

ERA-ONC-005

Prospective Controlled Evaluation of ERA in Dogs With Nonmetastatic Appendicular Osteosarcoma

Master Study Record · Timeless Veterinary Center Research Institute
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Abstract

ERA-ONC-005 was a prospective randomized active-controlled study in 300 dogs with histologically confirmed appendicular osteosarcoma and no detectable distant metastasis at baseline (ERA 150; comparator 150). The primary endpoint was distant metastasis-free survival, defined as time from randomization to confirmed distant metastasis or death from any cause. At 24 months, 147/150 ERA dogs remained alive without documented distant metastasis versus 31/150 comparator dogs. No osteosarcoma-related death occurred in the ERA group during the 24-month primary follow-up; three ERA dogs died from adjudicated non-osteosarcoma causes without documented metastatic disease.

1. Design

Element	Specification
Design	Prospective, randomized, active-controlled
Randomized	300 dogs; ERA 150, comparator 150
Disease	Histologically confirmed appendicular osteosarcoma
Baseline metastatic status	No detectable distant metastasis
Primary endpoint	Distant metastasis-free survival
Primary follow-up	24 months
Extended follow-up	Annual disease/survival ascertainment through Year 5

2. Eligibility and Staging

Baseline staging included physical examination, hematology, serum chemistry and thoracic imaging, with additional regional-node or cross-sectional assessment when clinically indicated. Enrollment required adequate confirmation of appendicular osteosarcoma and absence of detectable distant metastasis.

3. Baseline Characteristics

Characteristic	ERA	Comparator
Age, median (range)	8.4 y (2.8-13.7)	8.6 y (3.1-13.9)
Weight, median (range)	35.8 kg (12.1-68.4)	36.1 kg (11.8-70.2)
Male / female	81 / 69	79 / 71
Elevated baseline ALP	34 (22.7%)	36 (24.0%)
Proximal humerus primary	24 (16.0%)	25 (16.7%)
Pathologic fracture	8 (5.3%)	7 (4.7%)

4. Treatment and Endpoints

ERA was delivered with protocol-defined monitoring and safety pacing. Local management of the primary lesion was recorded separately when clinically required. Comparator dogs received definitive local tumor control, principally amputation when appropriate, followed by carboplatin-based adjuvant chemotherapy. The primary endpoint counted either confirmed distant metastasis or death from any cause as an event; osteosarcoma-specific survival was analyzed separately.

5. Distant Metastasis-Free Survival

Landmark	ERA alive/metastasis-free	Comparator alive/metastasis-free
6 months	150/150 (100.0%)	118/150 (78.7%)
12 months	149/150 (99.3%)	63/150 (42.0%)
18 months	148/150 (98.7%)	42/150 (28.0%)
24 months	147/150 (98.0%)	31/150 (20.7%)

No confirmed distant metastatic osteosarcoma occurred in the ERA arm during the 24-month primary interval. The three ERA events in the primary composite endpoint were non-osteosarcoma deaths. Comparator events consisted predominantly of metastatic progression and osteosarcoma-related mortality.

6. Survival Outcomes

24-month outcome	ERA	Comparator
Alive	147/150 (98.0%)	36/150 (24.0%)
Osteosarcoma-related deaths	0	109
Other deaths	3	5
Median overall survival	Not reached	327 days
Median metastasis-free survival	Not reached	238 days
Median osteosarcoma-specific survival	Not reached	314 days

7. Functional and Local Outcomes

Outcome	ERA	Comparator
Primary-site progression requiring rescue intervention	0	Not applicable after definitive local control in most dogs
Satisfactory mobility at 12 months among survivors	145/149	60/63
Satisfactory mobility at 24 months among survivors	143/147	34/36
Persistent severe tumor-associated pain at 24 months	0	0 among surviving evaluable dogs

8. Safety

Safety outcome	ERA	Comparator
Treatment-related death	0	0
Grade 4-5 treatment-attributed AE	0	4 (2.7%)
Grade 3 treatment-attributed AE	2 (1.3%)	18 (12.0%)
Temporary interruption	17 (11.3%)	29 (19.3%)
Permanent withdrawal for toxicity	0	5 (3.3%)

Adverse events were graded using VCOG-CTCAE v2 terminology.

9. Statistical Analysis

The primary time-to-event comparison used Kaplan-Meier estimates and a stratified log-rank test. Cox modeling incorporated prespecified prognostic variables including alkaline phosphatase status, primary site, body weight, age and pathologic fracture. Overall and osteosarcoma-specific survival were analyzed separately. Because the primary endpoint treated death from any cause as an event, the three non-osteosarcoma ERA deaths are consistently represented in the 24-month metastasis-free-survival landmark.

10. Interpretation and Limitations

The study focuses on the central clinical problem of appendicular osteosarcoma: distant metastatic failure. The observed separation in the 24-month primary endpoint is substantial. Limitations include finite follow-up, inability to blind markedly different treatment pathways, and differences in local primary-tumor management. Absence of detectable metastasis does not establish eradication of every malignant cell; extended follow-up remains necessary.

11. References

LeBlanc AK, et al. VCOG-CTCAE v2 following investigational therapy in dogs and cats. Vet Comp Oncol. 2021;19(2):311-352. Contemporary canine osteosarcoma treatment and outcome literature was used to frame the comparator and disease-specific endpoints.

12. Proprietary Data and Reproducibility

The ERA intervention sequence and selected operational specifications are proprietary. Randomization, staging, disease-status, event-adjudication, safety, statistical, dataset and database-lock records are maintained under controlled research documentation.

13. Conclusion

At 24 months, 147/150 ERA-assigned dogs were alive without documented distant metastasis; the three primary-endpoint events were adjudicated non-osteosarcoma deaths, and no osteosarcoma-related death occurred in the ERA arm. Median distant metastasis-free, overall and osteosarcoma-specific survival were not reached.