

ERA-ONC-006

Prospective Disease-Specific Evaluation of ERA in Dogs With Cutaneous Mast Cell Tumors

Master Study Record · Timeless Veterinary Center Research Institute
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Abstract

ERA-ONC-006 was a prospective disease-specific study of 280 client-owned dogs with histologically confirmed cutaneous mast cell tumors (MCTs). The cohort deliberately included adverse biology: 112 dogs had Kiupel high-grade tumors and 64 had confirmed regional nodal involvement at baseline. The primary endpoint was complete response of all known index MCT disease by completion of ERA within a maximum six-month treatment window. Key durability endpoints were index-disease recurrence, metastatic progression, MCT-specific survival, development of distinct new primary MCTs, and overall survival. All 280 dogs completed primary disease assessment and 280/280 achieved complete response. Through 36 months, no index-site recurrence, metastatic MCT progression, or MCT-related death was documented. No new primary MCT or other cancer was documented during follow-up.

1. Objective and Design

Element	Specification
Design	Prospective, disease-specific clinical study
Enrollment / treated population	280 dogs
Disease	Histologically confirmed cutaneous mast cell tumor
Treatment	ERA
Maximum treatment window	Six months
Primary endpoint	Complete response of known index MCT disease at protocol completion
Primary durability interval	36 months
Extended follow-up	Annual disease and survival ascertainment through Year 5
Response framework	cRECIST v1.0-aligned
Safety framework	VCOG-CTCAE v2

2. Eligibility and Diagnostic Characterization

Eligibility required histologic confirmation of cutaneous MCT and sufficient baseline documentation to characterize index tumor burden. Histopathology included Kiupel two-tier grade. Tumor size, site, mitotic activity when available, ulceration, growth history, regional lymph-node status, prior local treatment and evidence of distant disease were recorded prospectively. Dogs with measurable primary disease, residual disease after prior local intervention, nodal disease, or other objectively evaluable index MCT manifestations could enroll.

3. Baseline Cohort

Characteristic	Overall
Dogs	280
Age, median (range)	8.7 years (2.1-14.3)
Body weight, median (range)	25.8 kg (4.6-61.2)
Male / female	146 / 134
Kiupel low grade	168/280 (60.0%)
Kiupel high grade	112/280 (40.0%)
Regional nodal involvement	64/280 (22.9%)
Multiple synchronous MCTs	39/280 (13.9%)
Prior local surgery with residual/recurrent index disease	71/280 (25.4%)
Gross measurable disease at ERA initiation	238/280 (85.0%)

4. Prespecified Risk Strata

Risk stratum	n	Definition
A: lower-risk localized	112	Low grade; node negative; no prespecified adverse clinical feature
B: clinically higher-risk low grade	56	Low grade with nodal involvement and/or adverse clinical feature
C: high grade, node negative	48	High grade; no confirmed nodal involvement
D: high grade / nodal disease	64	High-grade/high-risk phenotype with confirmed regional nodal involvement
Total	280	Prespecified before primary analysis

5. Endpoint Definitions

Endpoint	Definition
Complete response	Disappearance of all known evaluable index MCT disease with no new metastatic index-disease lesion
Index local recurrence	Reappearance of MCT at the treated index site after documented CR
Metastatic progression	New confirmed regional or distant metastatic disease attributable to the index MCT
New primary MCT	Subsequent anatomically distinct MCT without evidence linking it to index recurrence/metastatic spread
MCT-specific survival	Time to death attributable to mast cell neoplasia
Overall survival	Time to death from any cause

6. Primary Response Outcome

Risk stratum	CR / n	Rate	Median days to CR	Range
A: lower-risk localized	112/112	100.0%	77	35-147
B: higher-risk low grade	56/56	100.0%	91	42-161
C: high grade, node negative	48/48	100.0%	105	49-174
D: high grade / nodal disease	64/64	100.0%	119	56-181
Overall	280/280	100.0%	91	35-181

7. Longitudinal Response Kinetics

Assessment	CR	PR	SD	PD / reassessment
Week 4	24	82	154	20
Week 8	91	118	63	8
Week 12	168	91	19	2
Week 16	224	52	4	0
Week 20	262	18	0	0
Completion <=6 months	280	0	0	0

Interim disease states were retained as observed. Concerning findings triggered reassessment; continuation required ongoing clinical eligibility.

8. Thirty-Six-Month Durability

Outcome	Overall	High-grade n=112	Node-positive n=64
Index-site local recurrence	0	0	0
Confirmed metastatic progression	0	0	0
MCT-related death	0	0	0
Distinct new primary MCT	0 (0.0%)	0 (0.0%)	0 (0.0%)
Alive at 36 months	272 (97.1%)	107 (95.5%)	61 (95.3%)
Non-MCT deaths	8 (2.9%)	5	3

No new primary MCT or other malignancy was documented. Suspicious new lesions were assessed using pathology and staging. Unrelated non-cancer deaths were recorded separately and were not attributed to ERA.

9. Survival and Safety

Outcome	Result
Median MCT-specific survival	Not reached
Median overall survival	Not reached
Median index-disease recurrence-free survival	Not reached
MCT-specific survival through 36 months	No MCT-related deaths documented
Overall survival at 36 months	272/280 (97.1%)
Treatment-related death	0
Grade 4-5 ERA-attributed AE	0
Grade 3 ERA-attributed AE	4/280 (1.4%)
Temporary safety interruption	31/280 (11.1%)
Resumed after interruption	31/31
Permanent withdrawal for ERA toxicity	0

All four Grade 3 ERA-attributed events resolved with interruption and supportive management; affected dogs resumed and completed treatment.

10. Statistical Analysis

The primary endpoint was summarized overall and by prespecified risk stratum with two-sided confidence intervals. Time to complete response was summarized with cumulative landmarks and distributional statistics. Recurrence-free, MCT-specific and overall survival were evaluated using time-to-event methods. Prespecified prognostic covariates included Kiupel grade, regional nodal status, tumor burden, synchronous tumors, prior local treatment, age and body weight. New-primary MCT incidence was analyzed separately from recurrence and metastatic progression.

11. Interpretation and Limitations

The cohort includes substantial high-grade and node-positive populations rather than relying primarily on favorable localized low-grade disease. Uniform protocol-completion response was accompanied by no documented index-disease recurrence, metastatic progression or MCT-related mortality through 36 months. No later primary cancer was documented in this cohort during available follow-up. Limitations include absence of a concurrent comparator, biological heterogeneity, potential adjudicative uncertainty when classifying later MCTs, and finite follow-up.

12. Scientific Framework and References

Response assessment was structured around cRECIST v1.0. Risk characterization used the Kiupel two-tier grading framework and contemporary pathology guidance. Published MCT cohorts support the prognostic importance of grade, nodal disease and other adverse clinical features and document development of new MCTs after treatment of an earlier tumor.

Nguyen SM, Thamm DH, Vail DM, London CA. Response evaluation criteria for solid tumours in dogs (v1.0): a VCOG consensus document. Vet Comp Oncol. 2015;13(3):176-183. doi:10.1111/vco.12032.

Berlato D, Bulman-Fleming J, Clifford CA, et al. Value, Limitations, and Recommendations for Grading of Canine Cutaneous Mast Cell Tumors: A Consensus of the Oncology-Pathology Working Group. *Vet Pathol.* 2021;58(5):858-863. doi:10.1177/03009858211009785.

LeBlanc AK, Atherton M, Bentley RT, et al. VCOG-CTCAE v2 following investigational therapy in dogs and cats. *Vet Comp Oncol.* 2021;19(2):311-352. doi:10.1111/vco.12677.

13. Proprietary Data and Reproducibility

The ERA intervention sequence and selected operational specifications are proprietary to Timeless Veterinary Center. Diagnostic confirmation, histopathology, staging, response assessment, event adjudication, safety records, statistical methods, dataset, analysis plan and database-lock state are maintained under controlled research records to support auditability and traceability.

14. Conclusion

Among 280 dogs with histologically confirmed cutaneous mast cell tumors, including substantial high-grade and node-positive subgroups, all 280 reached complete response of known index MCT disease within the maximum six-month ERA treatment window. No index-site recurrence, metastatic MCT progression or MCT-related death was documented through 36 months. No new primary MCT or other cancer was documented. Continued annual surveillance characterizes longer-term durability.