Osteosarcoma

BIOCERA-VET® OSTEOSARCOMA - EFFICACY AND SAFETY ASSESSMENT OF CEMENTOPLASTY BIOCERA-VET® IN DOGS WITH OSTEOSARCOMA

Collaborating Veterinary surgeons: Pr Olivier Gauthier, ONIRIS, Ecole Nationale Vétérinaire, France; Dr Guillaume Ragetly, CHV Frégis, France; Dr Aurélia Klajer, Eiffelvet, France; Dr Bertrand Vedrine, Seinevet, France; Dr Julien Letesson, CV Lameilhé, France; Dr Julien Carabalona, Clinique Olliolis, France.
Authors: Aquilino Villamonte, DVM, PhD, Veterinary Technical Manager and Céline Molle, PhD, Clinical Director (TheraVet®).

This study aimed to evaluate the efficacy and safety of BIOCERA-VET® used in percutaneous cementoplasty for the palliative care of osteosarcoma. The objective was to assess the effect of the cementoplasty using BIOCERA-VET® OSTEOSARCOMA in (i) improving limb function, (ii) reducing patient's pain, (iii) improving quality of life and (iv) limiting pathological fractures. The safety of the procedure was evaluated.

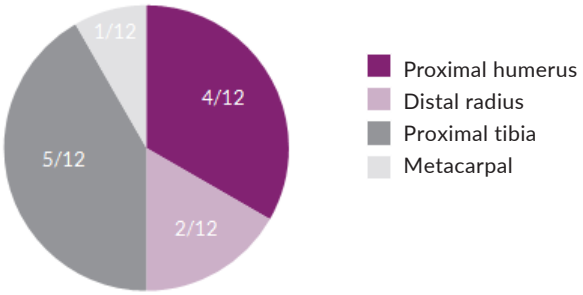
Materials & Methods

- Type of study: prospective, non-controlled clinical trial
- Evaluated product: BIOCERA-VET®* injectable synthetic self-hardening calcium-phosphate bone substitute
- Surgical procedure: percutaneous cementoplasty
- Study site: multicentric (6 sites in France)
- Eligibility criteria: client-owned dogs:
  - Physical examination: no chronic pain or long-term analgesic intake
  - Radiological evaluation: radiological signs consistent with appendicular osteosarcoma
  - No other treatment than cementoplasty[1]: no radiotherapy and no chemotherapy
- Study schedule: screening & treatment, follow-up visits at 1, 2 and 6 months post-treatment.
- Assessed variables at each visit:
  - Efficacy
    - Vet evaluation
      - Limb function: o NRS: Numerical Rating Scale regarding lameness, support, ease of lifting the contralateral limb and pain);
        o Pain: 4AVet (post-surgery pain questionnaire)
    - Owner evaluation
      - Pain: o VAS (visual analog scale)
        o CBPI (Canine Brief Pain Inventory) questionnaire with assessment of :
        - pain interference with function (PIS)
        - pain severity (PSS)
        - quality of life (QoL)
  - Safety
    - Complication rate
    - Pathological fracture rate

**The study was conducted with BIOCERA-VET® OSTEOSARCOMA 8cc version*
[1]In the context of this study, no concomitant treatment such as radiotherapy or chemotherapy was allowed.
If negative progression of the animal was noted requiring another treatment, the dog was excluded of the study to proceed with the treatment at the sole discretion of the veterinarian.

Demographics

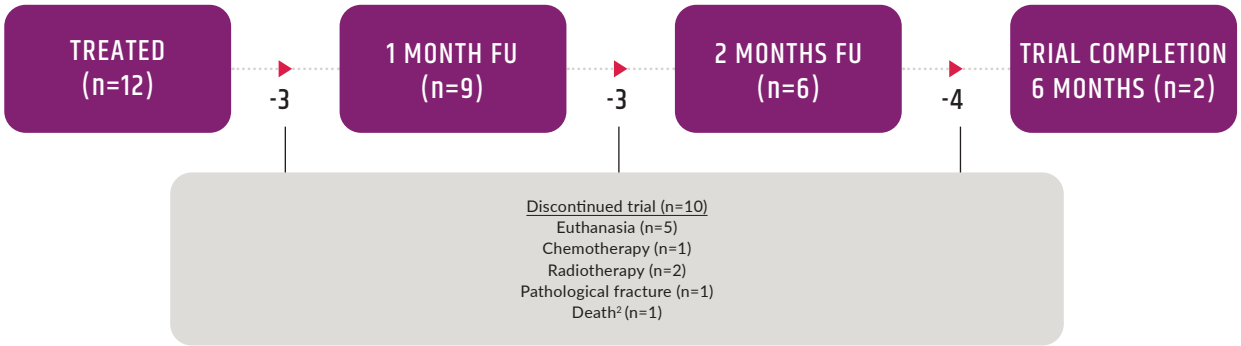
- 12 patients treated
- Median weight: 40 kg ranging from 30 to 75 kg
- Medium, large and giant sized breeds e.g. Great Dane, Labrador retriever, German shepherd, Dogue de Bordeaux
- 4 appendicular sites affected



Progression of patients

The advanced stage lesions of some patients and the required non-concomitant chemo/radiotherapy inclusion criteria led to an increasing number of discontinued patients through the course of the clinical trial. Patients were either euthanized, died[2], or left the study in order to start a more aggressive therapy protocol.

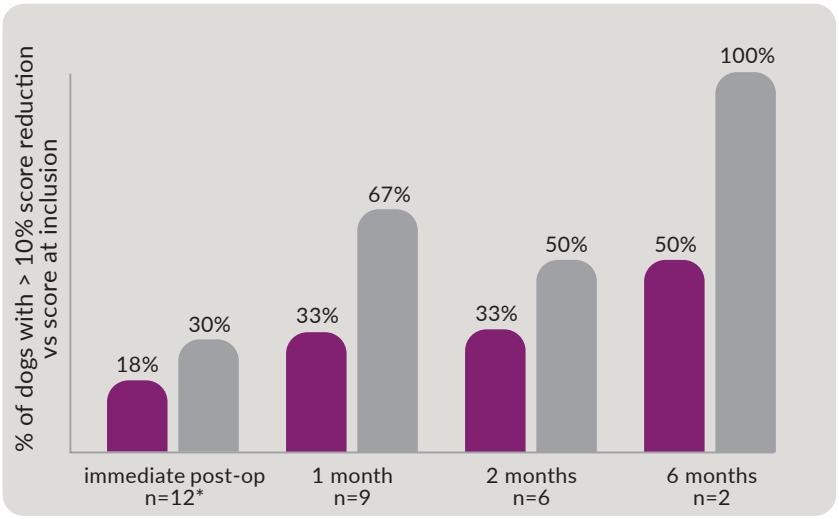
[2] *Natural death related to the evolution of the osteosarcoma.*



Efficacy results

Among the animals satisfying the different follow-up visits, an improvement of at least 10% of the score at inclusion for the limb function - evaluated by the veterinarian - using the NRS was observed in 18% of dogs immediately after treatment. Increasing percentages of responders were observed at later follow-up visits with 25%, 33% and 50% of patients responding to treatment respectively at 1, 2 and 6 months after treatment.

The pain assessment by the 4AVET questionary demonstrated that 30% of the dogs experienced a reduction of at least 10% immediately after treatment, 67% at one month, 50% at two months and a 100% improvement at 6 months.

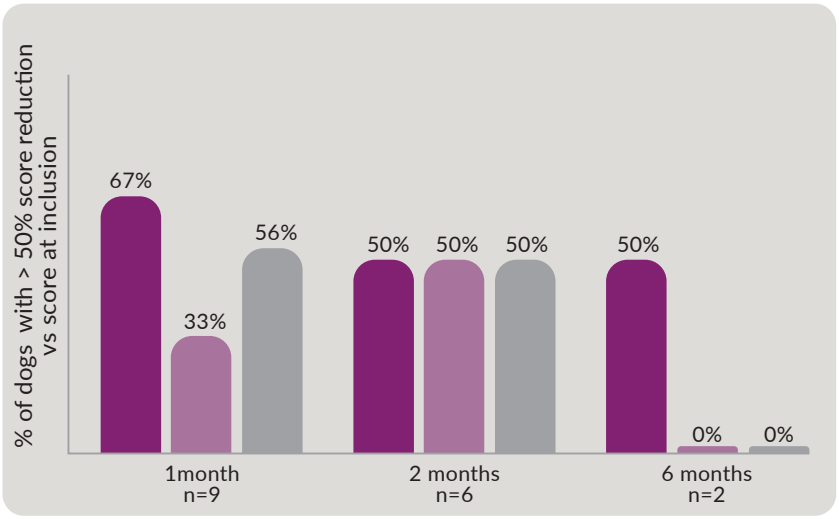


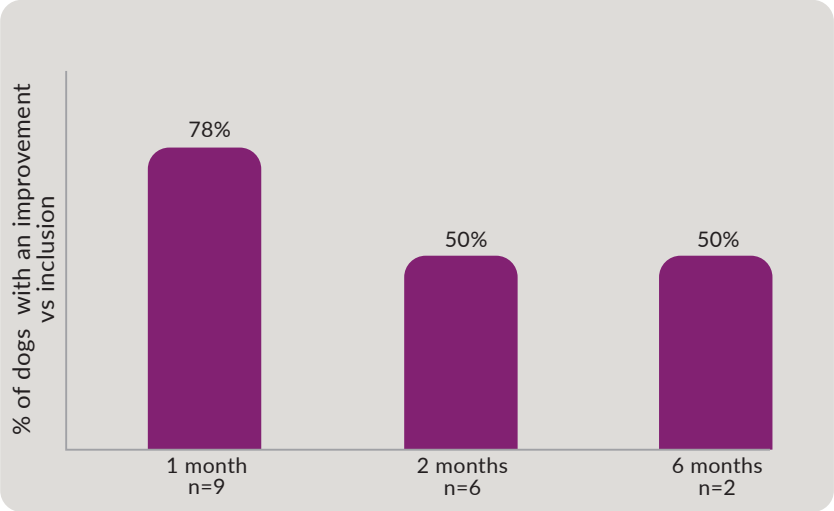
*n=12 including 2 missing data

The pain evaluation by owners is also important to consider since it allows a pain assessment in the usual living conditions of the dog using VAS and CPBI questionnaires. Among the animals satisfying the different follow-up visits, 67% of the dogs at 1 month and 50% at 2 and 6 months experienced a reduction of at least 50% in VAS pain at inclusion. The same reduction levels were measured at 1 and 2 months with the pain severity (PSS) and with the pain interference with the function (PIS) scores of the CBPI, although slightly less[3].

The QoL score was improved in 78% of the dogs at 1 month and 50% of the patients still showed an improvement at 2 and 6 months. The patients that discontinued the clinical trial due to the start of an additional different treatment plan and the patients subject to euthanasia showed an improvement of their QoL score for the majority of the follow-up evaluation until their last assessment.

[3] *PIS: 33% at 1 month, 50% at 2 months and 0% at 6 months; PSS: 56% at 1 month, 50% at 2 months and 0% at 6 months.*

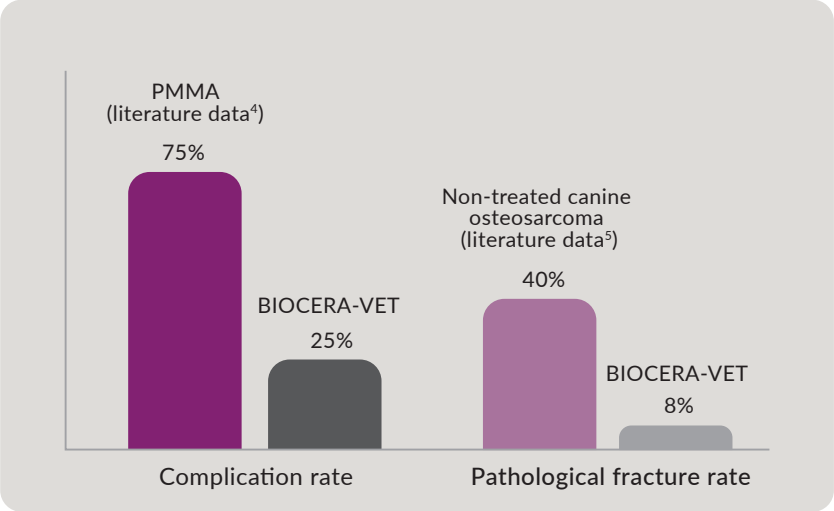




Safety results

Following the percutaneous BIOCERA-VET® cementoplasty, 3 complications (25%) were reported:

- Superficial surgical site infection n=1
- Swelling at surgical site n=1
- Pathological fracture on the adjacent bone n=1



When comparing our safety results to a similar approach of cementoplasty performed with PMMA (polymethyl methacrylate) in a multimodal management of canine osteosarcoma, complication rate reached 75% (including wound swelling, surgical site infection, exacerbation of the lameness, thromboembolism in combination with cough and anemia) for only limited benefit on lameness[4]. Furthermore, the pathological fracture rate of 8% in the BIOCERA-VET® study compares very favorably with the ~40%[5] incidence of fractures in canine osteosarcoma. (i.e. treated medically)

CONCLUSION

The data from this clinical study shows promising results for the cementoplasty with BIOCERA-VET® as a palliative option for dogs with osteosarcoma. Improved limb function, significant reduction of pain and better quality of life are the main benefits observed in the patients involved. The low complication rate also indicates that cementoplasty with BIOCERA-VET® is a safe alternative to other limb-sparing procedures and therefore represents a good palliative yet complementary option in the multimodal management of osteosarcoma.

Contact us for more information. A step-by-step guide of the cementoplasty procedure is also available. For your orders: www.bioceravet.com

SURGICAL TECHNIQUE TIPS

- Access point can be done by means of a biopsy trocar or with K wire and hollow drill bits
- Continuous surgical aspiration of the tumor cavity until injection allows a better filling of the cavity
- Fill the cavity retrogradely, from the furthest point towards the access point
- Cannula angulation should be adapted and checked with imaging tools, to fill in multiple directions
- Maximal filling of the bone tumor cavity is desired (minimum 50 % of filling is recommended)

[4] *Böttcher P et al., Percutaneous cementoplasty in the palliative, multimodal treatment of primary bone tumors of the distal aspect of the radius in four dogs. Vet Surg. 2009 Oct;38(7):888-901.*
[5] *Rubin J et al., Factors associated with pathological fractures in dogs with appendicular primary bone neoplasia: 84 cases (2007-2013). J Am Vet Med Assoc. 2015 Oct 15;247(8):917-23.*