VBX-1000, a new Cathepsin K inhibitor for treating periodontitis in dog : a proof-of-concept study

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Background

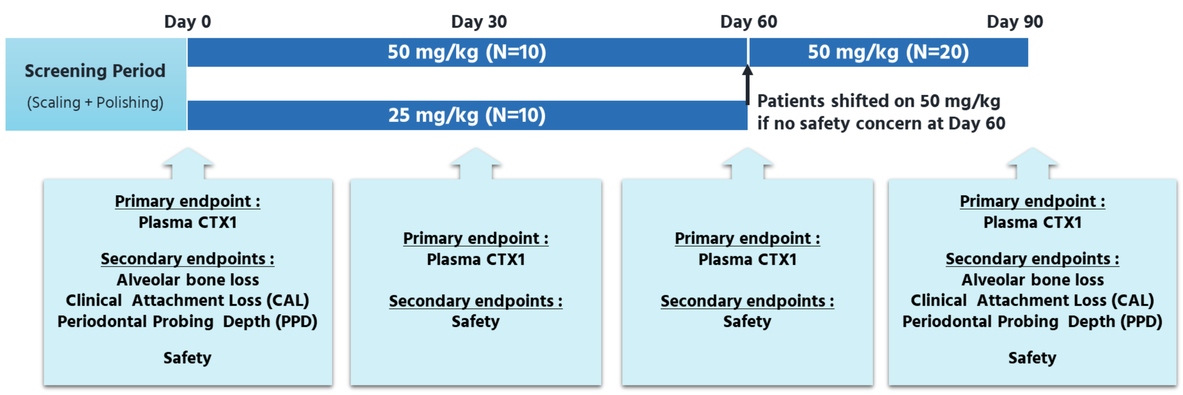
Periodontal disease (PD) is the most common dental condition in companion dogs. Prevalence in the UK primary-care veterinary setting was 12,52% [95% CI : 12,09 – 12,97] (O'Neill DG *et al.*, 2021). If effective measures are not taken early, PD will lead to a loss of clinical attachment of the affected teeth, which have a dramatic negative impact on the health and quality of life of the dogs. In most cases, PD is diagnosed too late and require the extraction of affected teeth. This calls for the development of new drugs for the treatment of periodontal disease.

Study design

This proof-of-concept clinical study (reference VBX1200-CL-1001) is an open-label, multicenter, European study (France, Poland) that aims to evaluate the safety and efficacy of repeated oral administration of the drug candidate VBX-1000, a novel cathepsin-K inhibitor, for 90 days in dogs with periodontitis (stage 2 and stage 3 of PD).

After scaling and polishing of the teeth, the dog patients with periodontitis were randomly divided into two groups and orally treated with the drug candidate VBX-1000 once-a-day :

- Group 1 (N=10 dogs, 3 teeth per dog) : dose of 25 mg/kg/day for 60 days. If at Day 60, treatment was well tolerated, a dose of 50 mg/kg/day was administered up to Day 90
- Group 2 (N=10 dogs, 3 teeth per dog) : dose of 50 mg/kg for 90 days



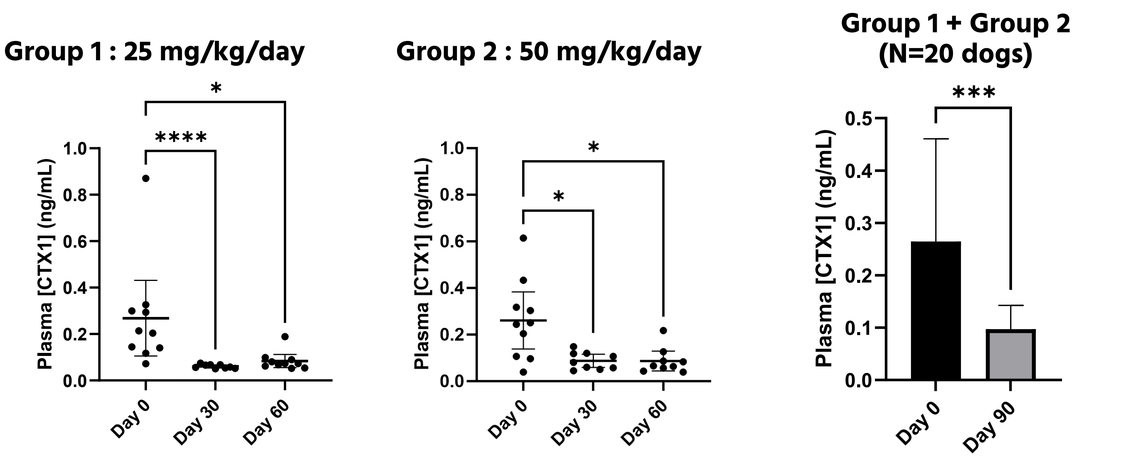
Study objectives

Primary objective : To assess the effects of VBX-1000 on plasma CTX-1 concentration (carboxy-terminal crosslinked telopeptide of type 1 collagen), a marker of bone resorption resulting from the activity of cathepsin K produced by osteoclasts

Secondary objectives :

- To measure the Height, Depth and Width of alveolar bone defect by X-ray radiography (N=20 dogs) and CBCT scan (Cone Beam Computed Tomography) (N=10 dogs) on mesial and distal sides of the selected teeth
- To assess clinical parameters of periodontal disease : Clinical Attachment Loss (CAL) and Periodontal Probing Depth (PPD)
- To evaluate the tolerance of repeated administration of VBX-1000

Primary endpoint : plasma CTX-1



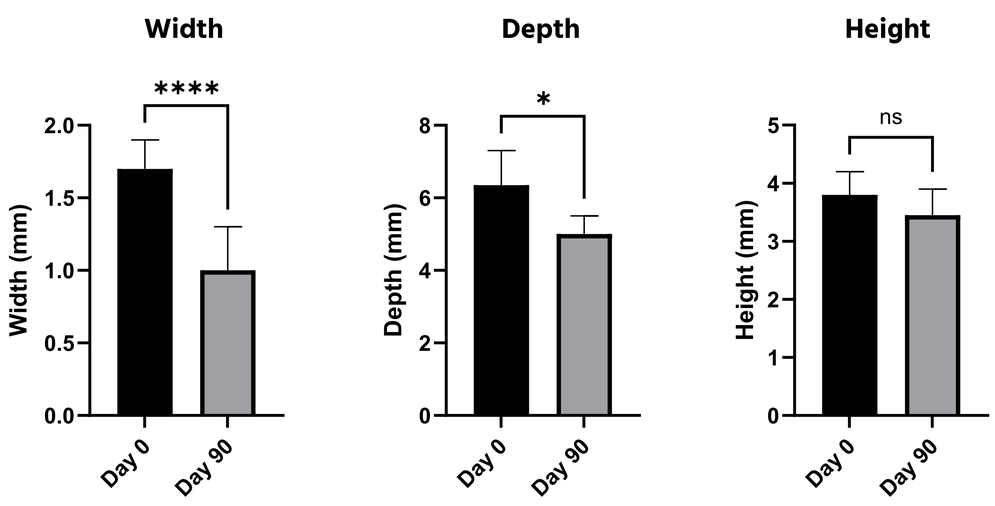
**p<0.05, ****p<0.0001 according to Dunn's multiple comparisons test*

**p<0.05, **p<0.01, ***p<0.001 according to Wilcoxon matched-pairs signed rank test*

- **VBX-1000 has a highly significant effect on the concentration of plasma CTX-1 :**
  - **Comparable effect of both doses of 25 mg/kg/day and 50 mg/kg/day**
  - **Rapid and dramatic decrease of CTX-1 plasma concentration after 30 days of treatment**
  - **Persistent effect of VBX-1000 up to 90 days**

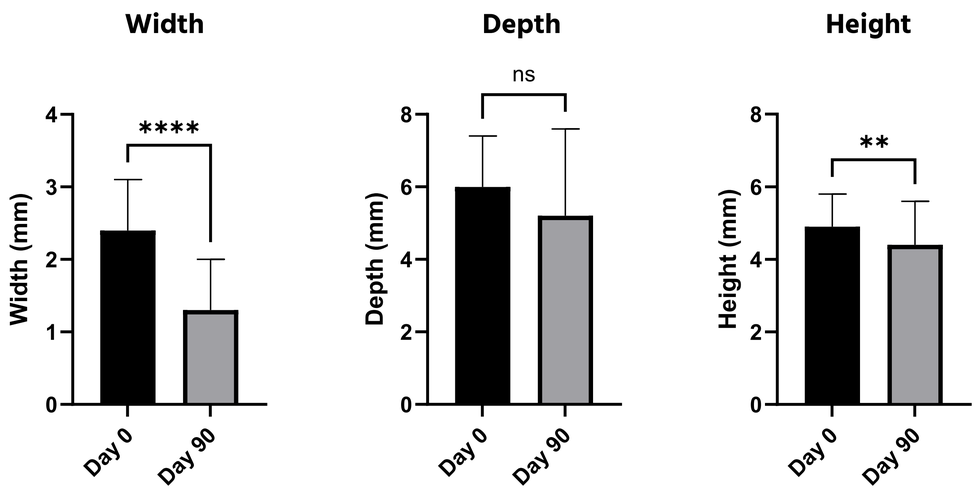
Secondary endpoint : Alveolar bone loss

Alveolar bone defect by X-ray radiography (N=20 dogs)



**p<0.05, ****p<0.0001, ns = not significant according to Wilcoxon test*

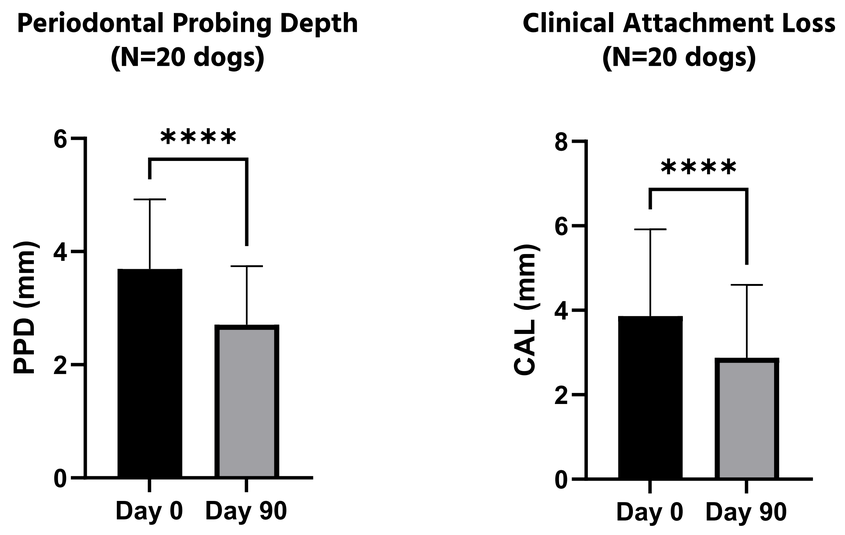
Alveolar bone defect by CBCT scan (N=9 dogs)



*****p<0.0001, ns = not significant according to Wilcoxon test*

- **VBX-1000 reduces significantly the alveolar bone loss as confirmed X-ray radiography and CBCT scan on Day 90**

Secondary endpoint : Clinical parameters of PD



*****p<0.0001 according to Paired t test*

- **VBX-1000 improves significantly (p<0.0001) clinical parameters of periodontal disease :**
  - **CAL was reduced by 0,99 mm [-1.27 to -0.70 mm] vs Day 0 (N=60 teeth)**
  - **PPD was reduced by 0,98 mm [-1.24 to -0.72 mm] vs Day 0 (N=60 teeth)**
- **In both groups, VBX-1000 was well tolerated up to Day 90 (data not shown)**

Conclusion

- **The rapid and continued decrease of CTX-1 plasma concentration suggests persistent inhibition of the resorption process that may promotes bone healing around affected teeth.**
- **This study supports VBX-1000 as a drug candidate to treat periodontal disease in dogs. A randomized, placebo-controlled trial in dogs should confirm VBX-1000 potential in this indication.**

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