

# **Comparison of Robenacoxib and carprofen in palliative management of cancer pain**

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## Abstract

When dogs with cancer are no longer (or not at all) treated for their illness, a palliative treatment should be given to increase the wellbeing of the dog. Dogs express pain in many different ways, sometimes by very subtle changes in behaviour. A brochure was created to inform owners about dogs that suffer from pain due to cancer and how to recognize this pain.

A blinded cross-over study was performed on 6 dogs with untreated tumors comparing Robenacoxib and carprofen as a palliative therapy. These two NSAIDs were compared using three forms (scoring pain, quality of life and adverse events), filled in weekly by the owners of the dogs. During 4 weeks every dog received either carprofen or Robenacoxib, they then had a wash-out period of one day without pain medication. Subsequently the other medication (either Robenacoxib or carprofen) was given during the next 4 weeks.

When looking at the interim results, using a paired samples t-test and an independent samples t-test no significant differences between the two medications were found. Further research by examining more dogs is necessary to obtain more data. It is important to see whether or not a significant difference could be acquired between the medications in the future.

## Introduction

In the veterinary practice cancer is a common diagnosis<sup>1</sup>. Not every dog-owner wants to treat his pet with radiation, chemotherapy or surgery. Furthermore, some cancers are untreatable with any of these therapies. Therefore, palliative treatment is an important part of a therapeutic plan. When trying to prolong a pet's life it is important to keep the quality of life as high as possible<sup>2</sup>.

It is difficult to determine how pain affects the quality of life in dogs with cancer. When looking at the human medicine field however, surveys tell us that 28% of the patients with newly diagnosed cancer experience pain, as well as at least 50% of the patients with existing cancer and 80% of the patients with advanced tumors and paraneoplastic disease<sup>3</sup>. It can be assumed that pets experience the same amount of pain when suffering from cancer.

The most painful tumors in dogs are<sup>4</sup>:

- Primary bone tumors and metastasis in bones
- Oral and pharyngeal tumors
- Urinary tract tumors
- Eye tumors
- Intranasal tumors
- Central nervous system tumors
- Gastrointestinal tumors
- Cutaneous tumors

Sometimes animals clearly show signs of pain, but unfortunately it happens a lot that pets suffer in silence. They do not show mild pain, and even moderate pain goes sometimes unnoticed.

The easiest way to assess a dog's pain from a tumor, is by palpating the tumor and cautiously apply pressure. If a dog shows pain with palpation of the tumor, it is likely the tumor will cause spontaneous pain as well<sup>4</sup>.

Another way to determine if a dog is in pain is by looking at behavioural changes. Chronic pain expresses itself by changes in behaviour.

Examples of these behavioural changes are listed below<sup>4</sup>.

- Decreased activity
- Decreased appetite
- Behavioural changes (aggression, dullness, shyness, clinginess, increased dependence)
- Sad facial expression, head carried low
- Less grooming, bad fur condition
- Increased respiratory rate
- Licking or scratching one certain area
- Urinating and defecating in inappropriate places
- Vocalization and making abnormal noises (whining, grunting)

Pain can induce a physiological stress reaction by elevating levels of cortisol, antidiuretic hormone (ADH), catecholamines, aldosterone, renin, angiotensin II and glucose. As well as decreasing levels of insulin and testosterone. All these metabolic changes bring the body in a chronic catabolic state which can decrease the rate of general healing. Stress due to pain also has a negative effect on the circulatory, respiratory and gastrointestinal organs<sup>2</sup>.

Therefore, it is ethically and clinically necessary to treat dogs with pain medication.

Veterinarians have several groups of analgesic drugs available to treat dogs. Non-steroidal anti-inflammatory drugs (NSAIDs) are often used in veterinary practice because of their long-lasting and good analgesic effects<sup>5</sup>.

The mechanism of action by which NSAIDs provide their analgesic effect is by inhibiting COX-1 and COX-2. These are the enzymes that induce the production of prostaglandins by converting

arachidonic acid. COX-2 is mainly responsible for causing pain, COX-1 is an enzyme that is necessary for housekeeping and physiological functions<sup>6</sup>. Therefore, the inhibiting of COX-1 leads to some of the side effects of NSAIDs. Because of the inhibiting of COX-1, NSAIDs can have toxic effects on the gastrointestinal tract, kidneys and haemostasis.<sup>7</sup>

By using a more selective COX-2 inhibitor, most of these adverse effects will be reduced compared with using a non-selective NSAID<sup>7</sup>.

Robenacoxib belongs to a group of selective COX-2 inhibitors, so the goal of this study is to prove that Robenacoxib is a more suitable NSAID than carprofen when used in canine cancer patients. It is expected that Robenacoxib will have significantly better quality of life and significantly less side effects compared to generic carprofen when treating dogs with cancer.

## Materials & methods

This research is a randomized cross-over study with blinded investigators and clients. The study is performed on client-owned dogs with one or more tumors that would or could not be treated (any more). The patients and owners were recruited at the University clinic for companion animals.

Inclusion criteria for the dogs are: The dogs must be in good health with no concurrent systemic disease. Exception for this rule is of course the diagnosis of cancer. The tumor will be diagnosed by history, clinical examination, FNAB (fine needle aspiration biopsy) and /or biopsy. Blood values can be out of reference range, if these are within expectation for this animal. Dogs must be expected to survive for at least 6 months.

Exclusion criteria are: Dogs that are receiving other pain medication (corticosteroids, other NSAIDs) or medication that could be nephrotoxic cannot participate in this study. In this case a wash out period of at least 3 days without these medications will be required before entering the dog in this study. Dogs with hepatic, gastrointestinal, cardiac, renal disease or severe organ failure, pregnant females, dogs that are hypersensitive to one of the excipients and dogs that are being treated with radiation- or chemotherapy will also be excluded.

When a dog met the inclusion criteria, the dog-owner was informed about the study both verbally and by written text. If an owner was willing to participate in the study, a complete case history was obtained and clinical examination was performed by a veterinary specialist or a veterinary student. At first clinical examination the tumor was measured and a FNAB or biopsy was taken to diagnose the tumor. A thoracic radiograph, abdominal echography or CT-scan was also made to check for tumor-metastasis. A 6 mL blood sample was taken in a heparin tube (4 mL) and an EDTA tube (2 mL) and tested on the following values: haematocrit, leukocytes (differentiated), thrombocytes, urea, creatinine, sodium, potassium, calcium, phosphate, ALP (alkaline phosphatase), ALT (alanine transaminase), bile acids, bilirubin, total protein, cholesterol and triglycerides. All dogs had to be sober for blood analysis.

During 4 weeks every dog received either carprofen (2 mg/kg) or Robenacoxib (1 mg/kg) (Onsior, Novartis Animal Health, Switzerland), then had a wash-out period of one day without pain medication. Subsequently the other medication (either Robenacoxib or carprofen) was given during the next 4 weeks. This research was blinded for investigators and clients. The pharmacy for companion animals at the university clinic prepared and delivered the right medication to the owners.

Before starting the study, suitable patients had to be recruited from the Small animal policlinic at Utrecht University or other veterinary practices. Up to now, 6 patients have entered and (partially) completed the study. One owner (with dog number 4) decided not to participate after the intake conversation.

All patients were followed during 57 days. Every owner had to fill in three questionnaire weekly: a pain scoring questionnaire, a quality of life (QoL) questionnaire and an adverse events questionnaire. At day 0, an intake conversation took place, as well as a clinical examination, tumor measurement, a check for metastasis and a blood analysis. At this first appointment all 3 questionnaires were filled in as well and the owner signed a compliance statement.

At day 1 the owner started with one of the medications (Robenacoxib or carprofen).

At day 14, 28, 42 and 57 owners with their dogs visited the clinic for physical examination, blood analysis and tumor measurement. If metastasis are present, these were measured as well, using the appropriate diagnostic methods.

All results were scored from the completed questionnaires (pain, QoL and adverse events). The adverse events were scored following the VCOG-CTCAE v1.1<sup>8</sup>. This form was adapted to fit in this

study by adding score 0 for no adverse event and leaving score 5 (death) out. Pain score could vary from 0 to 24, with 0 for no pain. QoL score could vary from 1 to 5 for each question, with 22 questions was 110 the maximum score for QoL.

#### *Statistical method*

All the scores were entered in de statistical program SPSS (Statistical Package for the Social Sciences). All statistical calculations and graphs have been made by using this program.

A *paired samples t-test* has been used 6 times (period 1 versus period 2 and during medication A versus during medication B, each with pain scores, QoL scores and AE scores) to determine whether or not the average scores of two groups differed significantly. This statistical model determines if the variation between the groups is a result of time/treatment or caused by coincidence. P values of less than 0,05 are considered significant.

An *independent samples t-test* has been used as well, to create more samples and thereby trying to get a better chance on a significant difference. With this test, more samples (n=31) are available to use because every weekly score can be used as an individual score and the scores of dog number 3 (survived only during period 1 and therefor received only medication B and could not be used in the paired samples t-test) can be used as well.

Because this study is still continuing when writing this report, the two used medications (Robenacoxib and carporal) are referred to as medication A and medication B, to keep this study as blind as possible for all researchers.

## Results

The mean results of the weekly questionnaires can be seen in Table 1. Some scores are missing because the owners of dog number 4 decided not to participate after all and dog number 3 was euthanized in week 4, therefore it did not receive its second medication (medication A). The scores of dog number 6 are not available because the owner was not able to send the questionnaires.

Patient number	Mean pain score A	Mean pain score B	Mean QoL score A	Mean QoL score B	Mean AE score A	Mean AE score B
1	0,75	0,75	76,5	93	2	2,25
2	0	3,5	96,75	67	1	7,5
3	-	8,3	-	66,33	-	8,5
4	-	-	-	-	-	-
5	1,5	0,5	96,5	100	2,5	1
6	-	-	-	-	-	-
7	6	8	75,5	67,25	3,25	4,75
<b>Mean</b>	<b>2,06</b>	<b>4,21</b>	<b>86,13</b>	<b>78,72</b>	<b>2,19</b>	<b>4,8</b>

**Table 1:** Mean scores obtained from the weekly questionnaires, when giving medication A and B. With pain scores and AE scores lower scores mean less pain and less adverse events. With QoL scores, higher scores mean better quality of life.

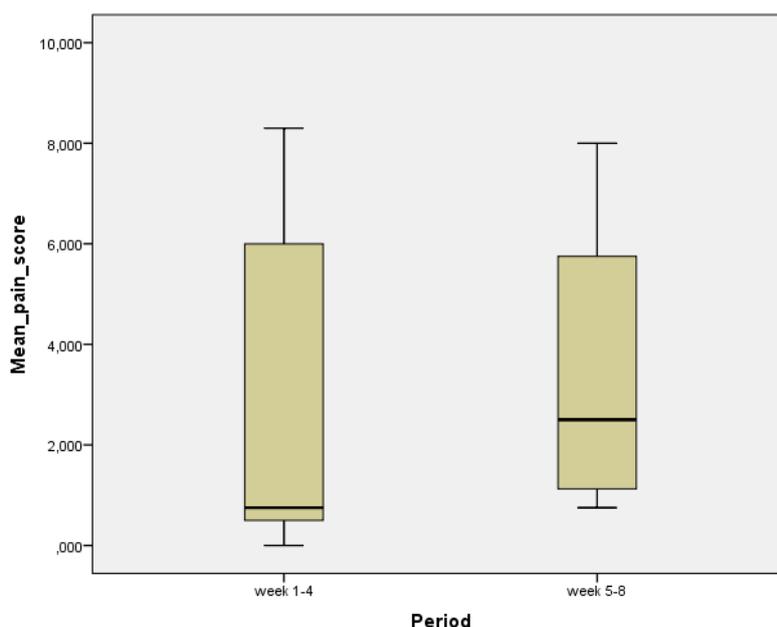
When looking at these numbers, scores for medication A seem to be better in every domain. Medication A results in lower pain scores and lower adverse events scores (thus less side effects), as well as higher scores on quality of life compared with medication B.

To determine whether or not these scores are significant statistical calculations were performed.

### **Paired samples t-test**

#### *Pain scores*

Graph 1 shows a boxplot of the mean pain scores obtained from all the weekly questionnaires, during period 1 and period 2.



**Graph 1:** Box plot with mean pain scores of all dogs, during period 1 and period 2.

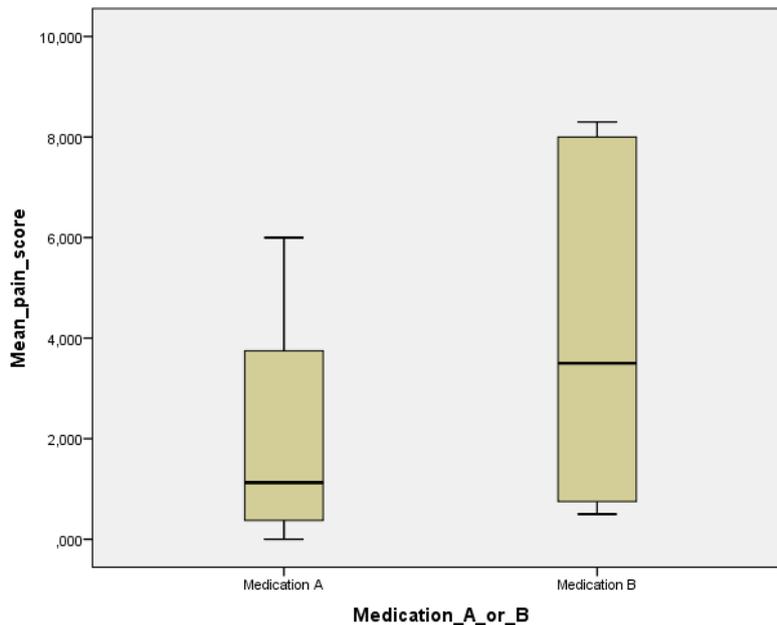
	Mean pain score	Standard deviation
Period 1	1,81	2,81
Period 2	3,44	3,26

Table 2: Mean pain scores and their standard deviation

See table 2 for the mean pain score during period 1 and 2 and their standard deviation.

When performing the paired samples t-test calculation on the pain scores during period 1 and 2, it shows that the mean pain scores do not differ significantly among the two groups ( $t(3) = -2,177, p = 0,118 > 0,05$ ).

Graph 2 shows a boxplot of the mean pain scores obtained from all the weekly questionnaires, during medication A and medication B.



Graph 2: Box plot with mean pain scores of all dogs, during medication A or B.

	Mean pain score	Standard deviation
Medication A	2,06	2,70
Medication B	3,19	3,48

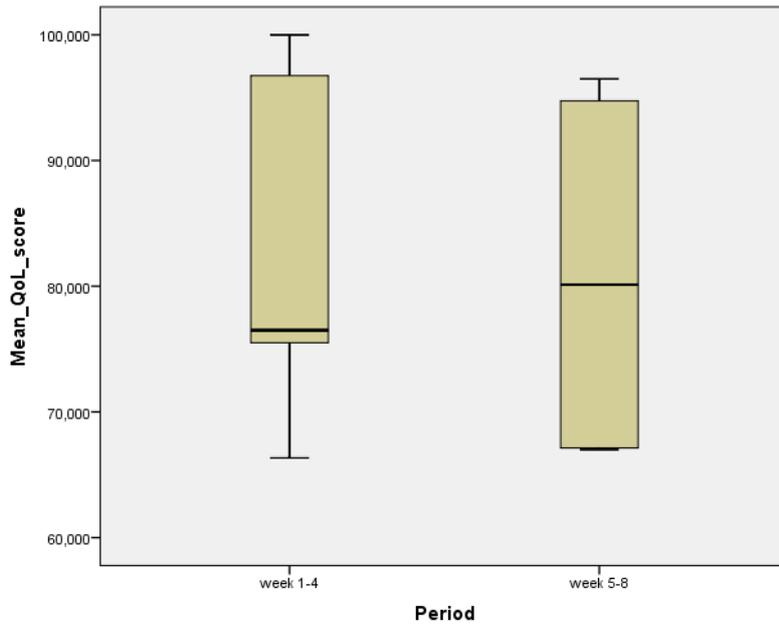
Table 3: Mean pain scores and their standard deviation

See table 3 for the mean pain score during medication A and B and their standard deviation.

When performing the paired samples t-test calculation on the pain scores during medication A and medication B, it shows that the mean pain scores do not differ significantly among the two groups ( $t(3) = -1,116, p = 0,346 > 0,05$ ).

### Quality of life

Graph 3 shows a boxplot of the mean QoL scores obtained from all the weekly questionnaires, during period 1 and period 2.



Graph 3: Box plot with mean QoL scores of all dogs, during period 1 and period 2.

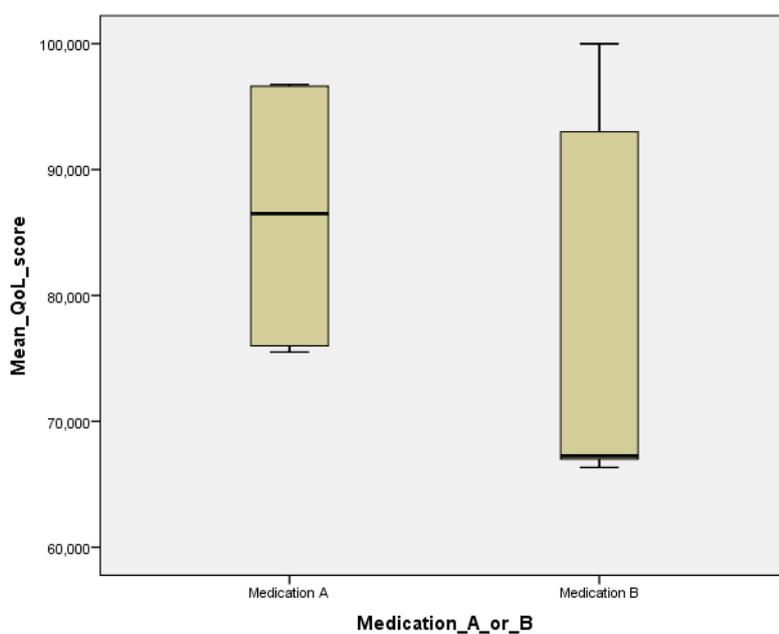
	Mean QoL score	Standard deviation
Period 1	87,19	12,99
Period 2	80,94	16,01

Table 4: Mean QoL scores and their standard deviation

See table 4 for the mean QoL score during period 1 and 2 and their standard deviation.

When performing the paired samples t-test calculation on the QoL scores during period 1 and 2, it shows that the mean QoL scores do not differ significantly among the two groups ( $t(3) = 0,658$ ,  $p = 0,557 > 0,05$ ).

Graph 4 shows a boxplot of the mean QoL scores obtained from all the weekly questionnaires, during medication A and medication B.



Graph 4: Box plot with mean QoL scores of all dogs, during medication A or B.

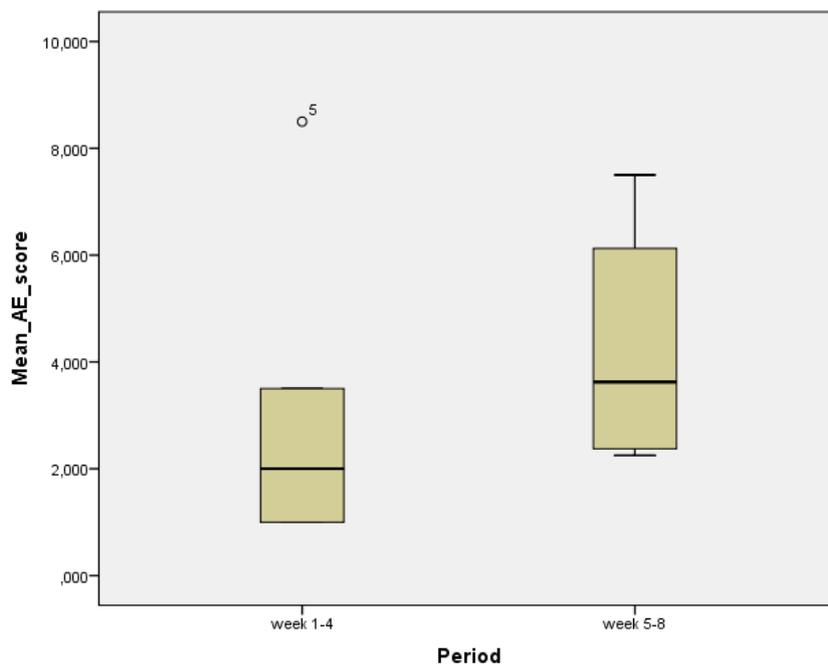
	Mean QoL score	Standard deviation
Medication A	86,31	11,92
Medication B	81,81	17,20

Table 5: Mean QoL scores and their standard deviation

See table 5 for the mean QoL score during medication A and B and their standard deviation. When performing the paired samples t-test calculation on the QoL scores during medication A and B, it shows that the mean QoL scores do not differ significantly among the two groups ( $t(3) = 0,458$ ,  $p = 0,678 > 0,05$ ).

#### Adverse events

Graph 5 shows a boxplot of the mean AE scores obtained from all the weekly questionnaires, during period 1 and period 2.



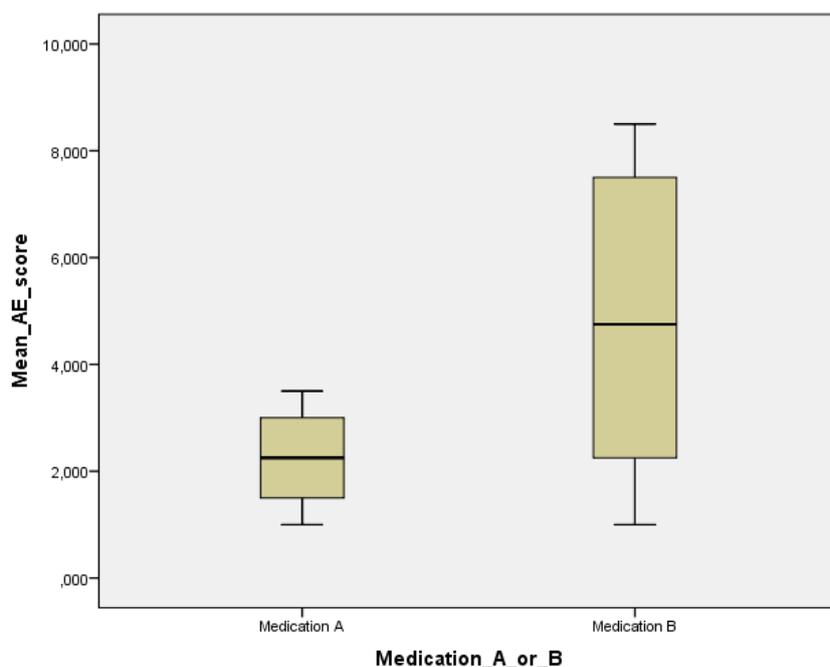
Graph 5: Box plot with mean AE scores of all dogs, during period 1 and period 2.

	Mean AE score	Standard deviation
Period 1	1,81	1,07
Period 2	4,25	2,44

Table 6: Mean AE scores and their standard deviation

See table 6 for the mean AE score during period 1 and 2 and their standard deviation. When performing the paired samples t-test calculation on the AE scores during period 1 and 2, it shows that the mean AE scores do not differ significantly among the two groups ( $t(3) = -1,759$ ,  $p = 0,177 > 0,05$ ).

Graph 6 shows a boxplot of the mean AE scores obtained from all the weekly questionnaires, during medication A and medication B.



Graph 6: Box plot with mean AE scores of all dogs, during medication A or B.

	Mean AE score	Standard deviation
Medication A	2,19	0,94
Medication B	3,88	2,88

Table 7: Mean AE scores and their standard deviation

See table 7 for the mean AE score during medication A and B and their standard deviation. When performing the paired samples t-test calculation on the AE scores during medication A and B, it shows that the mean AE scores do not differ significantly among the two groups ( $t(3) = -0,982$ ,  $p = 0,398 > 0,05$ ).

### **Independent samples t-test**

When performing an independent samples t-test, differences between the groups are not significant. All six comparisons (pain, QoL and AE scores during period 1 and 2 and during medication A and B) showed P-values higher than 0,05.

### *Pain scores*

Table 8 shows the means of all the individual weekly pain scores and their standard deviations.

	Mean pain score	Standard deviation
Period 1	2,84	3,70
Period 2	3,75	3,57
Medication A	2,14	2,82
Medication B	4,06	4,04

Table 8: Mean pain scores and their standard deviation

Comparing period 1 and 2:  $t(29) = -0,674$ ,  $p = 0,506 > 0,05$ .

Comparing medication A and B:  $t(29) = -1,497$ ,  $p = 0,145 > 0,05$ .

### QoL scores

Table 9 shows the means of all the individual weekly QoL scores and their standard deviations.

	Mean QoL score	Standard deviation
Period 1	87,89	15,42
Period 2	80,67	14,96
Medication A	90,29	12,78
Medication B	80,82	16,42

Table 9: Mean QoL scores and their standard deviation

Comparing period 1 and 2:  $t(29) = 1,286$ ,  $p = 0,209 > 0,05$ .

Comparing medication A and B:  $t(28,930) = 1,804$ ,  $p = 0,082 > 0,05$ . With this result, the Welch t-test results had to be used, instead of the pooled t-test results, because unequal variances were assumed.

### AE scores

Table 10 shows the means of all the individual weekly AE scores and their standard deviations.

	Mean AE score	Standard deviation
Period 1	2,87	3,03
Period 2	4,75	2,80
Medication A	2,79	2,58
Medication B	4,26	3,30

Table 10: Mean AE scores and their standard deviation

Comparing period 1 and 2:  $t(29) = -1,734$ ,  $p = 0,094 > 0,05$ .

Comparing medication A and B:  $t(29) = -1,368$ ,  $p = 0,182 > 0,05$ .

See appendix 2 for all SPSS tables.

## **Conclusion**

Pain scores, QoL scores and AE scores did not differ significantly when comparing medication A and B and neither when comparing period 1 and 2. This can have several reasons besides the two medications being alike. The most important reason to have insignificant results is the small sample size in this interim analysis. Continuation of this study is necessary to obtain more data to increase statistical power.

When a total of 10 dogs that have actually finished the study is reached, another interim evaluation should be made to see if there is a difference between the two medications.

## Discussion

Finding willing participants for this study was very difficult. Most dogs with a tumor that visited the University clinic were receiving treatment with chemotherapy, radiation or surgery. When eventually a dog was found that would not be treated otherwise, most owners thought the study would be too stressful for their dog. It also became clear that many owners were not sure about whether or not their dog was in pain. In some cases veterinary specialists thought a dog should get pain medication, but the owner stated that their dog was not suffering from pain. Sometimes animals clearly show their signs of pain, but most of the time it is not clear whether or not they are experiencing pain. Because of this indistinctness about their pet's pain, some owners were reluctant to participate in the study with their dogs.

This finding was interpreted as a sign that many dog-owners do not know how to see subtle pain in their pets. As a result, a brochure was created in Dutch and English to inform owners about what types of tumors cause pain and how to recognize it in dogs (see appendix 1 for the Dutch brochure). These brochures can be used to create awareness when talking about pain due to cancer and therefor people may be more willing to participate in the study in the future.

According to the inclusion criteria, only dogs that were expected to live for at least 6 months should be entered in the study. However, because of the difficulty to estimate a life expectancy, dogs who had a shorter life expectancy were entered too. A minimum life expectancy of 2 months was kept in practice. Two of six dogs were euthanized before their participation in the study ended (dog number 2 on day 45 and dog number 3 on day 22). The results of these dogs still could be used in the study. Dog number 7's tumor was never really diagnosed with biopsy or FNAB. A FNAB was performed at the referring veterinarian, but no conclusive diagnosis was formed.

Although the owners of dog number 5 first decided not to treat their dog and therefor entered the study, they later changed their mind and the dog was treated with a mandibulectomy on day 30. This dog received other medication during 5 days: tramadol, synulox and rimadyl. Therefor the results of these days plus 3 days wash-out (week 5 and 6) were left out during statistical calculations.

Pain, QoL and AE scores did not differ significantly among the groups. This can have several causes: it can be a sign that medication A and B give the same results and do not differ from each other.

Another reason why the differences are insignificant is the small sample size. With the paired samples t-test the sample size was  $n=4$  and with the independent sample t-test the sample size was  $n=31$ . By using too few cases when trying to prove a difference between two groups, the chance of a difference caused by coincidence is too high. The power analysis of this study showed that 20 dogs were needed to produce a significant level of difference.

A third problem with the tests is a low uniformity in the groups. Dogs were used from different breeds and with different diseases, therefor results varied a lot between dogs and inside the groups. This statistical model determines if the variation between the groups is a result of treatment or caused by coincidence. To achieve this, the variation between groups is compared with the 'natural' variation in the group. When this normal variation in the population is too large (thus a low uniformity), a more pronounced difference between the groups is necessary to prove a significant difference.

When using the independent samples t-test, it was hoped that by using a larger group ( $n=31$ ) a significant difference would determine a trend in a difference between the two medications. The difference between medication A and B when looking at QoL scores using the independent samples T-test came closest to being a significant difference ( $p = 0,082$ ). When  $p < 0,05$  a significant

difference is present between the groups. This value of 0,082 comes close to the significance value, but is still too big. This means that the difference between the means of the groups (in this case QoL scores during medication A and B) can still be caused by coincidence.

Blood samples were not considered in this report, because none of the blood values were outside their reference range. For further research blood samples could be looked into more critically, to maybe discover a trend in decreasing or increasing values during one of the medications.

All owners fill in the forms in their own way, this results in many variations between the scores of different dogs. For future research, it is advised to fill in questionnaires in concert with the dog owners or revise all questionnaires with the owners afterwards.

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## Appendix 1 – Brochure (Dutch version)

### HEEFT EEN HOND MET KANKER ALTIJD PIJN?

Niet alle tumoren zijn pijnlijk en de gevoeligheid pijn kan van dier tot dier sterk verschillen. Zelfs bij hetzelfde type tumor kan de pijnlijkheid per hond flink variëren. Onderzoek bij mensen heeft uitgewezen dat 20% tot 50% van de humane patiënten pijn heeft ten tijde van het stellen van de diagnose 'kanker'. Bij (ver)gevoerde kanker zijn deze percentages hoger. We kunnen ervan uitgaan dat dit bij honden vergelijkbaar is. Een groot verschil is dat honden niet weten dat ze kanker hebben en daarom meestal nog net zo vrolijk zijn, ondanks dat ze pijn kunnen hebben van hun ziekte. In dit geval kunnen wij met een passende pijnbestrijding ervoor zorgen dat ze zich toch beter voelen.

### WAARDOOR ONTSTAAT DE PIJN?

Pijn door kanker wordt veroorzaakt door verschillende processen in het lichaam. Ten eerste kan er sprake zijn van pijn doordat de tumor druk uitoefent op of ingroeit in omringende weefsels. Dit geldt ook voor uitzaaiingen op bepaalde plaatsen, zoals in bot. Daarnaast kan chronische verzwakking door langdurige ziekte bestaande pijn verergeren doordat de hond minder goed het aangedane lichaamsdeel kan ontlasten. Ook als een tumor ontstoken is zal dit pijn veroorzaken.



Een hond kan niet vragen om een pijnstiller. Een eigenaar, die de hond goed kent, kan wel zien dat er iets mis is met zijn of haar huisdier.



Universiteit Utrecht

## Heeft uw hond pijn? Over pijn bij kanker en hoe u deze pijn kunt herkennen

Een folder van het UU Kankercentrum voor Dieren



### Pijn checklist

- Sloomheid
- Kreupelheid
- Vermindering van specifieke activiteiten (springen, spelen, wandelen)
- Verminderde eetlust
- Veranderd gedrag (agressie, metheld, verlegenheid, aanhankelijkheid, verhoogde afhankelijkheid)
- Verdrietige gezichtsuitdrukking, laaghangende kop
- Minder vaak wassen, slechte vacht
- Pijnreactie op aanraken van de tumor
- Versnelde ademhaling
- Likken of krabben aan één plek
- Urineren en ontlasten op ongeschikte plaatsen
- Maken van vreemde geluiden (anken, grommen, kreunen)

## Universiteitskliniek voor Gezelschapsdieren UU Kankercentrum voor Dieren

Heeft u vragen naar aanleiding van deze folder, neemt u dan contact met ons op.

### OPENINGSTIJDEN

Maandag t/m vrijdag 08.00 – 16.45

Voor spoedgevallen zijn we 24 uur per dag, 7 dagen per week open. Neemt u hiervoor contact op met uw eigen dierenarts.

### UNIVERSITEITSKLINIEK VOOR GEZELSCHAPSDIEREN

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Voor de meest actuele informatie en route: [www.diergeneeskunde.nl](http://www.diergeneeskunde.nl)

### WELKE TYPEN TUMOREN ZIJN PIJNLIJK?

Tumoren die het vaakst pijnlijkheid geven bevinden zich op de volgende locaties:

- **Bot;** tumoren en uitzaaiingen in botten zijn erg pijnlijk.
- **Mondholte;** vooral tumoren achter in de bek en keel zijn pijnlijk, tumoren van het tandvlees minder.
- **Urinewegen;** aantasting van het kapoel van de nieren veroorzaakt pijn. Ook blaastumoren zijn vaak pijnlijk. Prostaat tumoren veroorzaken vaak pijn, vooral als er uitzaaiingen aanwezig zijn in bot.
- **Ogen;** tumoren in het oog zijn pijnlijk doordat ze de druk verhogen in de oogbol (ze veroorzaken glaucoom (groene staar)).
- **Neus;** tumoren in de neusholte zijn pijnlijk doordat ze weefsel en bot in de neus aantasten.
- **Hersenen en ruggenmerg;** massa's die drukken op de hersenen of het ruggenmerg kunnen veel pijn doen. Bij mensen met hersentumoren is bekend dat 60 – 90% last heeft van hoofdpijn.
- **Maag-darmkanaal;** vooral tumoren in de slokdarm, maag, dikke darm en endeldarm zijn pijnlijk.
- **Huid;** tumoren in de huid zijn vooral pijnlijk als er een wond of ontsteking ontstaat.

### HOE HERKENT U PIJN BIJ UW HOND?

Soms geven dieren duidelijk aan dat ze pijn hebben, maar helaas komt het vaak voor dat milde, of soms zelfs matige pijn niet duidelijk naar voren komt. In het herkennen van pijn heeft u als eigenaar van uw huisdier een zeer belangrijke rol.

De gemakkelijkste manier om te zien of een hond pijn heeft aan de tumor, is door de tumor vast te pakken en er voorzichtig op te duwen. Als uw hond hier pijnlijk op reageert (door bijvoorbeeld te piepen, aanraking probeert te vermijden of te happen) zal de tumor waarschijnlijk ook pijn doen als u er niet op drukt. In dit geval heeft uw hond dus pijnstilling nodig.

Een andere manier om pijn vast te stellen is door te kijken naar het gedrag van uw hond. Langdurige (chronische) pijn uit zich meestal door (soms subtile) veranderingen in het gedrag. De hoeveelheid pijn die



een hond moet voelen voor hij of zij zich er anders door gaat gedragen, verschilt aanzienlijk per hond en per ras.

Voorbeelden van veranderd gedrag door pijn zijn:

- Verminderde activiteit of specifieke activiteiten, zoals springen of spelen, niet meer uitvoeren.
- Verminderde eetlust
- Likken, bijten of krabben aan een bepaalde plek kan wijzen op pijn

Op de achterkant van deze folder vindt u een uitgebreide checklist waar de meest voorkomende gedragsveranderingen door pijn genoemd worden.

Zodra u weet welke gedragsveranderingen uw hond laat zien als hij of zij pijn heeft, kunt u deze kennis gebruiken om nauwlettend in de gaten te houden of en hoeveel pijn uw hond heeft. Een goed idee is om een pijnadagboek bij te houden. Zo weet u precies of de pijn erger of juist minder wordt, en of de pijnstillers die u geeft voldoende werken.

### HOE KUNT U UW HOND HELPEN?

Niet alleen voor de kwaliteit van leven van uw hond is het belangrijk om voor goede pijnstilling te zorgen.

Pijn kan een stressreactie veroorzaken in het lichaam waardoor de (wond)genezing langzamer verloopt. Daarnaast heeft stress een nadelige invloed op het hart- en vaatstelsel, longen en maag-darmkanaal.

Er zijn verschillende soorten pijnstillers die uw dierenarts uw hond kan voorschrijven om de pijn te verlichten. Het is belangrijk om samen met uw dierenarts na te gaan welke pijnstillers uw hond nodig heeft en of de pijnstillers effectief zijn bij uw hond. Niet alle pijnstillers zijn namelijk geschikt voor een bepaalde hond. Dit kan te maken hebben met bijwerkingen of andere ziektes die ook spelen (nieren, lever) of combinaties met andere medicatie. Daarnaast zijn pijnstillers die bij de mens gebruikt worden meestal niet geschikt voor honden en kunnen ernstige bijwerkingen veroorzaken. U kunt de effectiviteit meten door regelmatig (dus ook voor dat u bent gestart met de pijnstilling) de checklist na te gaan en de pijn van uw hond te 'scoren'. Het is ook van belang om uw dierenarts te informeren of uw hond last heeft van bijwerkingen.

Naast het geven van pijnstilling zijn er nog andere dingen die u kunt doen om het leven van uw hond met kanker zo aangenaam mogelijk te maken. Kleine veranderingen in de leefomgeving van uw hond kunnen de pijn flink verminderen. Voorbeelden hiervan zijn het maken van een helling in plaats van trages door middel van een houten plank, of tapijt leggen op gladde vloeren. De meeste dieren hebben ook veel baat bij een duidelijke regelmaat in hun dag. U kunt daar rekening mee houden door op vaste tijdstippen uw hond te voeren, medicijnen te geven en uit te laten.

### EUTHANASIE

Er komt ook een moment dat het niet meer verder kan. Op zo'n moment moet u zich realiseren dat uw hond zich niet meer beter gaat voelen, maar dat de kwaliteit van leven slechts zal afnemen. Het laten inslapen van uw huisdier is uiteindelijk ook een manier om hem of haar te helpen.

### BROMMEN

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## Appendix 2 – SPSS tables

### Paired samples t-test

**Paired Samples Correlations**

		N	Correlation	Sig.
Pair 1	Mean pain score in period 1 & Mean pain score in period 2	4	,889	,111
Pair 2	Mean pain score during medication A & Mean pain score during medication B	4	,817	,183
Pair 3	Mean QOL score in period 1 & Mean QOL score in period 2	4	,156	,844
Pair 4	Mean QOL score during medication A & Mean QOL score during medication B	4	,127	,873
Pair 5	Mean AE score in period 1 & Mean AE score in period 2	4	-,112	,888
Pair 6	Mean AE score during medication A & Mean AE score during medication B	4	-,487	,513

**Paired Samples Test**

		Paired Differences				t	df	Sig. (2-tailed)	
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower				Upper
Pair 1	Mean pain score in period 1 - Mean pain score in period 2	-1,625000	1,493039	,746520	-4,000759	,750759	-2,177	3	,118
Pair 2	Mean pain score during medication A - Mean pain score during medication B	-1,125000	2,015564	1,007782	-4,332213	2,082213	-1,116	3	,346
Pair 3	Mean QOL score in period 1 - Mean QOL score in period 2	6,250000	18,985740	9,492870	-23,960549	36,460549	,658	3	,557
Pair 4	Mean QOL score during medication A - Mean QOL score during medication B	4,500000	19,635215	9,817607	-26,744009	35,744009	,458	3	,678

Pair 5	Mean AE score in period 1 - Mean AE score in period 2	-2,437500	2,771695	1,385847	-6,847885	1,972885	-1,759	3	,177
Pair 6	Mean AE score during medication A - Mean AE score during medication B	-1,687500	3,436174	1,718087	-7,155220	3,780220	-,982	3	,398

*Independent samples t-test (period 1 and 2 compared)*

**Group Statistics**

	Period	N	Mean	Std. Deviation	Std. Error Mean
painscore	1,00	19	2,8421	3,70080	,84902
	2,00	12	3,7500	3,57071	1,03078
QoLscore	1,00	19	87,8947	15,41606	3,53669
	2,00	12	80,6667	14,95650	4,31757
AEscore	1,00	19	2,8684	3,02693	,69442
	2,00	12	4,7500	2,80016	,80834

**Independent Samples Test**

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
painscore	Equal variances assumed	,003	,954	-,674	29	,506	-,90789	1,34662	-3,66204	1,84625
	Equal variances not assumed			-,680	24,186	,503	-,90789	1,33542	-3,66294	1,84715
QoLscore	Equal variances assumed	,149	,702	1,286	29	,209	7,22807	5,62075	-4,26766	18,72380
	Equal variances not assumed			1,295	24,087	,208	7,22807	5,58118	-4,28872	18,74486

AEscore	Equal variances assumed	,028	,868	-1,734	29	,094	-1,88158	1,08517	-4,10101	,33785
	Equal variances not assumed			-1,766	24,930	,090	-1,88158	1,06566	-4,07666	,31351

Independent samples t-test (medication A and B compared)

**Group Statistics**

	Medication_A_or_B	N	Mean	Std. Deviation	Std. Error Mean
painscore	Medication A	14	2,1429	2,82454	,75489
	Medication B	17	4,0588	4,03842	,97946
QoLscore	Medication A	14	90,2857	12,77876	3,41527
	Medication B	17	80,8235	16,41735	3,98179
AEscore	Medication A	14	2,7857	2,57737	,68883
	Medication B	17	4,2647	3,29828	,79995

**Independent Samples Test**

	Levene's Test for Equality of Variances	t-test for Equality of Means								
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
painscore	Equal variances assumed	3,174	,085	-1,497	29	,145	-1,91597	1,27978	-4,53341	,70147
	Equal variances not assumed			-1,549	28,345	,132	-1,91597	1,23661	-4,44766	,61573
QoLscore	Equal variances assumed	4,273	,048	1,760	29	,089	9,46218	5,37624	-1,53346	20,45783
	Equal variances not assumed			1,804	28,930	,082	9,46218	5,24583	-1,26786	20,19223

AEscore	Equal variances assumed	1,222	,278	- 1,368	29	,182	-1,47899	1,08150	-3,69091	,73293
	Equal variances not assumed			- 1,401	28,941	,172	-1,47899	1,05566	-3,63824	,68026