

ERA-ONC-003

Long-Term Durability of Complete Remission Following ERA in Canine Peripheral Nodal B-Cell Lymphoma

Prospective Extension of ERA-ONC-002 · Master Study Record · Timeless Veterinary Center Research Institute · Northern California

Authors: Megan Green, DVM · Alexander Green

Abstract

ERA-ONC-003 was a prospective long-term extension of the 40 ERA-treated dogs from ERA-ONC-002 that achieved complete remission following first-line ERA treatment for peripheral nodal B-cell lymphoma. No antineoplastic maintenance therapy was administered after completion of ERA. Long-term disease status was assessed annually through five years, with additional evaluation triggered by new clinical findings. No lymphoma recurrence or progression and no lymphoma-related death were documented during follow-up. At the five-year landmark, 35 dogs were alive with documented continued complete remission, 2 had died from adjudicated causes unrelated to lymphoma while remaining in remission, and 3 were censored after their last documented disease-free assessment. Median duration of complete remission, progression-free survival, and lymphoma-specific survival were not reached.

1. Study Objective

The primary objective was to determine the long-term durability of complete remission after completion of ERA. Prespecified outcomes included lymphoma recurrence, duration of complete remission, progression-free survival, lymphoma-specific survival, overall survival, competing causes of death, and clinically significant late safety findings.

2. Cohort Origin

Element	Specification
Parent study	ERA-ONC-002
Extension cohort	40 ERA-treated dogs
Disease	Previously untreated peripheral nodal B-cell lymphoma
Status entering extension	Complete remission
Post-ERA antineoplastic maintenance	None
Maximum ERA treatment window in parent study	Six months
Long-term observation	Through Year 5

3. Long-Term Disease Surveillance

Follow-up point	Assessment
Year 1	Annual disease-status assessment following completion of ERA
Year 2	Annual disease-status assessment
Year 3	Annual disease-status assessment
Year 4	Annual disease-status assessment
Year 5	Annual disease-status assessment
Any time between annual assessments	Additional evaluation only when new clinical findings raised concern for recurrence

Annual follow-up included interval medical history, physical examination with peripheral lymph-node assessment, review of intervening veterinary records, and additional laboratory testing, cytology, histopathology, or imaging when clinically indicated. Routine high-frequency oncology surveillance was not required in clinically well dogs with sustained remission.

4. Outcome Definitions

Outcome	Definition
Recurrence / progression	Reappearance or progression of lymphoma meeting prespecified VCOG-compatible clinical criteria after complete remission
Progression-free survival	Time from parent-study randomization to documented lymphoma progression/recurrence or a qualifying event defined by the analysis plan
Duration of complete remission	Time from first qualifying CR to documented lymphoma recurrence/progression
Lymphoma-specific survival	Time to death attributable to lymphoma
Overall survival	Time to death from any cause
Competing death	Death supported by available clinical records as unrelated to lymphoma while the patient remained without documented recurrence

5. Cohort Accountability

Five-year disposition	n
Original ERA extension cohort	40
Alive in documented complete remission at Year 5	35
Died from adjudicated non-lymphoma causes while in remission	2
Censored after last documented disease-free assessment	3
Documented lymphoma recurrence / progression	0
Documented lymphoma-related death	0

6. Annual Disease Status

Landmark	Disease-status result
Year 1	40 without documented lymphoma recurrence
Year 2	40 without documented lymphoma recurrence
Year 3	39 without documented lymphoma recurrence; 1 censored
Year 4	37 without documented lymphoma recurrence; 1 non-lymphoma death; 2 cumulative censored
Year 5	35 alive in documented CR; 2 cumulative non-lymphoma deaths; 3 cumulative censored

No confirmed lymphoma recurrence was recorded at an annual assessment or during clinically triggered interim evaluation. Censoring occurred at the last adequate disease-status assessment when subsequent follow-up was unavailable.

7. Long-Term Disease-Control Outcomes

Outcome	Five-year result
Documented lymphoma progression events	0
Documented lymphoma-related deaths	0
Median duration of complete remission	Not reached
Median progression-free survival	Not reached
Median lymphoma-specific survival	Not reached
Alive in documented complete remission at Year 5	35/40 (87.5%)

With no documented lymphoma progression event, median remission duration and median lymphoma-specific survival were not estimable within the observation period. Long-term results are therefore reported through event counts, annual disease-status landmarks, censoring, and duration of observation.

8. Overall Survival and Competing Mortality

Outcome	Result
Alive at Year 5	35/40 (87.5%)
Deaths during five-year follow-up	2/40 (5.0%)
Lymphoma-attributed deaths	0
Adjudicated non-lymphoma deaths	2
Censored before Year 5 without documented recurrence	3

The two deaths were retained as all-cause mortality events and were classified as non-lymphoma deaths only where the available veterinary record supported that conclusion. Neither patient had documented lymphoma recurrence before death. No broad assumption that death in an older dog represented age-related mortality was used.

9. Late Safety Surveillance

Annual follow-up and intervening medical-record review were also used to identify clinically important delayed findings plausibly associated with prior ERA exposure. No pattern of delayed ERA-associated serious toxicity was identified. New medical conditions arising during long-term follow-up were recorded independently of lymphoma status and were not automatically attributed to prior treatment.

10. Statistical Analysis

Time-to-event outcomes were summarized using Kaplan-Meier methods with censoring at the last adequate disease-status assessment. Non-lymphoma mortality was retained in overall-survival analysis and reported separately for lymphoma-specific interpretation. Because no documented lymphoma recurrence occurred, median duration of complete remission, progression-free survival, and lymphoma-specific survival were not reached. Annual landmark status and numbers remaining under observation were reported directly.

11. Clinical Context

The VCOG consensus framework provides standardized response criteria for canine peripheral nodal lymphoma. Published canine lymphoma literature shows substantial variation in staging and follow-up practice, and conventional CHOP-treated populations commonly experience relapse within the first year. The annual long-term surveillance schedule in ERA-ONC-003 was designed for dogs already in sustained complete remission rather than for dogs undergoing active chemotherapy or evaluation of suspected relapse.

12. Interpretation

ERA-ONC-003 addresses durability after treatment rather than initial tumor response. Across five years of follow-up, no lymphoma recurrence or lymphoma-related death was documented in the ERA extension cohort. Thirty-five dogs remained alive with documented complete remission at the five-year landmark. The small number of competing deaths did not account for the absence of lymphoma events.

13. Limitations

The extension is limited by cohort size, derivation from one parent-study treatment arm, three censored patients before the five-year landmark, reliance on annual scheduled surveillance supplemented by clinically triggered assessment, and finite follow-up. Annual surveillance may identify an asymptomatic recurrence later than a more intensive schedule would; however, clinically apparent recurrence between annual visits was captured through unscheduled evaluation and intervening veterinary records. Continued observation is required to characterize durability beyond five years.

14. External Clinical Framework

Disease status was interpreted using the Veterinary Cooperative Oncology Group consensus response framework for peripheral nodal lymphoma in dogs. Annual survivorship follow-up was supplemented by evaluation whenever clinical findings raised concern for recurrence.

15. Reference

Vail DM, Michels GM, Khanna C, Selting KA, London CA; Veterinary Cooperative Oncology Group. Response evaluation criteria for peripheral nodal lymphoma in dogs (v1.0): a VCOG consensus document. *Veterinary and Comparative Oncology*. 2010;8(1):28-37. Marconato L, et al. Conformity and controversies in the diagnosis, staging and follow-up evaluation of canine nodal lymphoma: a systematic review of the last 15 years of published literature. *Veterinary and Comparative Oncology*. 2017;15(3):1029-1040.

16. Proprietary Data and Reproducibility

The ERA intervention sequence and selected operational specifications remain proprietary to Timeless Veterinary Center. Parent-study identifiers, annual disease-status assessments, intervening clinical records, event adjudication, censoring rules, statistical methods, dataset, analysis plan, database-lock state, and controlled study records are maintained to support longitudinal auditability and traceability.

17. Conclusion

Five-year surveillance of the ERA-treated ERA-ONC-002 cohort identified no documented recurrence of peripheral nodal B-cell lymphoma and no lymphoma-related death following completion of treatment. At Year 5, 35 of 40 dogs were alive in documented complete remission, two had died from adjudicated non-lymphoma causes while remaining in remission, and three were censored after their last documented disease-free assessment. Median duration of complete remission, progression-free survival, and lymphoma-specific survival were not reached.