Cardiovascular and Survival Outcomes in Adults Receiving Anthracyclines With Versus Without Dexrazoxane: A Real-World Propensity-Matched Analysis

Sandipta Banerjee, MD[1]; Chanchal Maheshwari, MD[2]; Humzah Abbas, MBBS[3]

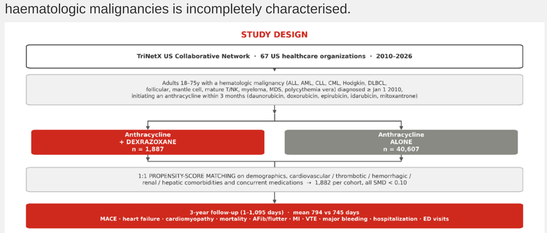
[1]BronxCare Health System, Bronx, New York, USA [2]Cleveland Clinic Akron General Hospital, Akron, Ohio, USA [3]Mega Medical Complex Hospital, Rawalpindi, Pakistan

Data source: TriNetX US Collaborative Network

INTRODUCTION

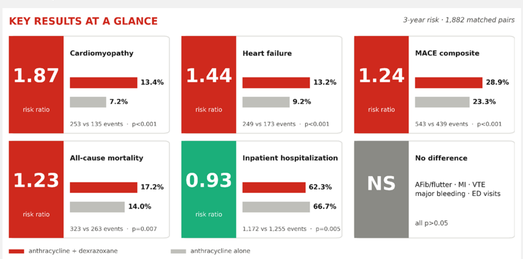
Anthracyclines remain central to the treatment of haematologic malignancy, but cumulative exposure carries a well-described risk of cardiomyopathy and heart failure.

Dexrazoxane is approved for cardioprotection during anthracycline therapy and reduces cardiotoxicity in randomised trials, yet its real-world effectiveness across haematologic malignancies is incompletely characterised.



AIM / OBJECTIVE

To compare 3-year cardiovascular, thrombotic, haemorrhagic, mortality and healthcare-utilisation outcomes in adults with haematologic malignancies receiving anthracyclines with versus without dexrazoxane.



METHOD

- Design: Retrospective propensity-score matched (PSM) cohort study, TriNetX US Collaborative Network (67 healthcare organisations), 2010–2026.
- Population: Adults 18–75 years with a haematologic malignancy (ALL, AML, CLL, CML, Hodgkin lymphoma, DLBCL, follicular, mantle cell, mature T/NK lymphomas, myeloma, MDS, polycythaemia vera) diagnosed on/after Jan 1 2010, initiating an anthracycline (daunorubicin, doxorubicin, epirubicin, idarubicin, mitoxantrone) within 3 months.
- Cohorts: anthracycline + concurrent dexrazoxane (n=1,887) vs anthracycline alone (n=40,607); 1:1 PSM on demographics, cardiovascular / thrombotic / haemorrhagic / renal / hepatic comorbidity and concurrent medications → 1,882 per cohort, all standardised mean differences <0.10.
- Follow-up: 1–1,095 days (3 years); mean 794 vs 745 days.
- Outcomes: composite MACE; heart failure; cardiomyopathy; all-cause mortality; atrial fibrillation/flutter; MI; VTE; major bleeding (intracranial/GI); inpatient hospitalisation; ED visits. Risk ratios (z-test p) and Kaplan–Meier hazard ratios (log-rank p) estimated.

CONCLUSIONS

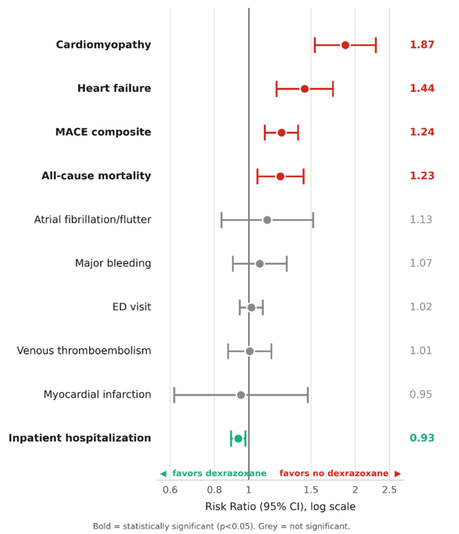
Dexrazoxane was paradoxically associated with HIGHER cardiomyopathy, heart failure, MACE and mortality — the opposite direction to randomised cardioprotection trials.

These results almost certainly reflect channelling bias: dexrazoxane is preferentially given to patients receiving high cumulative anthracycline doses or with pre-existing or emerging cardiotoxicity, none of which is captured by administrative coding.

Findings highlight the limits of propensity-score matching when key indication variables (cumulative dose, baseline LVEF, treatment intent) are unmeasured, and underscore the need for cumulative-dose-stratified analyses.

RESULTS

Figure 1. Three-Year Outcomes, Anthracycline + Dexrazoxane vs Anthracycline Alone (1,882 matched pairs)



Bold = statistically significant (p<0.05). Grey = not significant.

KEY FINDINGS

- **Cardiomyopathy nearly doubled: 13.4% vs 7.2% (RR 1.87, p<0.001)**
- **Heart failure: 13.2% vs 9.2% (RR 1.44, p<0.001)**
- **MACE: 28.9% vs 23.3% (RR 1.24, p<0.001)**
- **All-cause mortality: 17.2% vs 14.0% (RR 1.23, p=0.007)**
- **Inpatient hospitalisation was LOWER with dexrazoxane: 62.3% vs 66.7% (RR 0.93, p=0.005)**
- No difference in atrial fibrillation/flutter, MI, VTE, major bleeding or ED visits (all p>0.05)
- Direction is opposite to randomised trials — see channelling-bias panel

Figure 1 (left). Risk ratios with 95% CI for all ten 3-year outcomes.

Table 1 (right). Event counts, risks, risk ratios and Kaplan–Meier hazard ratios. RR = risk ratio; HR = hazard ratio; CI = confidence interval.

Outcome (3-year)	Anthracycline + dexrazoxane n (%)	Anthracycline alone n (%)	Risk Ratio (95% CI), p	Hazard Ratio (95% CI), p
Cardiomyopathy	253 (13.4)	135 (7.2)	1.87 (1.54–2.29), p<0.001	1.89 (1.53–2.33), p<0.001
Heart failure	249 (13.2)	173 (9.2)	1.44 (1.20–1.73), p<0.001	1.45 (1.19–1.76), p<0.001
MACE composite	543 (28.9)	439 (23.3)	1.24 (1.11–1.38), p<0.001	1.26 (1.11–1.42), p<0.001
All-cause mortality	323 (17.2)	263 (14.0)	1.23 (1.06–1.43), p=0.007	1.19 (1.01–1.40), p=0.040
Atrial fibrillation/flutter	88 (4.7)	78 (4.1)	1.13 (0.84–1.52), p=0.427	1.11 (0.82–1.51), p=0.493
Major bleeding (ICH/GI)	231 (12.3)	215 (11.4)	1.07 (0.90–1.28), p=0.420	1.05 (0.88–1.27), p=0.571
Emergency department visit	795 (42.2)	782 (41.6)	1.02 (0.94–1.10), p=0.668	0.98 (0.89–1.08), p=0.662
Venous thromboembolism	324 (17.2)	322 (17.1)	1.01 (0.87–1.16), p=0.931	1.00 (0.86–1.17), p=0.968
Inpatient hospitalization	1,172 (62.3)	1,255 (66.7)	0.93 (0.89–0.98), p=0.005	0.89 (0.82–0.96), p=0.004

ACKNOWLEDGEMENTS

We thank the contributing healthcare organisations of the TriNetX US Collaborative Network.

CONTACT INFORMATION

Sandipta Banerjee, MD — BronxCare Health System, Bronx, New York, USA
Email: sbanerjee021097@gmail.com

REFERENCES

1. de Baat EC, Mulder RL, Armenian S, et al. Dexrazoxane for preventing or reducing cardiotoxicity in adults and children with cancer receiving anthracyclines. Cochrane Database Syst Rev. 2022;9:CD014638.
2. Swain SM, Whaley FS, Gerber MC, et al. Cardioprotection with dexrazoxane for doxorubicin-containing therapy in advanced breast cancer. J Clin Oncol. 1997;15(4):1318–1332.
3. Lipshultz SE, Rifai N, Dalton VM, et al. The effect of dexrazoxane on myocardial injury in doxorubicin-treated children with acute lymphoblastic leukemia. N Engl J Med. 2004;351(2):145–153.
4. Salas M, Hofman A, Stricker BH. Confounding by indication: an example of variation in the use of epidemiologic terminology. Am J Epidemiol. 1999;149(11):981–983.
5. Data source: TriNetX, LLC. TriNetX US Collaborative Network (www.trinetx.com).