



## TOLERABILITY AND EFFICACY OF INTRAVENOUS COMBRETASTATIN A4-PHOSPHATE INFUSION IN DOGS WITH SPONTANEOUS CANCER

### Introduction

Combretastatin A4-phosphate (CA4P) is a vascular targeting agent which selectively blocks tumour blood flow. Research on CA4P in rodent tumour models is extensive; however, knowledge of its effect on spontaneous cancer is scarce. The objectives of this research were to assess the adverse effects and the efficacy of a therapeutic dose of CA4P in dogs with various spontaneous tumours.

### Materials and Methods

Eight dogs with a spontaneous mesenchymal, epithelial, or round cell tumour were enrolled and treated intravenously with a single dose of CA4P at 75 mg m<sup>-2</sup>. After injection, clinical, haematological, and biochemical values were monitored during a maximum of 6 months. Pre- and post-treatment tumour blood flow was analysed *in vivo* by power Doppler ultrasound (PDUS) and contrast-enhanced ultrasound (CEUS) at T<sub>0</sub>, T<sub>24h</sub>, and T<sub>72h</sub>. Vessel destruction and tumour necrosis were assessed by histopathological evaluation at T<sub>72h</sub>.

### Results

Clinically relevant toxicity was limited to one case of temporary paraparesis that lasted for 96h. Further, mild and transient gastrointestinal signs (nausea, anorexia, and/or diarrhea) and subtle changes in blood parameters (neutropenia, lymphopenia, thrombocytopenia, and/or anaemia) were noticed. Macroscopic tumour size reduction was evident in 2 dogs. Based on PDUS, CEUS, and histopathology, 75 mg m<sup>-2</sup> CA4P induced a significant decrease in vascularity index and tumour blood flow and a significant increase in necrotic tumour tissue.

### Conclusions

This is the first study reporting the administration of CA4P to canine cancer patients with *in vivo* and *ex vivo* assessment. Anti-vascular and necrotizing effects of CA4P were documented in a variety of canine spontaneous cancers with only minimal side effects, supporting further development towards implementing CA4P in a combination therapy in veterinary medicine.

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