

Interim data favourable for use of systemic squalamine lactate as PDT adjunct

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in Fort Lauderdale**

COMBINED treatment with intravenous squalamine lactate (Evizon™, Genaera Corporation) and verteporfin photodynamic therapy (Visudyne®, Novartis) is safe, well tolerated and may afford functional and anatomic benefits compared with PDT alone for the treatment of subfoveal choroidal neovascularisation associated with age-related macular degeneration.

Thomas A. Ciulla MD, Midwest Eye Institute, Indianapolis, Indiana, US, provided preliminary results from an ongoing clinical trial at the annual meeting of the Association for Research in Vision and Ophthalmology.

The randomised, double-masked Phase II study enrolled 46 patients aged 50 years and older with subfoveal neovascular AMD of any angiographic subtype

deemed suitable for PDT (predominantly classic, minimally classic, or active occult) that had received no prior treatment.

Patients were randomised into four groups to receive PDT plus vehicle injection or PDT plus intravenous infusion of squalamine 10, 20 or 30 mg. Squalamine or vehicle is administered at weeks one, two, four, five, and monthly thereafter. Infusion times range from 10 to 40 minutes. PDT is performed at week three and is optional, depending on the investigator's determination and using established PDT re-treatment criteria, at weeks 15 and 27.

Preliminary results suggest combined regimen superior

In a pre-planned, nine-week interim analysis, visual acuity assessments have shown a trend to vision stabilisation or

improvement, with patients receiving squalamine plus PDT having an average gain of 1.3 letters. That compared to a 0.9 letter loss in the PDT plus vehicle group. OCT analysis showed anatomic improvement. Eighty percent of patients enrolled had bilateral active CNV, and in the fellow eyes, there was also a trend toward stabilisation of visual acuity with squalamine plus PDT treatment compared with control.

"This is a small study with limited follow-up and while the results are not statistically significant, the preliminary evidence is encouraging in suggesting squalamine has favourable biologic activity," said Dr Ciulla.

Side effects generally mild

The safety review showed 29 patients had experienced an adverse event. To date, most

adverse events have been mild and involved peripheral infusion site reactions, and there have been no drug-related serious adverse events or ophthalmic adverse events. There were eight adverse events deemed as being probably related to the study treatment and all occurred in the squalamine plus PDT group. Only four adverse events were rated as moderate or severe. With the exception of one episode of hyperglycaemia, all of those occurrences were injection site reactions.

Eligibility requirements for the Phase II trial require that subfoveal CNV in the study eye have a greatest linear dimension of up to 5,400 microns, an area of fibrosis of less than 25%, and an area of subretinal blood of less than 50%. Snellen visual acuity in the study eye must be between 20/32 and 20/200 (equivalent to 78 to 34 ETDRS letters).

The patients enrolled were similar in their demographic and baseline features across the various treatment groups. Roughly one-third of patients had predominantly classic CNV, about 20% had minimally classic CNV, and the rest had active occult lesions. Only 20% of patients had unilateral disease.

"The high proportion of patients with bilateral active CNV enrolled in this study was interesting and probably reflected the tendency of investigators and patients to enrol in a study offering a systemic treatment," Dr Ciulla observed.

Squalamine is a small molecule with anti-angiogenic, anti-inflammatory, and antimicrobial effects. It undergoes rapid systemic clearance but has a long intracellular half-life and effects that allow for intermittent dosing. It is absorbed specifically by activated endothelial cells and has been shown in animal models to have dramatic effects on inhibiting CNV and iris neovascularisation

A Phase III study is now underway.

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