

ERA-BIO-002

Safety, Tolerability, and Physiologic Recovery During Repeated ERA Exposure in Adult Dogs

Master Study Record · Timeless Veterinary Center Research Institute · Northern California
Authors: Megan Green, DVM · Alexander Green

Abstract

ERA-BIO-002 was a randomized, controlled, repeated-exposure study designed to characterize safety, tolerability, physiologic adaptation, and recovery during ERA exposure. Sixty healthy adult dogs were allocated to ERA (n=40) or Control (n=20) and followed over a 12-week active period with protocol-defined recovery surveillance. All 60 completed planned follow-up. No death, life-threatening event, Grade ≥ 3 treatment-emergent adverse event, or serious adverse event was observed. Four ERA animals (10.0%) met temporary-interruption criteria; all recovered, resumed exposure, and completed follow-up.

1. Objectives and design

The primary objective was to characterize clinically adverse events and intervention-limiting physiologic instability during repeated ERA exposure. Monitoring emphasized clinical examination, hydration/hemodynamics, body weight and composition, hematology, serum chemistry, glucose/electrolytes, activity/behavior, and recovery. Expected physiologic adaptations were prospectively distinguished from adverse events.

2. Baseline characteristics

Characteristic	ERA (n=40)	Control (n=20)
Age, years, mean (SD)	4.8 (1.6)	4.7 (1.5)
Body weight, kg, mean (SD)	12.5 (1.7)	12.4 (1.8)
Body-condition score, median (IQR)	5 (5–6)	5 (5–6)
Male / female	20 / 20	10 / 10
Clinically significant screening abnormality	0	0

Baseline variables were selected to document broad comparability of the randomized groups; the study was not powered to test baseline differences.

3. Disposition and safety outcomes

Outcome	ERA	Control
Completed planned follow-up	40/40	20/20
Temporary protocol interruption	4/40 (10.0%)	0/20
Permanent safety-related withdrawal	0	0
Grade ≥ 3 TEAE	0	0
Serious adverse event	0	0
Death	0	0

4. Physiologic adaptation and recovery

Body-weight change during active ERA phases was evaluated as a monitored physiologic variable rather than automatically classified as an adverse event. Interpretation integrated individualized weight trajectory, body condition/composition, hydration, functional status, laboratory findings, and recovery. Gastrointestinal toxicity was not a defining treatment-emergent signal. All four temporarily interrupted ERA animals satisfied recovery and resumption criteria and completed follow-up.

5. Laboratory safety

No persistent clinically important hematologic, renal, hepatic, electrolyte, or glucose/metabolic abnormality was present at study completion. Transient out-of-range measurements remained in the record and were interpreted according to magnitude, persistence, associated clinical findings, and recovery.

6. Statistical interpretation

The study was estimation-focused. Zero observed serious adverse events among 40 ERA-exposed animals does not imply zero underlying risk. By the conventional rule-of-three approximation, zero observations in 40 exposures corresponds to an approximate upper 95% risk bound of 7.5% for an unobserved event type.

7. External evidence framework

The safety framework was informed by published medically supervised prolonged-fasting safety research, while mechanistic context was informed by experimental work on fasting-associated IGF-1/PKA signaling, hematopoietic stem-cell responses, and fatty-acid-oxidation–dependent intestinal stem-cell function. These external findings informed monitoring domains; they do not establish ERA-specific safety or efficacy.

8. Limitations

Limitations include the healthy research population, modest sample size, limited precision for uncommon events, finite follow-up, and incomplete generalizability to older, medically fragile, or oncology patients.

9. Proprietary Data & Reproducibility

The ERA intervention sequence and selected operational specifications are proprietary to Timeless Veterinary Center. Event definitions, safety thresholds, monitoring domains, statistical methods, dataset, analysis plan, database-lock state, and document history are maintained under controlled research records for auditability and traceability.

10. References

Finnell JS, Saul BC, Goldhamer AC, Myers TR. Is fasting safe? A chart review of adverse events during medically supervised, water-only fasting. *BMC Complementary and Alternative Medicine*. 2018;18:67. Cheng CW, et al. Prolonged fasting reduces IGF-1/PKA to promote hematopoietic-stem-cell-based regeneration and reverse immunosuppression. *Cell Stem Cell*. 2014;14(6):810–823. Mihaylova MM, et al. Fasting activates fatty acid oxidation to enhance intestinal stem cell function during homeostasis and aging. *Cell Stem Cell*. 2018;22(5):769–778.e4.

11. Conclusion

Under the ERA-BIO-002 study conditions, repeated ERA exposure was completed without an observed serious adverse event, Grade ≥ 3 treatment-emergent event, death, persistent clinically important laboratory abnormality, or permanent safety-related withdrawal. The findings support progression to disease-specific clinical investigation with continued safety surveillance.