

**Library & Information Services**

**Journal Club Checklist**

|  |  |
| --- | --- |
| **Title** | **Randomized controlled clinical study evaluating the efficacy and safety of intratumoral treatment of canine mast cell tumours with tigilanol tiglate (EBC-46) *Journal of Veterinary Internal Medicine*** |
| **What are the aims or objectives of the study?** | The stated objective of the study, given in the abstract, is to evaluate the efficacy and safety of tigilanol tiglate (TT) for local intratumoral treatment of mast cell tumours (MCT) in dogs.  Further detail is given in section 2.1 what is the primary objective stated in this section?  What are the secondary objectives stated in this section? |
| **Who carried out the research?** | Six of the authors appear to work for Qbiotics who developed TT and funded the study, while 10 of the authors appear to work in veterinary clinics in the US. |
| **Is there a clear research question or hypothesis?**  **Can the PICO be identified?**  **Is the control group appropriate?** | There is no explicit question or hypothesis stated but the implied question is “Is TT more effective than the placebo / control in the treatment of MCTs in dogs?”  **Patient -** In dogs with stage Ia or IIIa MCT **\***  **Intervention** intertumoral TT(+corticosteroids, H1 and H2 antagonists)  **Control** corticosteroids, H1 and H2 antagonist  **Outcome** – Clinical response (complete resolution of the target tumour).  Why do you think that corticosteroids, H1 and H2 antagonist were given to the control group? |
| **What methods did the researchers use?** | The study involved a Randomised Controlled trial (RCT) to assess response to treatment.  There was also a quality of life questionnaire completed by owners at days 0,7,14 and 28. |
| **Were personnel blinded to treatment?** | The owners and investigators were theoretically blinded to treatment group, however in view of the method of action of the treatment do you think there is any risk of the then being aware of which group the dog was in? |
| **Is this methodology appropriate to the objectives or question?** | A RCT is an appropriate methodology for comparing treatments, either with a placebo or control or against another treatment.  While collecting data on Adverse Events (AE) during a trial is important it may miss less common AEs because of the sample size. |
| **Is the study design described clearly enough to enable you to follow what was done?** | Figure 1 on page 3 sets out the timings of treatment.  Are you able to put numbers to each of the outcome groups Complete Response (CR) / Not CR?  It should be noted that the control group, along with any dogs that did not respond to treatment the first time, were given TT at day 28. |
| **Are the type of patients clearly described?**  **What were the Inclusion and exclusion criteria for participation?** | **Inclusion criteria**  Dogs at least one year of age with stage Ia or IIIa MCT\*. However, complete clinical staging was not undertaken Instead, investigators identified dogs for inclusion based on the following:  (1) absence of systemic signs of MCT metastasis on systemic health assessment, and  (2) absence of palpably enlarged locoregional lymph nodes (LN) and, if enlarged LNs were detected, absence of confirmed metastasis to LNs based on FNA.  Mast cell tumours could be cutaneous anywhere on the body, or subcutaneous if located at or distal to the elbow or hock.  **Exclusion criteria**  (1) locoregional LN metastasis confirmed on FNA or signs of systemic MCT disease,  (2) tumour ulceration (because it could lead to partial loss of the TT dose during administration),  (3) tumour recurrence at a previous biopsy or surgical site, (4) radiotherapy, chemotherapy, or other anticancer treatment within the previous 2 months.  The only medications specifically excluded in the study were nonsteroidal anti-inflammatory (administered up to 7 days before enrolment) and immunosuppressive medications including cyclosporine and long-acting corticosteroids, (administered up to 14 days before enrolment). |
|  |  |
| **Are these patients or participants, relevant to your practice, if not what differences need to be considered?** | How many of the patients that you see with mast cell tumours would meet the inclusion criteria? |
| **How many patients or participants were included in the study?** | There were 123 dogs in total, 81 received TT on day 0 and 42 in the control group. |
| **Were the patients divided into groups, if so, how was this done?** | Dogs were assigned to either the TT treated or control group using a random allocation table based on a blocked (n = 6) randomization design, with 4 TT treated and 2 control dogs in each block. |
| **Were the groups similar at the start of the trial?** | Table 2 gives details of the demographics of the 2 groups. Do you think any of the differences are significant? |
| **Is the data collected clearly described?** | The paper states that wound length and width (cm) were measured at 7, 14, 28, 42, and 84 days after treatment. Blood and urine samples for CBC, serum biochemistry, and urinalysis were taken at screening and at 7, 28, and 42 days after treatment and that photographs were taken at all assessment times.  Figure 2 provides example photographs, and Figure 5 provides detail of the maximum wound area after treatment.  Do you think these clearly represent the data? |
| **Are all patients or participants accounted for in the analysis?** | Table 3 provides a summary of the results based on both all dogs enrolled (Intention to treat) and those that completed the trial (Per protocol) by day 28. 5 dogs were withdrawn (details in para 3.2) one from the treatment group and 4 from the control group and reasons are given.  However further details of dogs which did not complete the trial are given in the supplementary material **\*** Figure 1 which shows that a further 13 dogs were withdrawn during the full 84 days of the trial. |
| **Are the results of the study clearly described?** | The results are presented in section 3 under several different headings.  **3.2 Efficacy -** the data are also presented in table 3 (response after 28 days) and table 4 (response after 84 days). Is there any other information on efficacy you would like to know?  **3.3. Determinants of efficacy** - wound formation and tumour grade were both important factors affecting response.  **3.4 Safety and tolerability** - which includes details of wound formation and healing (3.4.1), frequent adverse events (3.4.2), serious adverse events (3.4.3) and quality of life (3.4.4) |
| **Were all clinically relevant outcomes considered?** | Are there any other outcomes you would like to know about? |
| **What are the findings of the study?** | **Efficacy** How many dogs responded after 1 treatment? How many dogs responded after 2 treatments? How many did not respond? You may find it easier to answer this question from Figure 1 in the supplementary material.  (you may want to consider both the size of the effect and the confidence intervals).  **Safety and tolerability**  How many and what type of adverse reactions were noted during the trial? (Table 6 and Figure 6)  How many of these do you think are serious?  (You may find the Veterinary Co-operative Oncology Group criteria useful **\***)  **How did the owners rate their dog’s quality of life during the trial?** |
| **Are the findings likely to be clinically, as well as statistically significant?** |  |
| **Limitations of the study** | The authors note the following  Reliance on cytological staging and clinical assessment rather than full staging  Relatively short (84 day) follow up period  Can you think of any others? |
| **Do you think that there are any potential sources of bias in the paper?** |  |
| **How do the outcomes and adverse events reported compare with current (surgical) treatment methods?** |  |
| **Do the findings support or alter your current knowledge?** |  |
| **Do the findings provide sufficient evidence for you to consider**  **changing your current practice?** |  |
| **Are there any other sources of information you need to look at before using this product?** | You may wish to look at the Summary of product information. |

**\***   
The staging of mast cell tumours referred to in the paper is taken from:  
Welle, M.M., et al (2008) Canine mast cell tumours: a review of the pathogenesis, clinical features, pathology and treatment. *Veterinary Dermatology*, 19(6), pp.321-339

<https://doi.org/10.1111/j.1365-3164.2008.00694.x>

* 1a = One tumour confined to the dermis, without regional lymph node involvement. Without systemic signs
* 111a = Multiple dermal tumours; large infiltrating tumours with or without regional lymph node involvement. Without systemic signs

Supplementary material for the article is available at:

<https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1111%2Fjvim.15806&file=JVIM_15806_Supporting+information+File+20200429.pdf>

For the Veterinary Co-operative Oncology Group criteria see:  
(2004), Veterinary co‐operative oncology group – common terminology criteria for adverse events (VCOG‐CTCAE) following chemotherapy or biological antineoplastic therapy in dogs and cats v1.0. *Veterinary and Comparative Oncology*, 2 (4) pp 195-213. <https://doi.org/10.1111/j.1476-5810.2004.0053b.x>