UCDAVIS
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Efficacy and toxicity of carboplatin in the treatment of macroscopic mesenchymal neoplasia in dogs

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Introduction

- Soft tissue sarcomas (STSs) and hemangiosarcomas (HSAs) are common mesenchymal tumors diagnosed in dogs.
- Both are locally invasive but metastatic behavior varies based on location and grade.

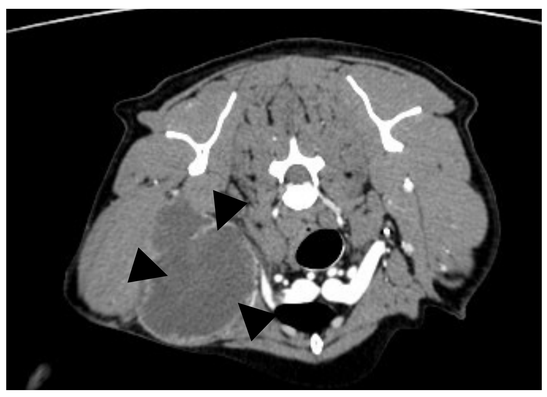

Figure 1. CT scan (Transverse view) of a canine patient diagnosed with an invasive, recurrent soft tissue sarcoma (black arrows). The tumor recurred after two surgeries, definitive radiation therapy and failed doxorubicin chemotherapy. The patient received carboplatin and was included in this study.

- When local control with surgery and/or radiation therapy is not an option, doxorubicin-based chemotherapy protocols may be considered as palliative treatment.

Tumor type	Chemotherapy used		Response rate
STS	Metronomic	CCNU, chlorambucil, thalidomide, cyclophosphamide	0-36%
	Dose intense	Doxorubicin, ifosfamide, mitoxantrone	
HSA	Metronomic	Chlorambucil, cyclophosphamide	0-47.4% (86%)
	Dose intense	Doxorubicin, mitoxantrone, multiagent DAV, VAC	

Table 1. Summary of agents used as palliative chemotherapy for STS or HSA. Dose-intense chemotherapy or metronomic chemotherapy protocols as a single treatment modality have not proven to be effective in local tumor control with variable response rates and often short control times.

- Carboplatin is a chemotherapy effective against canine osteosarcoma, with a favorable toxicity profile compared to doxorubicin. It is not an ABCB-1delta substrate and is not cardiotoxic.
- The use of carboplatin in the treatment of canine non osseous sarcomas has been limited, and data is direly needed to investigate its efficacy against this heterogenous family of tumors.

Aims

- To determine the efficacy of carboplatin in the treatment of macroscopic non osseous sarcoma in dogs.
- To describe the toxicity profile and adverse events (AEs) associated with carboplatin in this patient population using VCOG adverse events consensus.

Material and methods

Retrospective study

Computer search using combination of key words
"canine" "carboplatin" "sarcoma" "Sarcoma-(minus)bone" "Soft tissue sarcoma" "hemangiosarcoma" "peripheral nerve sheath tumor" "schwannoma" "neurofibrosarcoma"" "perivascular wall tumor" "hemangiopericytoma" "fibrosarcoma" myxosarcoma" "pleomorphic sarcoma" "liposarcoma" "spindle cell tumor"
Between 1990 and 2021

622 dogs

Inclusion Criteria
At least one dose of carboplatin
Macroscopic tumor
Tumor description
Follow up tumor assessment
STS or HSA (cytology or histopathology)
Presumptive cardiac HSA (based on echo appearance)
Any stage
Any prior therapy

29 cases included

Exclusion Criteria
Lack of Tumor assessment
No Follow up post carboplatin
Bone sarcoma
Microscopic disease
Cardiac masses with appearance of nonvascular sarcoma or chemodectoma on echocardiogram

593 cases excluded

- **Data collected**: signalment, stage, tumor type, previous treatments and responses, carboplatin administered, duration and type of response, AEs, other therapies given, date & cause of death.

Material and methods

- **Data assessed:**

Tumor response using **RECIST criteria** when possible
Toxicity using **VCOG criteria**
Response rate (RR) and Response duration [complete (CR) or partial response (PR)] as time of initiation of carboplatin to time of progression of disease (PD)
Progression free survival as time from initial carboplatin to date of identification of PD or death without evidence of PD, impact of stage and pretreatment with chemotherapy.

Results

Table 2. Demographics for the 29 patients included.

Patient demographics – 29 dogs	
Sex	16 spayed females
	11 castrated males
	2 intact males
Median Age	9.7 years (range 2.5-13.8)
Median Body weight	24.7 kg (range 5.6-45)
MDR mutation present	3
Tumor type	12 HSA
	17 STS
Stage	12 Local only
	17 Distant metastases
Previous treatments	18 patients received prior chemotherapy
	11 chemotherapy naive
Median # chemo prior to carboplatin	1 (range 0-4)

Table 3. Carboplatin treatments and response characteristics.

Treatments and response		
Median carboplatin dose	263.7 mg/m^2 (range 148.2-332.8)	
Median doses of carboplatin given	2 (range 1-12)	
PR	3/29	
CR	1/29	
Overall RR	13.8% (4/29)	0% (0/17) for **STS**
		33% (4/12) for **HSA**
Median duration of response	103 days (range 39-252)	

Figure 3 - Kaplan Meyer curves. (a) Progression interval for naïve vs pretreated. **(b)** Progression interval for naïve vs pretreated patients. **(c)** Progression interval for patients with local only vs metastatic disease.

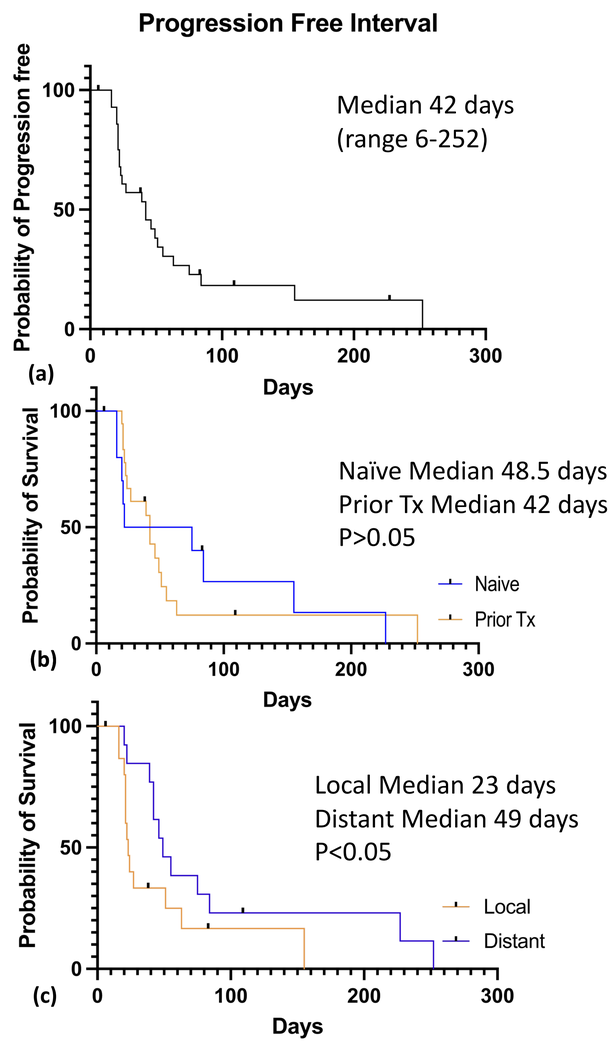

Table 4. Adverse events(AEs) characteristics graded using VCOG criteria.

VCOG Grade	Thrombocytopenia	Neutropenia	Constitutional	GI
Grade I	6.9 %	5.5%	0 %	13.9%
Grade II	8.3%	2.7%	1.4%	2.8%
Grade III	4.1 %	1.4%	0 %	0 %
Grade IV	2.7%	1.4%	0 %	1.4 %
Grade V	0%	1.4%	0 %	0 %

Discussion

- Response rate (RR) was low (13.8%) and of short duration in this heavily pretreated population.
- HSA may be more sensitive to carboplatin (33% RR), but this is based on a low number of patients.
- The toxicity profile seen in our patient population was acceptable.
- Patients with distant metastasis may have better response, but this may be due to the type of sarcoma (HSA) associated with metastatic status.
- Limitations of this study inherent to retrospective nature.

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References