

Outcome of first-rescue cyclophosphamide treatment for relapse small cell gastrointestinal lymphoma in cats

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BACKGROUND

- Lymphoma is the most common tumor type found in the intestines of cats.
- The small cell variant of gastrointestinal (GI) lymphoma in cats carries a good prognosis.
- First line treatment with chlorambucil and steroids results in response rates of > 90% and survival times of ≥ 2 years.
- Standard rescue protocols have not been established for relapse feline small cell GI lymphoma.
- Rescue drugs typically include other alkylating agents, although response data are limited.

OBJECTIVES

- To determine the progression free survival (PFS) and overall survival time (OST) of cats with relapse small cell GI lymphoma treated with first-rescue cyclophosphamide/steroids after failing chlorambucil/steroids
- To evaluate potential prognostic factors associated with outcome

MATERIAL AND METHODS

- Multi-institutional retrospective case series
- Inclusion criteria
 - Cats with small cell GI lymphoma confirmed histologically or via PARR/flow cytometry
 - Cats treated with cyclophosphamide/steroids after failure from first-line treatment with chlorambucil/steroids
 - Cats with no concurrent cancers nor prior chemotherapies
- Response to therapy was based on clinical signs (CS).
 - Complete response (CR): complete resolution of CS (VCOG grade 0) ≥ 30 days
 - Partial response (PR): improvement but not complete resolution of CS (VCOG grade 1) ≥ 30 days
 - Progressive disease (PD): worsening of CS (VCOG grade > 1)
 - Stable disease (SD): neither improvement nor progression of clinical signs
 - Responses lasting < 30 days were considered either SD or PD, depending on severity of CS compared to pre-cyclophosphamide treatment
- Outcome definitions
 - PFS: days between initiation of cyclophosphamide and disease progression or death
 - OST: days between initial diagnosis and death
- Statistical analysis
 - Kaplan-Meier product limit estimates to compare survival times among cats grouped by categorical variables of interest
 - Cox proportional hazards regression analysis to assess associations between all variables and outcome in univariate analyses

RESULTS

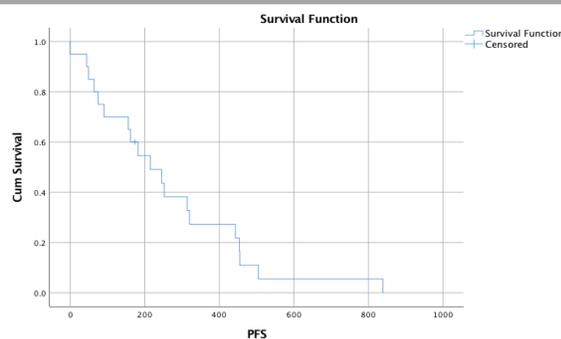


Fig 1. Kaplan-Meier survival curve depicting progression free survival (PFS). Median PFS was 215 days (95% CI 102-328)

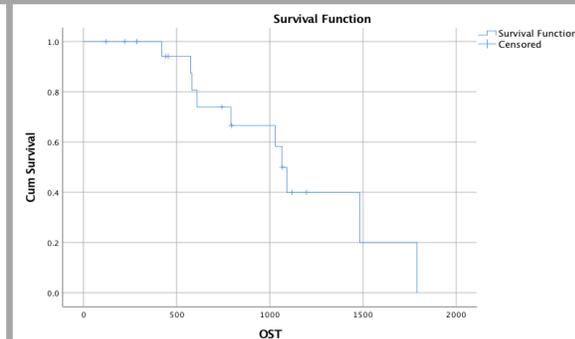


Fig 2. Kaplan-Meier survival curve depicting overall survival time (OST). Median OST was 1065 days (95% CI 974-1156)

- 20 cats met the inclusion criteria.
- Demographic data
 - Gender: 14 castrated male and 6 spayed female
 - Median age: 14.8 year old (range 6.2-19.8)
 - Median weight: 4.04 kg (range 2.8-5.1)
- CS
 - Weight loss (n=15)
 - Vomiting (n=10)
 - Diarrhea (n=8)
 - Anorexia (n=7)
 - Lethargy (n=5)
 - Median duration of CS: 100 days (range 3-1095).
- Cyclophosphamide/steroid treatment
 - Median dose of cyclophosphamide: 206.9 mg/m² (range 161.3-281.8 mg/m²) every 2 weeks
 - Median number of cyclophosphamide treatments: 13 (range 3-54)
 - Response
 - CR: 18/20 (90%)
 - SD: 1/20 (5%)
 - PD: 1/20 (5%)
 - 17 cats discontinued therapy due to progression of CS.
 - Median PFS: 215 days (95% CI 102-328, Fig 1)
 - Clinical factors associated with longer PFS in univariate analysis was achievement of CR (p=0.02, HR=0.14, Table 2).
 - Median OST: 1065 days (95% CI 974-1156, Fig 2)
 - Clinical factors with significant impact on OST include duration of clinical signs (p=0.03, HR=1.003) and response to prior chlorambucil therapy (p=0.01, HR=0.995, Table 1).
 - Adverse events
 - Anemia most common (n=5)
 - Dose limiting toxicity: grade 3 neutropenia (n=1), grade 3 anorexia (n=1)

Predictive factors	P value	HR	95% CI Lower	95% CI Upper
Duration of clinical signs	0.033	1.003	1	1.006
Duration of response to chlorambucil treatment	0.012	0.995	0.992	0.999

Table 1. Univariate cox proportional hazard regression of prognostic factors with statistically significant impact (P < 0.05) on OST

Predictive factors	P value	HR	95% CI Lower	95% CI Upper
CR vs Non-CR	0.024	0.139	0.025	0.768

Table 2. Univariate cox proportional hazard regression of prognostic factors with statistically significant impact (P < 0.05) on PFS

CONCLUSION

- Cyclophosphamide was well-tolerated.
- Treatment with cyclophosphamide for relapse small cell GI lymphoma in cats resulted in moderate response duration with a high complete response rate.
- Overall prognosis of feline small cell GI lymphoma is favorable with chemotherapy.
- A prospective randomized study is necessary to determine the superiority of cyclophosphamide over other rescue therapies.

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