PAPER

Clinical response of masitinib mesylate in the treatment of canine macroscopic mast cell tumours

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Objectives: To retrospectively evaluate the clinical response and toxicity associated with masitinib mesylate (Masivet®) treatment of macroscopic mast cell tumours in the dog.

Methods: Retrospective review of medical records of 39 dogs that had undergone treatment with masitinib for macroscopic mast cell tumours. Patient signalment, tumour location, tumour grade, tumour stage, previous treatments, concurrent medications, dose of masitinib, side effects, response, time to tumour progression, survival time and cause of death were documented. Response was assessed according to RECIST criteria.

Results: Clinical response was observed in 32 (82·1%) dogs receiving masitinib, with 15 dogs (38·5%) exhibiting a complete response and 17 dogs (43·6%) achieving a partial response. The median time to progression was 79 days (range: 14 to 667 days). Adverse effects were seen in 25 dogs (64·1%) with serum alanine aminotransferase elevation (n=9; 23·1%) and vomiting (n=6; 15·4%) being most common. Median survival time following initiation of masitinib was 159 days (range: 14 to 1339).

Clinical Significance: Masitinib appears to be a well-tolerated and effective drug against macroscopic mast cell tumours.

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INTRODUCTION

Mast cell tumours are among the most common tumours affecting domestic dogs, accounting for 17 to 21% of all canine cutaneous tumours (Bostock 1986). The biological behaviour of mast cell tumours can differ widely within a population of affected animals with some having a benign clinical course, while others are rapidly fatal as the result of aggressive local growth or distant metastases (Simoes *et al.* 1994). Approximately 11 to 14% of dogs are affected with multiple cutaneous mast cell tumours that may occur synchronously or successively (Mullins *et al.* 2006, Murphy *et al.* 2006).

It is well documented that a majority of patients with mast cell tumours can be treated effectively with surgery and, in some cases, adjunctive radiation therapy. However, in a proportion of dogs with Patnaik intermediate grade mast cell tumours and the majority of dogs with Patnaik and Kiupel high-grade mast cell tumours, chemotherapy is also indicated (Patnaik *et al.* 1984, Kiupel *et al.* 2011, Blackwood *et al.* 2012). In such cases, chemotherapy can be used before surgical resection, as adjuvant postoperative treatment for control of metastatic disease, or for primary control of the local tumour when surgery and radiation are not feasible or recommended. The chemotherapy agents that have been shown to be effective in the treatment of mast cell tumours include chlorambucil/prednisolone (overall response rate: 38%) (Taylor *et al.* 2009), lomustine (overall response rate: 42%) (Rassnick *et al.* 1999), vinblastine/prednisolone (overall response rate: 47%) (Thamm *et al.* 2006), vinblastine/lomustine (overall response rate: 57%) (Cooper *et al.* 2009) and vinblastine/lomustine/prednisolone (overall response rate: 65%) (Rassnick *et al.*

2010). Despite this reported efficacy, the response of mast cell tumours to chemotherapy is transient, with the median time to progression only 77 days for lomustine alone (Rassnick *et al.* 1999), and 141 days for the vinblastine/lomustine/prednisolone regime (Rassnick *et al.* 2010). Consequently, the development of new anti-tumoural agents beyond conventional chemotherapy has been necessary for more effective management of non-resectable, recurrent or metastatic mast cell tumours.

Substantial progress in molecular biology has resulted in the development of a new class of drugs for treatment of mast cell tumours in dogs: tyrosine kinase inhibitors. Tyrosine kinase inhibitors are specific small-molecule inhibitors that, through competitive inhibition of ATP binding, target and block the activity of a group of specific cell-surface receptors, the receptor tyrosine kinases (London *et al.* 2009). While normal receptor tyrosine kinase activity is critical for cell growth, differentiation and proliferation, dysfunction of several receptor tyrosine kinases has been demonstrated in certain cancers. One of the receptor tyrosine kinases expressed in normal mast cells is the mast/stem cell growth factor receptor, KIT, encoded by the c-KIT proto-oncogene, and mutations in c-KIT have been implicated in the pathogenesis of canine mast cell tumours (Webster *et al.* 2006). C-KIT mutations have been identified in approximately 15% of canine cutaneous mast cell tumours, and a higher prevalence (30 to 50%) in higher grade mast cell tumours (Downing *et al.* 2002). These mutations can potentially result in uncontrolled signalling and are associated with higher mast cell tumour grade, increased incidence of recurrent disease and higher chance of mast cell tumour-related death (Webster *et al.* 2006).

The first evaluation of tyrosine kinase inhibitors in veterinary mast cell tumour patients was carried out using the tyrosine kinase inhibitor toceranib (SU11654; Palladia®, Pfizer, New York, USA). In this study, the overall response rate was 42·8% with a median time to progression of 18·1 weeks. It was also determined that dogs with c-KIT mutations had a higher rate of response to toceranib (82 *vs* 55%) (London *et al.* 2009). In November 2009, a tyrosine kinase inhibitor which was a potent and selective inhibitor of KIT was launched: masitinib (Masivet®/Kinavet®, AB Science). Masitinib also potentially targets platelet-derived growth factor receptor α and β, lyn and fibroblast growth factor receptor 3 and the focal adhesion kinase pathway (Lyles *et al.* 2012). The first study investigating the efficacy and safety of masitinib in dogs with non-metastatic, recurrent or nonresectable mast cell tumours revealed that it significantly improved time to progression, with the time to progression of dogs receiving masitinib 118 days in comparison to 75 days on placebo (Hahn *et al.* 2008). A second study carried out on the same group of dogs found that masitinib significantly increased survival rates at 12 and 24 months in dogs with non-resectable mast cell tumours compared with placebo, with 59 of 95 (62·1%) and 9 of 25 (36·0%) dogs alive at 12 months and 33 of 83 (39·8%) and 3 of 20 (15·0%) dogs alive at 24 months, respectively. In this study, control of disease at 6 months was predictive of long-term survival (Hahn *et al.* 2010). More recently, an overall response rate of 50% (57% frontline; 25% rescue) and median survival time of the responders was 630 days were reported in a study of masitinib as both a frontline agent and rescue agent for the treatment of non-resectable mast cell tumours (Smrkovski *et al.* 2013).

The purpose of the current study was to further evaluate the clinical response, time to progression, survival time and the toxicity associated with the use of masitinib for the treatment of macroscopic, non-resectable or metastatic mast cell tumours in dogs. The relationships between patient signalment, mast cell tumour location, tumour size, mast cell tumour grade and histopathological characteristics, previous treatments, masitinib dose and the effects of concurrent medications (including steroids) on tumour response, time to progression and survival were also evaluated.

MATERIALS AND METHODS

The clinical records of 39 client-owned dogs that received masitinib for the management of cytologically or histopathologically confirmed macroscopic mast cell tumours were reviewed retrospectively. The patients were treated at three private veterinary referral institutions between May 2009 and April 2013.

A questionnaire for each case was completed by the participating centres. Information regarding patient age, gender, breed and mast cell tumour location, size, grade and histopathological characteristics (if applicable) was recorded. Immunohistochemical results were also collected when available. Any previous treatments were noted. Clinical staging results were classified according to the World Health Organisation (WHO) clinical staging guidelines for mast cell tumours (Owen 1980). The dose of masitinib administered to each patient was documented (taking into account the recommended dose of 12·5 mg/kg) as well as any concurrent medications.

Baseline measurements and response data were recorded using the 2009 Response Evaluation Criteria for Solid Tumours: Revised RECIST Guidelines (v1.1) (Nguyen *et al.* 2013). Adverse events were assessed and reported using the Veterinary Co-operative Oncology Group (VCOG) – Common Terminology Criteria for Adverse Events (v1.1) (VCOG 2011). Masitinib was administered to all patients until disease progression was noted, unless a severe adverse event precluded further use. Patients were examined at two-week intervals for the first month of treatment and then monthly. Time to maximal tumour response was defined as the number of days between the initiation of masitinib and the recorded date of maximum response. Time to tumour progression was defined as the number of days between masitinib initiation and first clinically documented signs of disease progression. Survival time was defined as the number of days between the date of masitinib initiation and the date of death, both death resulting from the mast cell tumour as well as non-mast cell tumour-related causes. Progression-free survival and survival data were censored for patients that were disease-free and still alive at the end of the study.

Statistics

Data were entered into an Excel spreadsheet (Microsoft Corporation, 2007, USA) and were analysed using IBM SPSS Statistics 20 (New York, USA). Survival times and time to progression were examined using Kaplan–Meier methodology.

RESULTS

Population data and tumour characteristics

Of the 39 dogs included in the study 20 were male and 19 were female; their median age was 10 years (mean: 9·25; range: 3 to 17). There was an assortment of breeds with the most common being Labrador retriever (n=8; 20·5%), boxer (n=5; 12·8%), Staffordshire bull terrier (n=4; 10·3%) and shar pei (n=4; 10·3%) in addition to a small numbers of different breeds. None of the dogs in the study were lost to follow-up and all were included in the statistical evaluation.

The location of the mast cell tumour was a limb in 17 dogs (43·6%), the head in 5 (12·8%), the flank in 2 (5·1%), perianal region in 2 (5·1%), prepuce/scrotum in 2 (5·1%) and the neck, thoracic wall and tail in 1 dog (2·9%) each. In 8 dogs the mast cell tumour was located in a metastatic regional lymph node (20·5%). The median tumour diameter was 5 cm (range: 1 to 15 cm).

The diagnosis of mast cell tumour was reached via cytology in 7 dogs (17·9%) and histopathology in 32 dogs (82·1%). Of these 32 dogs, 29 had their mast cell tumour graded according to the Patnaik system (Patnaik *et al.* 1984), with 19 dogs classified as intermediate grade and 10 dogs as high grade. Three dogs had subcutaneous mast cell tumours that underwent Kiupel grading only (Kiupel *et al.* 2011), while four dogs had both Kiupel and Patnaik grading performed on their tumour. The Ki-67 (Scase *et al.* 2006), Kiupel grading results and mitotic index (Romansik *et al.* 2007) are shown in Table 1. None of the tumours had undergone immunohistochemistry staining for KIT or PCR analysis for c-KIT mutations.

Staging results

Thirty-five dogs in the study (89·7%) underwent some form of clinical staging including regional lymph node aspiration, chest radiographs, abdominal ultrasound, and/or bone marrow aspiration prior to initiation of masitinib (Table 2). Overall 19 (54·3%) dogs had evidence of metastatic disease. Five (12·8%) dogs had at least one other cutaneous mast cell tumour.

Treatment

Of the dogs included in this study, 32 patients (82·1%) had undergone previous surgery, radiation and/or chemotherapy prior to receiving masitinib (Table 3).

Table 1. Histopathological tumour grading and proliferation markers

		Patnaik grading (Patnaik *et al.* 1984)	Kiupel grading (Kiupel *et al.* 2011)	Mitotic Index[a]	Ki-67[b]
Cytopathology	7 (17·9%)				
Histopathology	32 (82·1%)	Grade 1: 0			
		Grade 2: 19 (48·8%)	Low: 2	≤5: 11	<1·8%: 1
			High: N/a	>5: 2	>1·8%: 7
				N/a: 6	N/a: 11
		Grade 3: 10 (25·6%)	Low: N/a	≤5: 1	
			High: 2	>5: 8	
				N/a: 1	
		N/a: 10 (25·6%)	Low: 2	≤5: 2	
			High: 1	>5: 1	
				N/a: 7	

[a]Mitotic index was defined as the number of mitotic figures/10 high-power fields. MI cut-off based on data from Romansik *et al.* (2007)
[b]Ki-67 score for intermediate grade tumours: 1·8% cut-off based on study by Scase *et al.* (2006)

Table 2. Results of staging prior to treatment with masitinib

Variable	n/Total			% Patients	Description
Thoracic radiographs	9/39	Evidence of metastatic disease[a]	1	11·1	Mediastinal LN enlargement
		No abnormalities detected	8	88·9	
Abdominal ultrasound	31/39	Evidence of metastatic disease[b]	11	35·5	Medial iliac LN (n=5); subaortic LN (n=4); hepatic (n=1) splenic (n=1)
		No abnormalities detected	20	64·5	
Regional lymph node cytology	30/39	Evidence of metastatic disease[c]	17	56·7	
		No abnormalities detected	13	43·3	
Bone marrow cytology	10/39	Evidence of metastatic disease[d]	1	10	
		No abnormalities detected	9	90	
Staging[e]	35/39	Stage 1	7	17·9	
		Stage 2	7	17·9	
		Stage 3	18	46·1	
		Stage 4	3	7·7	
		Unknown	4	10·4	

[a]Metastatic disease defined by marked enlargement of thoracic lymph node
[b]Metastatic disease confirmed by fine needle aspiration of lesion and cytology
[c]Metastatic disease confirmed by fine needle aspiration of lymph node and cytology
[d]Metastatic disease confirmed by bone marrow aspiration and cytology
[e]Denoted patients undergoing some form of staging prior to treatment – classified according to WHO clinical staging guidelines for MCT (Owen 1980)

Table 3. Table describing treatment of mast cell tumour prior to receiving masitinib

Variable		N	% Dogs		N	% Dogs
Treatment prior to masitinib	Surgery	8	20·5			
	Surgery and radiation	1	2·6			
	Surgery and chemotherapy	14	35·9			
	Surgery, radiation and chemotherapy	4	10·3			
	Chemotherapy alone (including TKIs)	3	7·7			
	Prednisolone	2	5·1			
	No previous treatment	7	17·9			
Surgery	Surgery	27	69·2	Surgical Excision×1	18	46·1 (66·7)[a]
				Initial Surgery+Revision/s	9	23·1 (33·3)
	No surgery undertaken	12	30·8			
Radiation	Radiation	4	10·3	4×9 Gy	1	2·6 (25)[b]
				12×4Gy	1	2·6 (25)
				16×3Gy	2	5·1 (50)
	Brachytherapy	1	2·6			
	No radiation undertaken	34	87			
Chemotherapy	Chemotherapy	21	53·8	Vinblastine (2 mg/m^2)×4 to 8 cycles	10	25·6 (47·6)[c]
				Lomustine: 60 mg/m^2×4 cycles	1	2·6 (4·8)
				Vinblastine/Lomustine: Alternating: Vinblastine: 2 mg/m^2×3 cycles; Lomustine 60 mg/m^2×3 cycles	8	20·5 (38·1)
				Toceranib: 2·75 to 3·25 mg/m^2 eod	3	7·7 (14·3)
	No chemotherapy undertaken	18	46·2			

[a]% in brackets is percentage of patients undergoing surgery receiving this number of surgeries
[b]% in brackets represents % of patients undergoing radiation receiving this dose
[c]% in brackets represents % of patients undergoing chemotherapy receiving this chemotherapy drug/protocol

There were several reasons for treatment with masitinib (Table 4). The median dose of masitinib was 11·1 mg/kg (mean: 10·8 mg/kg; range: 7·5 to 13·1 mg/kg). The majority of dogs received concurrent medications, with 26 (66·7%) receiving prednisolone as part of their treatment regime. Thirteen dogs (33·3%) received antihistamines (chlorpheniramine) and 23 dogs (59%) received gastrointestinal protectants (omeprazole, cimetidine, ranitidine and/or sucralfate).

Response data

The overall response rate to masitinib in this study was 82·1% (n=32). Fifteen dogs (38·5%) exhibited a complete response and 17 (43·6%) achieved a partial response. The disease appeared stable in an additional five dogs (12·8%) but 2 (5·1%) had progressive disease. The median time to maximum tumour response was 28 days (range: 7 to 77 days). The mean reduction in tumour diameter in the partial responders was 39% of the original diameter.

Time to tumour progression

Time to progression data was available on 25 patients but was censored for the remaining 14 animals. The median follow-up time for these 14 dogs that did not show progression of the tumour in the study period was 405 days. The overall median time to progression was 79 days (mean: 127 days; range: 14 to 667 days). Complete responders exhibited a median time to progression of 147 days (mean: 240 days; range: 68 to 667) while the time to progression for the partial responders was 49 days (mean: 61 days; range: 14 to 126) and those dogs with stable disease had a median time to progression of 36 days (mean: 55·2; range: 26 to 113; Fig 1). The median time to progression for the responders was 88 days (mean: 145; range: 14 to 667 days). Four dogs (10·3%) achieved complete response for greater than 1 year following initiation of treatment.

Table 4. Rational for use of masitinib

Reason for choosing masitinib	N	% Dogs
Size or location of MCT prevents surgical management	20	51·3
Presence of metastatic disease prevents surgical excision	10	25·6
Multiple MCT present	4	10·3
MCT is recurrence and further surgery not possible	3	7·7
Systemic condition unrelated to MCT prevents anaesthetic for surgical resection	2	5·1

Discontinuation of treatment

In total 32 dogs discontinued treatment with masitinib: 22 because of progression of disease, 5 because of durable complete response (greater than 6 months), 3 because of side-effects and 2 dogs because of unrelated illness or death.

Survival time and clinical outcome

The overall median survival time of dogs following initiation of masitinib was 159 days (mean: 265; range: 14 to 1339 days). Complete response was associated with a median survival time of 263 days (mean: 397; range: 88 to 1339 days) while partial responders had a median survival time of 81 days (mean: 148; range:14 to 831); dogs with stable disease had a median survival time of 239 days (mean: 348; range:92 to 667) and patients with progressive disease had a median survival time of 58 days (mean: 58 days; range:45 to 71; Fig 2). The median survival time of the responders was 155 days (mean: 264 days; range: 14 to 1339).

At the end of the study a total of 22 dogs had died from their mast cell tumour (56%) with 19 dying within 6 months and 22 within 12 months of starting treatment. Four dogs died from causes unrelated to their mast cell tumour. Survival data were therefore available for 26 dogs that died during the study period,

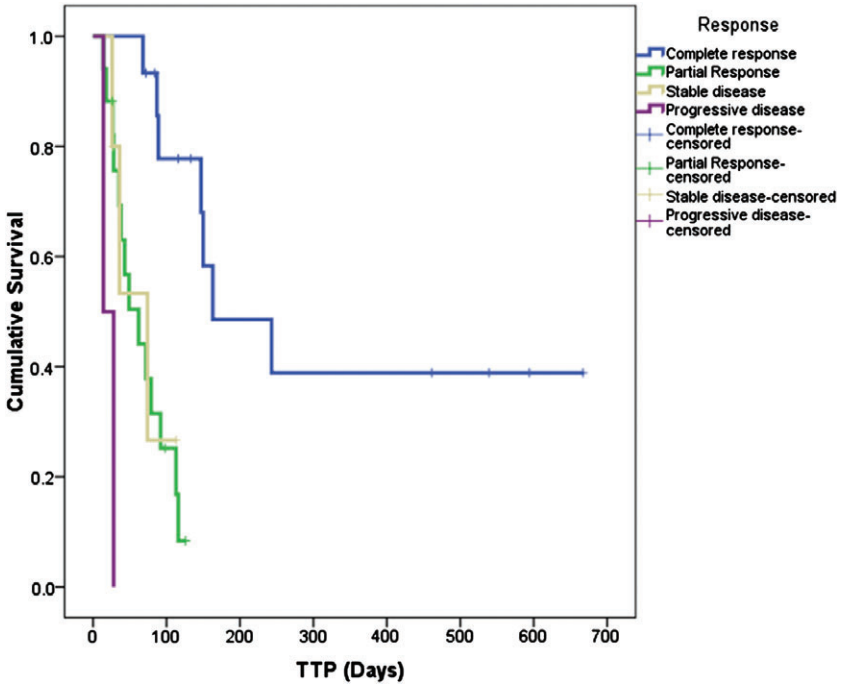

FIG 1. Kaplan–Meier curve showing time to progression from initiation of masitinib for dogs according to response (CR, PR, SD and PD) to masitinib

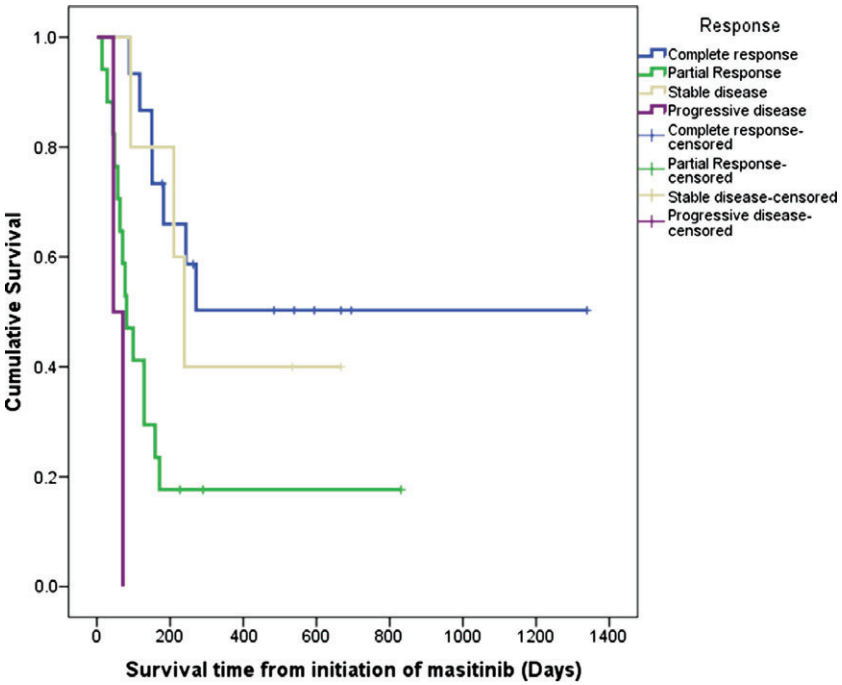

FIG 2. Kaplan–Meier curve showing survival time from initiation of masitinib for dogs according to response (CR, PR, SD and PD) to masitinib

with the remaining 13 dogs having their survival times censored because they remained alive at the end of the study. The median follow-up time for these 13 dogs, that was censored based on survival, was 534 days (range: 150 to 1339 days).

Adverse events

Twenty-five dogs (64·1%) exhibited side effects to masitinib. Clinical toxicities or laboratory abnormalities (haematological or biochemical) were observed in 15 (38·5%) and 21 (53·8%) dogs, respectively (Table 5). Vomiting was the most frequent adverse clinical effect (n=6; 15·4%). The most frequently observed laboratory abnormality was alanine aminotransferase (ALT) elevation (n=9; 23·1%). Severe side-effects (VCOG-CTCAE grade 3 to 4) were described in 10 dogs (25·6%). Eight dogs underwent dose adjustments and four dogs discontinued masitinib because of the side-effects.

Table 5. Treatment-related adverse clinical and pathological events

Adverse event	N	% Total dogs in study	VCOG-CTCAE Grade 3 or 4 (n; % total dogs affected by adverse events)	VCOG-CTCAE Grade 3 or 4 (% total)
Clinical adverse event				
Vomiting	6	15·4		
Diarrhoea	2	5·1		
Weight loss	2	5·1		
Anorexia	2	5·1		
Tumour Lysis	1	2·6	1 (100)	2·6
Pancreatitis	1	2·6	1 (100)	2·6
Cough	1	2·6		
Laboratory abnormalities				
Elevated ALT	9	23·1	4 (44·4)	10·25
Neutropaenia	5	12·8	1 (20)	2·6
Anaemia	4	10·3	1 (25)[a]	2·6
Elevated ALKP[b]	3	7·7	2 (66·7)	5·1
Elevated UPC	2	5·1		
Abnormal canine pancreas-specific lipase	1	2·6	1 (100)	2·6
Total number of dogs affected by adverse events	25	64·1		
Total number of dogs affected by Grade 3 or 4 adverse events			Number of Grade 3 to 4 adverse events 12	Total number of dogs affected 10 (25·6)

[a]Dog with VCOG-CTCAE Grade 3 or 4 anaemia had grade 3 haemolytic anaemia
[b]Elevated ALKP recorded in patients not receiving prednisolone only

DISCUSSION

The results of this study suggest that, overall, masitinib is an effective drug against mast cell tumours with a reported overall response rate of 82·1%. In another recent study the overall response rate was 50% (Smrkovski *et al.* 2013), considerably lower than that seen here. Investigation into this disparity showed that the previous report assessed response using the WHO criteria (Miller *et al.* 1981), rather than the RECIST criteria, making a direct comparison of response between the studies impossible. Consequently the response rates for this study were recalculated based on the WHO guidelines. The revised results revealed that nine dogs (23·1%) had a partial response to masitinib, in contrast to 17 dogs (43·6%) when using the RECIST criteria. Subsequently the recalculated overall response rate in the present study was 61·5%, closer to that reported in by Smrkovski *et al.* (2013).

Curiously the higher overall response rate in this study has occurred despite much pre-treatment of the patients. Smrkovski *et al.* (2013) reported a significant difference in the overall response rate between the naïve and the pre-treated groups (pre-treatment overall response rate=25%; naïve overall response rate: 57%). In contrast 82·1% of the patients in our study underwent another form of treatment prior to receiving masitinib but pretreatment appeared not to alter response rate (pretreatment overall response rate=84·4%; naïve overall response rate: 71·4%). One explanation for the high overall response rate despite pre-treatment is that these dogs could have a sub-group of mast cell tumours that remained sensitive to masitinib despite developing general resistance mechanisms to conventional chemotherapy. In a previous study, the c-KIT mutation was associated with longer time to progression in dogs receiving masitinib despite previously receiving conventional chemotherapy (Hahn *et al.* 2008). Unfortunately, the c-KIT status is unknown for the current group of patients.

Another hypothesis for the superior response to masitinib in this study may be the use of prednisolone in a large number of our patients. It is well documented that prednisolone is an effective treatment for mast cell tumours (McCaw *et al.* 1994, Stanclift & Gilson 2008, Bisping *et al.* 2009) and, as reported by De Vos & Brearley (2011), the highest complete response rates to masitinib (complete response: 77%) occurred in protocols incorporating prednisolone. A prospective study would be required to further investigate this potentially synergistic relationship.

In this study, the median time to progression for the responders, based on RECIST criteria, was 88 days (105·5 days based on WHO criteria). This was significantly shorter than the median time to progression for the responders of 453 days reported by Smrkovski *et al.* (2013) (Table 6). This is likely to be because the majority of patients in our study received masitinib as a final rescue agent. Likewise the overall median survival time of responders in our paper was only 155 days (204·5 days based on WHO criteria), considerably less than that (630 days) reported by Smrkovski *et al.* (2013) (Table 6). This is possibly secondary to the shorter time to progression as well as the high proportion of animals found to have metastatic mast cell tumours during staging (54·3%).

In veterinary medicine quality of life is a significant factor in making decisions regarding various therapies. In this study 64·1% of dogs experienced some form of toxicity and, while this was comparable to other studies examining masitinib (Hahn *et al.* 2008, Smrkovski *et al.* 2013), it was higher than that reported for conventional chemotherapy. For example only 9% of patients experienced side-effects of the vinblastine/prednisolone combination (Miller *et al.* 2014). Hepatic toxicity was the most frequent reported adverse event and in each case was an incidental finding. One dog discontinued treatment due to alanine aminotransferase elevation (ALT), and eight dogs were placed on S-adenosyl methionine (SAM-E) and silymarin, four of which

Table 6. Smrkovski study findings comparison

Published study	Number of dogs	CR	ORR (CR+PR)	TTP		MST		Toxicity (n; % dogs)
Smrkovski study (Smrkovski *et al.* 2013)	26	7 (27%)	13; 50%	ORR 453	NR 282	ORR 630	NR 137	19 (61·5%)
Present study	39	15 (38·5%)	32; 82·1%[a] 24; 61·5%[b]	ORR 105·5[b]	NR 32[b]	ORR 204·5	NR 92	25 (64·1%)

CR Complete response, ORR Overall response rate, NR Non-responders, TTP Time to progression, MST Median survival time
[a]RECIST criteria (Nguyen *et al.* 2013)
[b]WHO criteria (Miller *et al.* 1981)

also had masitinib dosage reduced. All animals normalised their alanine aminotransferase following these protocol modifications. In this study only two dogs (5·1%) were diagnosed with proteinuria in contrast to 23% reported by Smrkovski *et al.* (2013). This highlights the study limitations, because only 12 dogs (30·8%) underwent the recommended urine protein:creatinine ratio diagnostics during their treatment, and the number of dogs with proteinuria is likely to have been underestimated. No patients developed azotaemia during the study period.

The retrospective nature of this study and the inclusion of patients from three separate centres resulted in a lack of standardisation of staging, masitinib dose and concurrent medications. There was also a lack of consistency in the management of adverse side-effects and, in some cases, the management of toxicities was not in line with the data sheet. Finally, as in many veterinary studies, there is only a small number of patients, making it difficult to draw strong conclusions.

In conclusion, this article provides support for use of masitinib as an effective agent against mast cell tumours. There was no association between tumour grade, location, tumour size, pretreatment or concurrent treatment, with response. Larger prospective studies are required to examine the relationship between response, time to progression and survival. In addition, further investigation into the role of prednisolone as part of a masitinib treatment protocol and the effect of c-KIT mutations on response to masitinib would also be beneficial in the future.

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Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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