

**Library & Information Services**

**Journal Club Checklist**

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| **Title** | **A prospective, randomized, placebo-controlled, double-blinded clinical trial comparing the incidence and severity of gastrointestinal adverse events in dogs with cancer treated with piroxicam alone or in combination with omeprazole or famotidine**  *Journal of the American Veterinary Medical Association*, 259 (4), pp385-391. |
| **What are the aims or objectives of the study?**  A clearly stated aim or objective will make it easier for you to assess whether the research has been appropriately designed to meet these aims. | The stated objective of the study is to assess the impact of the prophylactic use of omeprazole and famotidine on the incidence and severity of gastrointestinal (GI) adverse events (AEs) in dogs with cancer treated with single agent piroxicam. |
| **Who carried out the research?**  Do the researchers have appropriate knowledge or supervision to carry out the research?  **Who is paying for the study?**  Do you think that this could bias the results? | The study was carried out by veterinary clinical staff at Purdue University Veterinary Teaching Hospital.  In the acknowledgements the authors state that the study was funded by the Veterinary Cancer Society’s Resident Research Award and that the funding source did not have any involvement in the study design, data analysis and interpretation, and writing of the manuscript. |
| **Are there any potential sources of bias?**  **What steps were taken to reduce this bias?** | The authors note that because of the study design, owners were biased to identify even low-level adverse events. |
| **Is there a specific research question or hypothesis?** | Based on a previous retrospective study the authors hypothesised that the prophylactic administration of gastric acid suppressants would result in an increase in the frequency and severity of gastrointestinal adverse events in dogs with cancer treated with piroxicam. |
| **Why do you want to review this paper?** |  |
| **What methods did the researchers use?**  **Can you pick out the elements of a PICO question from the materials and methods section?**   * Patients/participants * Intervention * Comparator * Outcome | This study is described as a prospective, randomized, placebo-controlled, double-blinded clinical trial |
| **Is this methodology appropriate to the objectives or question?**  More detailed guidance on how to critically appraise different types of study can be found in the [EBVM Toolkit Section 3](https://knowledge.rcvs.org.uk/evidence-based-veterinary-medicine/ebvm-toolkit/) | The randomised controlled trial is considered the best (least likely to bias) study design for comparing outcomes. This can include adverse events (AEs), but it should be remembered that for rare AEs large sample sizes and meta-analyses of multiple studies may be required. |
| **Is the methodology described clearly enough to enable you to follow what was done?**  **Is there any additional information you would like to know?** |  |
| **Are the type and selection of patients clearly described?**  Are the inclusion and exclusion criteria clearly described?  What effect do you think that these criteria would have on recruitment? | This information in given in the Animals section of Materials and Methods |
| **How many patients were included in the study?**  The sample size calculation gave a recruitment target of 72 dogs (24 per group). Was this target met?  What reason was given for stopping recruitment to the study early? |  |
| **Are the patients divided into groups, if so, how was this done?**  Is the method of randomisation and blinding clearly described? |  |
| **How were each of the three groups treated?** |  |
| **Is the data collected clearly described?**  What data was collected from each dog? |  |
| **Are the results of the study clearly described?**  **How were adverse events described and reported?**  **Which adverse events would you consider most important?** | Did you find Table 2 a useful way of presenting the results? |
| **Which results are statistically significant?**  **Which results were not statistically significant, and why might this be the case?** | The authors state that *In addition to experiencing more GI AEs overall, significantly (P = 0.034) more dogs that received omeprazole, versus placebo, had AEs that were graded as ≥ 2 (*Severe)  Differences in the percentages of dogs that had AEs of ≥ 2 were not significant (P > 0.197) between the famotidine and omeprazole groups and between the famotidine and placebo groups.  Because the study was stopped early it may have been underpowered to detect differences between the groups. |
| **What other result did the authors report and why might it be significant?** | The authors also reported on whether raised liver enzymes (ALT/ALP/GGT) impacted on adverse events, with the authors reporting *Differences in the numbers of dogs that had GI AEs on the basis of whether serum ALT, ALP, and GGT activities were increased were not significant (P > 0.521).*  Famotidine and omeprazole are metabolized by the liver; thus, liver dysfunction may result in prolonged or possibly higher serum or tissue concentrations of these drugs. |
| **What is the main recommendation from the study, and do you agree with it?**  **What mechanism do the authors propose for this recommendation?**  **Do you think that the same recommendation would apply to other situations?** | The authors state that *On the basis of the results of the present (evidence-based) study, veterinarians should not prescribe H2RAs or PPIs in an attempt to minimize the risk of GI AEs for dogs that are being administered piroxicam.*  The authors suggest two possible mechanisms, either that the use of H2RAs or PPIs may have resulted in changes in the GI microbiome.  Or that co-administration of piroxicam and famotidine or omeprazole may have altered piroxicam pharmacokinetics, resulting in prolonged or possibly higher piroxicam concentrations and therefore more GI AEs. |
| **What are the limitations of the study?** | Some limitations that you may think of include:   * Small sample size * Using owner reports of Adverse events * Narrow inclusion criteria |
| **Do the findings provide sufficient evidence for you to consider changing your current practice?** |  |
| **Having read the paper are there any other sources of information you need to look at before changing your current practice?** | Some references that may be of interest are given below |

Marks, S.L. et al (2018)ACVIM consensus statement: support for rational administration of gastrointestinal protectants to dogs and cats. *Journal of Veterinary Internal Medicine*, 32(6), pp. 1823-1840. <https://doi.org/10.1111/jvim.15337>

LeBlanc, A.K., et al (2021) Veterinary Cooperative Oncology Group—Common Terminology Criteria for Adverse Events (VCOG‐CTCAE v2) following investigational therapy in dogs and cats. *Veterinary and Comparative Oncology*, 19(2), pp. 311-352. <https://doi.org/10.1111/vco.12677>

Hunt, J.R. et al (2015) An analysis of the relative frequencies of reported adverse events associated with NSAID administration in dogs and cats in the United Kingdom. *The Veterinary Journal*, 206(2), pp. 183-190. <https://doi.org/10.1016/j.tvjl.2015.07.025>