Eplerenone for chronic central serous chorioretinopathy

We congratulate Andrew Lotery and colleagues[1] for their excellent work on eplerenone for chronic central serous chorioretinopathy (CSCR). However, we have several concerns about the study.

First, seven (13%) of the 54 patients in the placebo group analysed for the primary endpoint received photodynamic therapy or subthreshold laser therapy compared with three (5%) of the 57 patients in the eplerenone group analysed for the primary endpoint. Because further treatments were offered only if best-corrected visual acuity deteriorated by 15 or more letters from baseline,[2] the greater proportion of patients treated in the placebo group than in the eplerenone group could reflect the greater proportion of patients without resolution in the placebo group. However, by treating these patients with photodynamic therapy or subthreshold laser therapy, best-corrected visual acuity at 1 year follow-up was modified.

Second, the presence of choroidal neovascularisation complicating CSCR is the major negative predictor of response to eplerenone.[3] Of note, Lotery and colleagues[1] based the diagnosis of choroidal neovascularisation only on structural optical coherence tomography (OCT) and dye angiographies, which do not detect choroidal neovascularisation in about a third of patients and are less sensitive alone than when used with OCT angiography.[4] Given that OCT angiography was not used, Lotery and colleagues[1] have possibly erroneously included patients with choroidal neovascularisation without randomisation.

Third, several biomarkers have been previously reported to be associated with the response to eplerenone.[3,5] In particular, the presence of a hotspot in the late phase of indocyanine green angiography seems to indicate a positive response to eplerenone.[3] A subanalysis of the data from the study should be done according to these predictors.

Finally, a target sample size of 104 patients was chosen to detect a difference of five or more letters between the two groups.[1] However, the mean baseline best-corrected visual acuity for the whole study population was 78 letters (SD 73–81),[1] only seven letters less than that recorded for healthy patients. Therefore, if the placebo group had shown an improvement of at least two letters during follow-up (natural history), any improvement in the eplerenone group would not have been statistically significant (ie, the ceiling effect).

Taking together all these observations, based only on this study, we feel that the conclusion "ophthalmologists who currently prescribe eplerenone for CSCR should discontinue this practice" is too strong. Further studies without all the limitations of this trial should be done to confirm the non-efficacy of eplerenone.

GQ is a consultant for Alimera Sciences, Allergan, Bayer Shering-Pharma, Heidelberg Engineering, Novartis, Sandoz, and Zeiss. All other authors declare no competing interests.

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The VICI trial[1] was necessary because of the uncertainty surrounding eplerenone, an off-label drug, in the management of chronic central serous chorioretinopathy (CSCR). Andrew Lotery and colleagues[1] concluded that eplerenone was not superior to placebo for improving best-corrected visual acuity in patients with chronic CSCR after 12 months of treatment. Nevertheless, this study raises a few concerns.

In the eplerenone group, treatment was stopped as soon as resolution of subretinal fluid occurred (17 [40%] of 42 patients treated). 17 (30%) of 57 patients received eplerenone for less than 3 months. However, in previous studies,[2,3] treatment with eplerenone of between 6 and 12 months resulted in resolution of subretinal fluid and improvement of vision in 60–80% of patients. In these same studies,[2,3] CSCR recurred when treatment ceased.

Seven (12%) of the 57 patients in the placebo group received photodynamic therapy or subthreshold laser therapy, compared with three (5%) of 57 patients in the eplerenone group in the case of non-resolution of subretinal fluid. That such a difference did not have a role in the outcome of the study is hard to believe. The number of patients in the placebo group who had pigment epitheliopathy doubled, but no increase was observed for the treatment group. How can this difference be explained?

Lotery and colleagues[1] extrapolated their results by adding two previous randomised controlled trials of eplerenone versus placebo.[4,5] These trials did not use the same duration of treatment (8 weeks and 3 months) and should therefore not be considered to

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