MEDICAL TREATMENT OF CANINE OSTEOSARCOMA: BIBLIOGRAPHIC REVIEW

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INTRODUCTION

Osteosarcoma (OS) is the most common primary bone tumor in dogs (85%). At the time of diagnosis, 80–90% of patients already have micrometastases in the lungs but are not evident by conventional imaging techniques. Approximately 90% of these will die within a year of diagnosis.

OBJECTIVE

Since the **final cause of mortality is the metastasis** caused by osteosarcoma, the aim of this review has focused on the search for **treatments or therapies directed and focused on the treatment of metastases** (mostly pulmonary)

Losartan → inhibits monocyte recruitment, tumor angiogenesis, ↓ TFG-ß production and micrometastasis

Toceranib → inhibits VEGFR and PDGFR, antiangiogenic, ↓ circulating regulatory T lymphocytes

L-MTP-PE → activates monocytes and alveolar macrophages due tu the production of inflammatory cytokines, ↑ cytotoxicity

Gemcitabine → antitumor activity mediated by the regulation of the Fas receptor expression on the surface of metastatic cells

Table 1. Summary of treatments and average survival times of the reviewed articles

Treatment	Median survival time: review studies
Amputation alone	102 – 168 days
Amputation + chemotherapy with cisplatin	262 – 365 days
Amputation + chemotherapy with carboplatin	321 days
Amputation + chemotherapy with doxorubicin	366 days
Amputation + toceranib	90 days and 34 months (two studies)
Amputation + toceranib + losartan	148 days
Amputation + L-MTP-PE	222 days and 435 (two studies)
Inhaled PTX + additional therapy	>325 days
Inhaled gemcitabine	262 days
Inhaled IL-2	360 – 600 days

IL-2 → ↑ cytotoxicity of CD8+ T lymphocytes and NK cells, induces B cell proliferation, activates APCs and ↑ inflammatory cytokines

CONCLUSIONS

- The development of **pulmonary metastases** is the most common complication and the most frequent form of treatment failure in dogs with OS.
- **Chemotherapy** does not prevent the formation of lung metastases.
- **Multimodal therapeutic** approaches are necessary for the management of OS.
- **Activation of innate immune cells** is key to stopping metastatic progression (immunotherapy, L-MTP-PE).
- **Inhaled administration** of drugs reduces systemic adverse effects.
- Effective treatment of lung metastases in dogs remains a **clinical challenge** and future research is needed in this field.

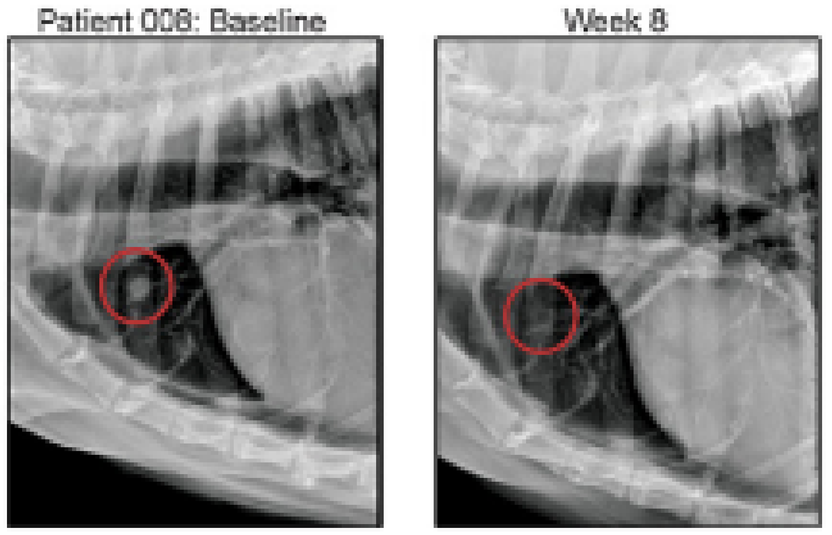

Figure 1. A 70% reduction in lung lesion diameter post-treatment with losartan (Regan *et al.*, 2022)

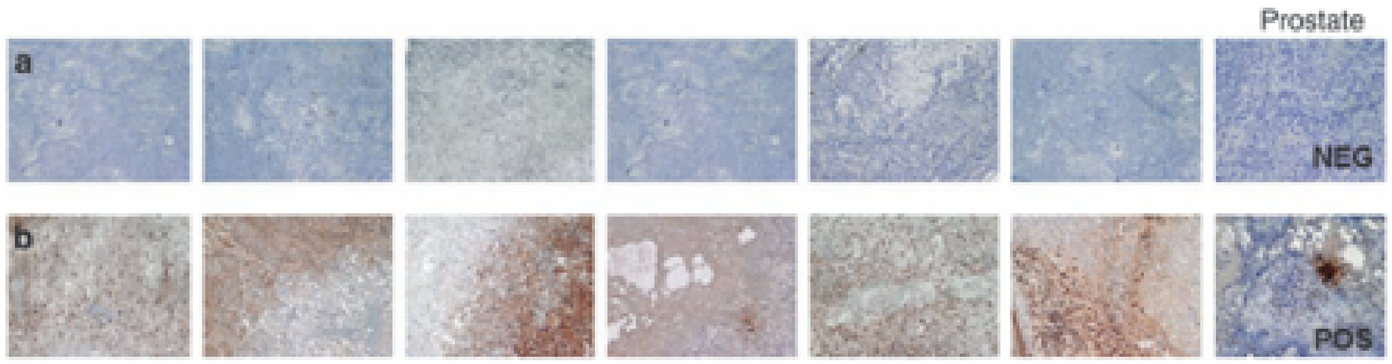

Figure 2. Sections of canine metastatic bone lesions from dogs untreated (a) or treated with aerosolized gemcitabine (b) with TUNEL (Rodríguez *et al.*, 2010)