trials (CATT) and from an interim analysis after one year in the two-year Inhibition of VEGF in Age-related Choroidal Neovascularisation (IVAN) study.

Findings from both studies showed visual acuity outcomes in patients with exudative AMD are similar whether they receive intravitreal anti-VEGF treatment with ranibizumab (Lucentis, Genentech) or bevacizumab (Avastin, Genentech).

In CATT and in an analysis pooling data from both studies, the rate of serious systemic adverse events was higher for bevacizumab than ranibizumab. However, the interpretation of the latter difference is uncertain for now as is the clinical relevance of small, but statistically significant differences identified between drugs and dosing regimens in various functional and morphological endpoints.

Daniel F Martin MD, study chair for CATT and chairman, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, US, noted the new data will help clinicians and their patients make informed treatment decisions. He said that based on the outcomes of CATT, clinicians can proceed with confidence using either anti-VEGF agent. Deciding between the monthly dosing and as needed regimens may involve more of a discussion, he told EuroTimes.

Dr Martin explained, “There was more gain in visual acuity with monthly administration, but the difference was small, only 2.4 letters, and required giving 10 more injections over the course of two years. Furthermore, looking at broader metrics of visual acuity, there was not much difference between dosing groups.

In IVAN, where patients had systemic bevacizumab exposure, “The differences between drugs in CATT are very nonspecific and diffuse. They may be due to chance, perhaps there is some unidentified imbalance between groups at baseline that we did not adjust for, or the difference could be something meaningful. We are still trying to sort that out,” said Dr Martin.

Dr Chakravarthy began her presentation by noting that determining the relative effects of the two drugs and two regimens is important in the context that bevacizumab is much cheaper than ranibizumab and because fewer treatments with prn treatment is safer and helps keep costs down, particularly when using ranibizumab.

Cost analyses she presented, which included costs for medication, administration, monitoring and the costs of serious expected adverse events (hospitalisations and treatment of these events), showed a range from £9656 per patient per year for ranibizumab monthly to £1509 for as needed bevacizumab. These estimates were calculated explicitly in the context of the economic evaluation and did not include value-added tax, Dr Chakravarthy noted.

Dr Martin also reported cost data, noting cost was a pre-specified secondary outcome for CATT but never drove the study, and he put the per-patient difference into a larger perspective. “Extrapolating to the 220,000 AMD patients treated annually, there is a US$5bn difference between ranibizumab monthly and either bevacizumab group and a difference of $3bn comparing prn ranibizumab and the bevacizumab regimens,” he said.

The CATT investigators also undertook further analyses to try to understand if the higher risk of serious systemic adverse events with bevacizumab is true. Curiously, there was a higher risk with prn versus monthly treatment, and dissecting deeper into the data, they found most of the excess events associated with bevacizumab were not previously reported in oncological trials where patients had systemic bevacizumab exposure. “The differences between drugs in CATT are very nonspecific and diffuse. They may be due to chance, perhaps there is some unidentified imbalance between groups at baseline that we did not adjust for, or the difference could be something meaningful. We are still trying to sort that out,” said Dr Martin.

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