



### Student CAT competition! And the winner is...Nicole Taurisano!

Earlier this year, Banfield Pet Hospital and the Evidence-Based Veterinary Medicine Association (EBVMA) invited veterinary students to compete in a student writing competition. Students were asked to write and submit a Critically Appraised Topic (CAT)—a synthesis of published evidence that answers a clinical question. A panel of veterinarians reviewed the entries and selected the winner, Nicole Taurisano, on the basis of specific criteria.

As a winner, Nicole will receive a \$500 honorarium, and her CAT appears below.

**Congratulations Nicole!**

## CRITICALLY APPRAISED TOPIC:

# Does treatment with pimobendan increase survival time for cats with congestive heart failure due to naturally occurring cardiac disease?

BY NICOLE TAURISANO  
CONTRIBUTING AUTHOR

### CLINICAL QUESTIONS

For cats with congestive heart failure (CHF) due to naturally occurring cardiac disease, does treatment with pimobendan, in addition to traditional treatments with diuretics, anti-thrombotics and angiotensin-converting enzyme (ACE) inhibitors, increase survival time? Is the incidence of adverse effects severe enough to limit the administration of pimobendan in cats?

### SEARCH STRATEGY

A literature search was performed in December 2012 using the CABDirect and PubMed databases with the MeSH terms “(cat OR feline) AND (pimobendan).” The PubMed database yielded 11 search items, while CABDirect returned 20. Articles discussing other species such as humans, mice and dogs were eliminated. Only original research studies were considered, yielding one pharmacokinetic study<sup>1</sup> in clinically normal cats, one retrospective cohort study<sup>2</sup> and two retrospective case series<sup>3,4</sup> in which the effect of pimobendan on the median survival time (MST) of cats in CHF was evaluated.

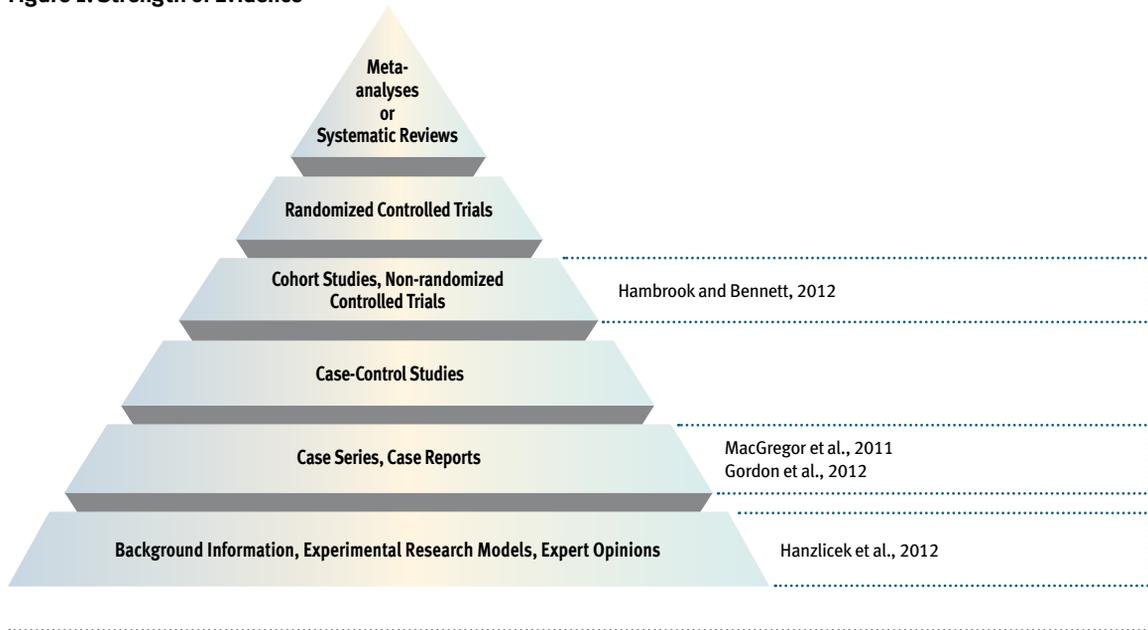
### CLINICAL BOTTOM LINE

- Pimobendan can be used to assist other traditional medications in relieving clinical signs associated with ventricular systolic dysfunction in cats and may increase survival time.
- The drug appears to be generally well-tolerated. In cats presenting with anterior motion of the mitral valve, pimobendan should be avoided because of the possibility of inducing severe hypotension and worsening mitral regurgitation.

### MAIN RESULTS

- The available evidence suggests that use of pimobendan (0.24 to 0.26 mg/kg, PO, q 12 h), in conjunction with ACE inhibitors, diuretics and anti-coagulants, may be effective at extending the survival time of cats with CHF.
- Pimobendan treatment was generally well-tolerated in healthy cats, as well as in cats with ventricular systolic dysfunction secondary to non-aurine responsive dilated cardiomyopathy, hypertrophic cardiomyopathy with

**Figure 1: Strength of Evidence**



focal hypokinesis, arrhythmogenic right ventricular cardiomyopathy and congenital heart disease.

- In cats with anterior motion of the mitral valve, pimobendan has the potential to cause severe hypotensive adverse effects.<sup>3</sup>

## COMMENTS

Pimobendan is a positive inodilator that increases cardiac contractility and decreases peripheral resistance through vasodilation.<sup>5</sup> Use of pimobendan in cats is currently off-label, and limited information is available regarding the safety and efficacy of using pimobendan to treat cats with CHF.

The pharmacokinetic study<sup>4</sup> in clinically normal cats established that pimobendan is generally well-tolerated and is absorbed after oral administration, producing blood concentrations equal to or greater than those reportedly achieved in dogs given an equivalent dose. Of the remaining studies available for review, all were retrospective. Two of the retrospective studies<sup>3,3</sup> assessing MST of cats treated with pimobendan did not focus on one particular form of cardiovascular disease but on several forms. Hambrook and Bennett (2012) reviewed cases specific to dilated cardiomyopathy not attributable to taurine deficiency, yielding results specifically helpful to practitioners dealing with that disease. Conversely, MacGregor et al. (2011) and Gordon et al. (2012) reviewed cases of dilated cardiomyopathy, hypertrophic

cardiomyopathy, and arrhythmogenic right ventricular cardiomyopathy, generating results that favor the use of pimobendan but are not specific to any one of the array of causes related to CHF in cats. Although the MST of cats after treatment with pimobendan was increased, factors such as lifestyle and medical history have the potential to rein in the full benefits of the drug on survival time.

Future randomized, controlled studies specific to systolic cardiovascular diseases in cats are necessary to build on the information gained from retrospective studies. Available research suggests that cats with ventricular systolic dysfunction in CHF can benefit from pimobendan, although the evidence is limited and of a low evidentiary value.

Table 1: Evidence Summary

Study	Study Type	Participants	Intervention	Results	Adverse Effects	Limitations
MacGregor et al., 2011	Case series	164 client-owned cats with CHF due to naturally occurring heart disease	Pimobendan (median dose, 0.24 mg/kg, PO, q 12 h) in conjunction with various combinations of ACE inhibitors, diuretics, anti-thrombotics	Median survival time (MST) was 151 days (range, 1 to 870 days)	5, or 3% of cats, had adverse effects coinciding with pimobendan initiation: unusual agitation (2), anorexia (1), vomiting (1) and constipation (1). Unusual agitation was pronounced enough to prompt treatment discontinuation in 1 cat.	No control group; testimonies from owners have the potential to lack credibility regarding appropriate medication administration; validity dependent on accurate reports from referring veterinarians; form of heart disease varied among patients.
Hambrook and Bennett, 2012	Retro-spective cohort study	32 client-owned cats with non-aurine responsive dilated cardiomyopathy	16 cats received pimobendan (median dose, 0.26 mg/kg, q 12 h) in conjunction with furosemide, taurine and either benazepril or enalapril; the remaining 16 received all but pimobendan, and 9 in this group also received digoxin	MST was significantly greater ( $P < 0.05$ ) for the pimobendan group (49 days; range, 1 to > 502 days) than for the control group (12 days; range, 1 to 244 days)	Not reported	Medications administered to the control group were not consistent, as some (n=9) were given digoxin in addition to the other drugs; phone communication with owners as a follow-up may not yield reliable information; a wide range of diets, environmental conditions and pre-existing medical conditions existed across the control and experimental groups, possibly affecting MST.
Gordon et al., 2012	Case series	27 client-owned cats with heart failure with ventricular systolic dysfunction secondary to one of several forms of heart disease	Pimobendan (mean $\pm$ SD dosage, 0.26 $\pm$ 0.08 mg/kg); other drugs used in combination were not specified	MST was 167 days (95% confidence interval, 33 to 339 days)	Hypotension in one subject with systolic anterior motion of the mitral valve	Validity dependent on accurate follow-up information from owners; since patients in the study had different types of heart disease, the MST calculated in the study would not necessarily be applicable to all types of heart disease.
Hanzlicek et al., 2012	Pharmacokinetic study (without surrogate endpoints)	18 healthy cats, purpose-bred to assess pharmacokinetics of pimobendan	Pimobendan (mean $\pm$ SD dose, 0.28 $\pm$ 0.04 mg/kg)	The terminal half-life of pimobendan was longer in cats than what is reported in dogs. The maximum plasma concentration was likewise slightly higher in cats versus dogs.	Two cats showed adverse gastrointestinal (GI) effects when given a single dose after food withholding. No reports of adverse GI effects were seen in non-fasted cats given multiple doses.	Only healthy cats were assessed in this study, leaving adverse effects in cats with heart disease undetermined.

## References

1. MacGregor JM, Rush JE, Laste NJ, et al. Use of pimobendan in 170 cats (2006-2010). *J Vet Cardiol.* 2011;13(4):251-260.
2. Hambrook LE, Bennet PF. Effect of pimobendan on the clinical outcome and survival of cats with non-aurine responsive dilated cardiomyopathy. *J Fel Med Surg.* 2012;14(4):233-239.
3. Gordon SG, Saunders AB, Roland RM, et al. Effect of oral administration of pimobendan in cats with heart failure. *JAVMA.* 2012;241(1): 89-94.
4. Hanzlicek AS, Gehring R, KuKanich B, et al. Pharmacokinetics of oral pimobendan in healthy cats. *J Vet Cardiol.* 2012;14(4):489-496.
5. Pouleur H, Hanet C, Schröder E, et al. Effects of pimobendan (UD-CG 115 BS) on left ventricular inotropic state in conscious dogs and in patients with heart failure. *J Cardiovasc Pharmacol.* 1989;14(Suppl. 2):S18-S22.

### ABOUT THE AUTHOR

Nicole Taurisano is in her first year at St. George's University in Grenada, currently enrolled in a dual degree program working toward an MSc in Anatomic Pathology in addition to her DVM. She is originally from Yonkers, N.Y., and spent two years working as a veterinary assistant at Banfield Pet Hospital® in East Hartford, Conn. Her interest in feline heart disease therapy began when her 2-year-old cat was diagnosed with hypertrophic cardiomyopathy, and he passed away four months later. 🐾

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