Critical appraisal – Standard questions

Loescher et al 2004 Epilepsia paper

Introduction	
Are the aims clearly stated?	To compare the efficacy of ELB138 in dogs with newly diagnosed epilepsy with that of phenobarbitone and primidone and to assess the efficacy of ELB 138 as an additional therapy.
Methods	
Is the study design suitable for the aims?	Difficult to determine as a combination of different study type appear to have been utilized. In addition, the aim of our BET was not the primary aim of this study.
What population of animals was being studied?	Dogs with spontaneously recurrent epilepsy that had had two generalized tonic clonic seizures, treated at the Department of Small Animal Medicine in Hannover
Is it clear what measurements were carried out in the study?	• Owners used a seizure calendar to note frequency, type and duration of spontaneous seizures. • Seizure types were determined using video in selected cases. • Adverse event data
Were the correct measurements chosen? Do they that reflect (or are they strongly related to) the outcome of interest?	Yes Yes
Were previously established validated methods used to make the measurements? (e.g. Glasgow pain score, International Units etc)	No
Are the statistical methods described?	Yes
Was the statistical significance level stated?	No

Was the sample size justified?	No
Was ethical approval obtained?	Not stated
Overall, are the methods described in enough detail that you could repeat them?	No; there is inadequate description of the dogs included, particularly in the phenobarbital group, or how dose escalation was conducted in dogs that did not respond to 10mg/kg ELB-138, and not enough description of the owners' seizure log to understand the nature of the data collected (free text versus some form of scale). In addition from a study design perspective, it is unclear why these different study designs were put together in this way.
Results	
Were the basic data adequately described?	Little data on the type of dog included, e.g. breed, sex.
Do the numbers add up? Are all subjects accounted for?	Yes, where given Yes
Was the statistical significance (p value) stated in the results? Is this consistent with the methods? (It should be stated in the sample size or power calculation)	Yes P values are not described in the methods and neither a sample size calculation or power calculation are provided.
What were the main findings/key results?	The authors conclude that median seizure frequency was statistically significantly reduced versus baseline for dogs that responded to ELB138, but only if the "non-responders" (defined as dogs whose seizure frequency remained unchanged or increased) were removed from the analysis. Median seizure frequency was reduced in dogs that received phenobarbital when both responders and non-responders were included in

	analysis. In addition, dogs receiving phenobarbitone that had generalized tonic-clonic seizures showed a significant decrease in seizure frequency, but this was not found in dogs with generalized seizures receiving ELB138.
Discussion and conclusion	
What do the main findings/key results mean?	The small number of dogs included in the ELB138 group combined with the lack of sample size calculation means that these data are difficult to interpret.
Are the negative findings discussed? How are the negative findings interpreted?	No
Does the discussion reflect the results?	Yes, broadly
Interpretation	
What are the clinical implications of this study? Are the subjects in the study similar to those in the BET/your own?	Hard to conclude any as no sample size calculation provided and multiple subgroup analyses were performed, the statistical validity of which is difficult to determine. In addition, use of data from prospective and retrospective studies raises further concern about the validity of these results. Difficult to be confident
General	
Who funded this study?	Not stated