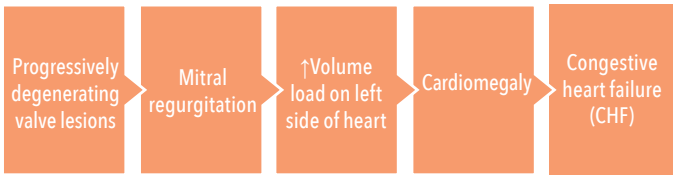
A SUMMARY OF THE EPIC STUDY[1]

Background

Mitral valve disease (MVD) is the most common cardiovascular disease in the dog.

The pathophysiology of MVD, which can lead to heart failure, is summarised here:



Dogs with MVD can progress through various stages of the disease:

- Stage A – those at risk of developing the disease
- Stage B – those with mitral regurgitation but no signs of CHF
- Stage C – those with signs of CHF
- Stage D – those with signs of CHF that are refractory to treatment

Stage B can be further subdivided:

- Stage B1 – those with disease but no evidence of cardiomegaly
- Stage B2 – those with disease and cardiomegaly

A number of therapies are considered effective in dogs with Stage C disease, including pimobendan (Vetmedin®), which has been shown to significantly improve survival and maintain quality of life.

Currently, there is no consensus about the effectiveness of medical treatment in Stage B. There are 2 published, prospective, randomised clinical trials evaluating ACE inhibitor (ACEi) treatment at this stage, however, no clearly beneficial effect of ACEi was found in either trial.

Due to the long duration of the asymptomatic period, any treatment that is effective in prolonging it could have a major impact on the longevity and quality of life of affected dogs.

Hypothesis/Objectives

To determine whether the administration of Vetmedin (0.4 - 0.6 mg/kg/day) to dogs with asymptomatic MVD and cardiomegaly would delay the onset of signs of CHF and cardiac-related death or euthanasia.

Materials and Methods

The EPIC trial was the largest prospective, randomised, placebo-controlled, blinded, multicentre clinical trial in veterinary cardiology ever to be conducted. The investigators were guaranteed the right to publish the results of the study irrespective of the outcome.

The study involved:

- 360 dogs
- 36 investigators
- 11 countries
- 4 continents

Inclusion criteria:

- ≥ 6 years of age
- Body weight 4.1 - 15 kg
- Stage B2 MVD:
  - Evidence of asymptomatic MVD on auscultation (≥ grade 3/6 murmur) and echocardiography
  - Evidence of cardiomegaly on radiography and echocardiography

Dogs were randomised into two groups:

- 180 dogs into the Vetmedin group
- 180 dogs into the placebo group

Study endpoints

Primary endpoint – this was defined as the point at which the dog either developed CHF or experienced cardiac-related death or euthanasia.

Secondary endpoints - there were two secondary endpoints in the EPIC study. The first was "all-cause mortality", which was death due to any cause. The second was "time to first event" which was the point at which the dog experienced any event; this could include reaching the primary endpoint, having an unscheduled veterinary visit, receiving a precluded medication, or the owner becoming non-compliant.

Results

The study was terminated early after the interim analysis demontrated a significant benefit in favour of administering Vetmedin to dogs with asymptomatic MVD.

Boehringer Ingelheim

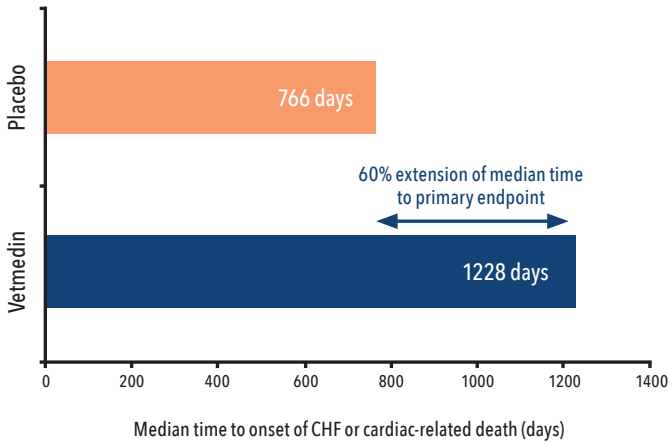
A SUMMARY OF THE EPIC STUDY[1] CONTINUED

Primary endpoint analysis

The median time to the primary endpoint for each group was:

- Vetmedin – 1228 days
- Placebo – 766 days

Dogs receiving Vetmedin took on average an additional 462 days (approximately 15 months) to either develop CHF or die from cardiac disease (p=0.0038). This represents around a 60% extension of the asymptomatic period.



Secondary endpoint analysis

Dogs receiving Vetmedin had an extended time to first event (p=<0.0001) and lived longer (p=0.012) compared with dogs receiving placebo.

Safety

There were no significant differences in adverse event occurrence between the Vetmedin and placebo groups.

Conclusions and clinical importance

MVD is the leading cause of heart disease, and the development of CHF results in substantial morbidity and mortality. The EPIC study has shown, for the first time, convincing evidence of the benefit of a treatment before the onset of CHF in dogs with asymptomatic MVD (Stage B2). Dogs receiving Vetmedin:

- Experienced a 60% extension in the asymptomatic period
- Took on average, an additional 15 months to develop clinical signs
- Had an overall longer survival time
- Took longer to experience an event
- Did not experience any increase in adverse events compared to the placebo group

This substantial degree of prolongation of the asymptomatic period is of clinical relevance and is of importance to vets and owners of dogs affected by this common disease.

Reference: 1. Boswood A, Häggström J, Gordon S, *et al.* Effect of Pimobendan in Dogs with Preclinical Myxomatous Mitral Valve Disease and Cardiomegaly: The EPIC Study—A Randomized Clinical Trial. J Vet Intern Med. 2016