Evaluation of lomustine, L-asparaginase and prednisone as a first rescue protocol for resistant canine non-Hodgkin high-grade B-cell lymphomas following a 19 week University of Wisconsin (UW-19) induction protocol

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Introduction

The combination of lomustine, l-asparaginase, and prednisone (LAP) has been previously evaluated as an effective rescue treatment for canine lymphoma (LSA).[4,5] The aim of this study was to evaluate efficacy and toxicity of this protocol, in a Spanish cohort of resistant canine B-cell multicentric lymphomas previously treated with a UW-19 protocol.

Materials and methods

Medical records were searched retrospectively for dogs with resistant B-cell multicentric lymphomas treated initially with a UW-19 protocol that received LAP as a first rescue treatment from 2014-2018.
Clinical variables (staging) at initial diagnosis and relapse were recorded

Pretreatment Evaluation
Complete history
Physical examination -Measure Target and non-target lesions if not done previously
CBC, chemistry profile, and UA (within 1 week of starting treatment)
Thoracic radiographs (only if clinically necessary)
Cytology confirmation of PD when new VCOG v1.0 applied

Lomustine (70-90mg/m²) was administered orally at 3-week intervals for a total of 5 doses, concurrently with subcutaneous l-asparaginase (10000 IU/m²) administered the first two doses of the protocol. Prednisone was administered at a tapering dose for the duration of the protocol and a liver protectant consisting in S-adenosilmetionine and silibilin (Hepatosil®)
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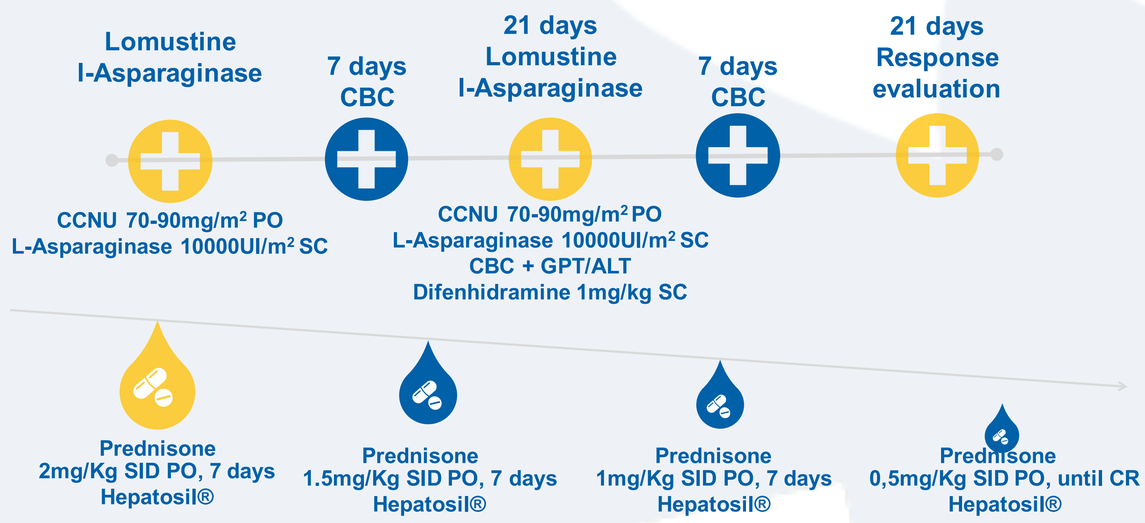
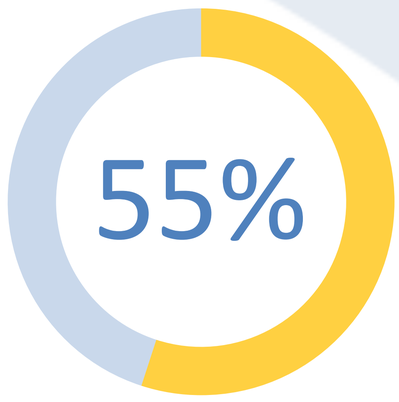


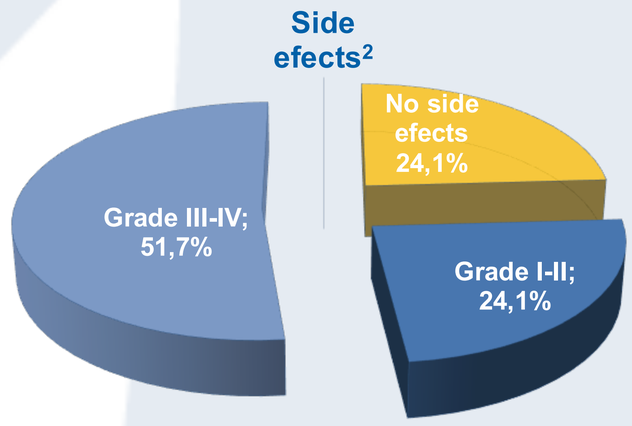
Responses were evaluated according to the Veterinary cooperative oncology group's (VCOG) response evaluation criteria for peripheral nodal lymphoma in dogs (v1.0). Outcome was measured as progression free survival. Evaluation of response was performed at day 30 and with every dose of lomustine thereafter. Monitoring will continue on a monthly basis after finishing the protocol. Adverse events were graded according to the Veterinary cooperative oncology group's common terminology criteria for adverse events (VCOG-CTCAE).

Results

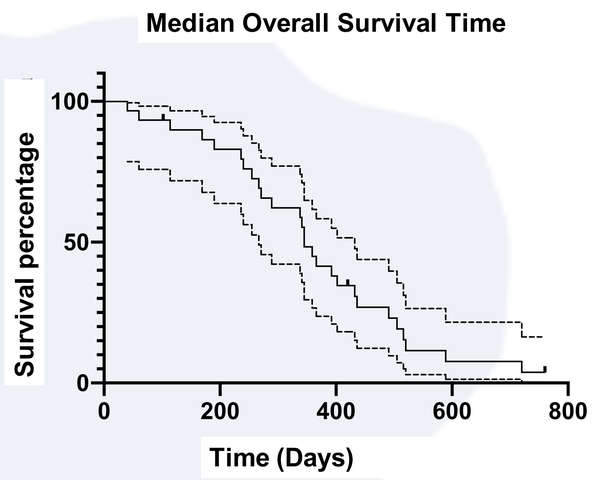
Twenty-nine patients fulfilled the requirements for inclusion in the study. Median weigh 19 Kg (3-41.8 Kg). Fourteen males and 15 female. Diagnosis was made by flow cytometry in 23 cases and IHC in 6. At diagnosis 20 patients were stage IV, 7 stage III, and 2 stage V. Fifteen substage A and 14 substage B
Nine patients did not complete the UW-19 protocol and in 2 cases they had completed two UW-19 protocols. The PFS for the first UW-19 protocol was 200 days.
The response rate to the protocol was 55% (15 cases). Twelve dogs achieved a complete response (RC) (44%), 3 a partial response (RP) (9%) and a 1 stable disease (EE) (3%). Eighteen patients (66%) did not complete the rescue protocol, 1 due to dilated cardiomyopathy while in CR at the time of death and 17 due to progressive disease. Three patients are still alive and in CR. The median PFS was 59 days. Eleven patients received another rescue protocol and Vinblastine was the most frequently used (n=9)

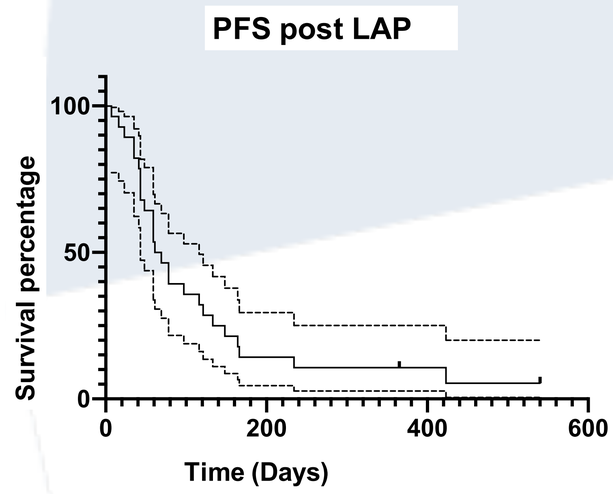


Response rate
16/29



9 dose reductions
1 hospitalization
1 death related with hepatic failure





The median PFS was 59 days. Overall MST was 372 days. Eleven patients received another rescue protocol and Vinblastine was the most frequently used (n=9)

Discussion

- B-cell lymphomas treated with a LAP protocol had a lower response rate 59% compared with previously described lomustine based rescue protocolos 77-87%.[4,5]
- Similar median progression free survival of 59 days compared with previously described lomustine rescue protocols 63-70 days.[4,5]
- Less than 50% patients were rescued with 3th or 4th protocol.
- Adverse side effects rate and severity similar to what has been reported with lomustine protocols, typically mild and selflimiting.

Conclusion

Despite a lower response rate compared to previous published data, the LAP protocol can be considered as a safe and useful first rescue treatment protocol for dogs with B-cell multicentric LSA, previously treated with a UW-19 weeks protocol.

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