Reviewer’s report

Title: (R)-[11C]Verapamil PET studies to assess changes in P-glycoprotein expression and functionality in rat blood-brain barrier after exposure to kainate-induced status epilepticus

Version: 2 Date: 4 November 2010

Reviewer: Mark Muzi

Reviewer’s report:

Comments on the manuscript “(R)-[11C]Verapamil PET studies to assess changes in P-glycoprotein expression and functionality in rat blood-brain barrier after exposure to kainite-induced status epilepticus”. Reviewed by Mark Muzi and Sara Eyal.

Synopsis: The authors describe a PET and IHC study of P-gp expression and function at an early time point in the kainate model for spontaneous seizures in rats. NONMEM analysis detected small differences between kainate-treated and control rats in verapamil BBB kinetics when P-gp was inhibited.

The changes introduced to the manuscript “(R)-[11C]Verapamil PET studies to assess changes in P-glycoprotein expression and functionality in rat blood-brain barrier after exposure to kainite-induced status epilepticus” address most of the issues raised by us. We now have only the following comments:

1. We are aware of the papers cited along this manuscript evaluating the interaction of AEDs with P-gp. However, these studies altogether indicate that AEDs are either not substrates or at best very weak substrates of P-gp (see Anderson GD, Shen DD. Where is the evidence that p-glycoprotein limits brain uptake of antiepileptic drug and contributes to drug resistance in epilepsy? Epilepsia. 2007 Dec;48(12):2372-4).

2. P. 22, second paragraph, last sentence: either “hence” or “therefore” should be used.

3. P. 26, line 5: please change “a” to “an”.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests