Survival and Organ Outcomes in AL Amyloidosis in the Daratumumab Era

A propensity score–matched real-world analysis across 173 health systems

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Background

- AL amyloidosis is a plasma cell disorder in which misfolded light chains deposit in heart, kidney, liver and nerve. Proteotoxicity, not tumour burden, drives outcome.
- Cardiac involvement ~75%; renal ~2 in 3. Six-month mortality reaches 43% in advanced cardiac disease.
- ANDROMEDA (2021): daratumumab + VCd tripled complete haematologic response (53% vs 18%) and doubled cardiac and renal organ response.
- Approved 15 January 2021 — the first regimen ever approved for this disease.
- The trial excluded Mayo stage IIIB, NT-proBNP >8,500 ng/L, NYHA IIIB–IV and eGFR <20: precisely the patients who account for most early mortality.

Objective

- To determine whether diagnosis in the daratumumab era is associated with better survival and less organ damage than diagnosis in the era immediately before, in an unselected real-world population.

Methods

- TriNetX Global Collaborative Network; 173 healthcare organisations.
- Adults ≥18 years with ICD-10 E85.81 (light chain amyloidosis).
- Daratumumab era: index ≥15 Jan 2021. Pre-daratumumab era: 1 Jan 2016 – 14 Jan 2021.
- 1:1 propensity score matching on 20 covariates (8 demographic, 12 diagnostic), re-run within each outcome set.
- Kaplan–Meier, log-rank and Cox proportional hazards at 1, 3 and 5 years.
- 30 endpoints in six systems: survival; cardiac (incl. BNP); renal; haematologic (incl. free light chain); hepatic; utilisation and infection.
- Hazard ratio <1.00 favours the daratumumab era.

9,093	4,441	4,173–4,412
identified daratumumab era	identified pre-daratumumab era	matched pairs per outcome set

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Overall survival

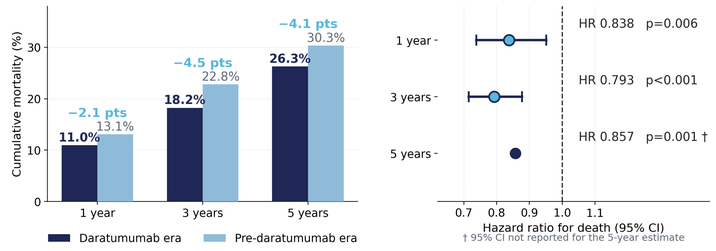
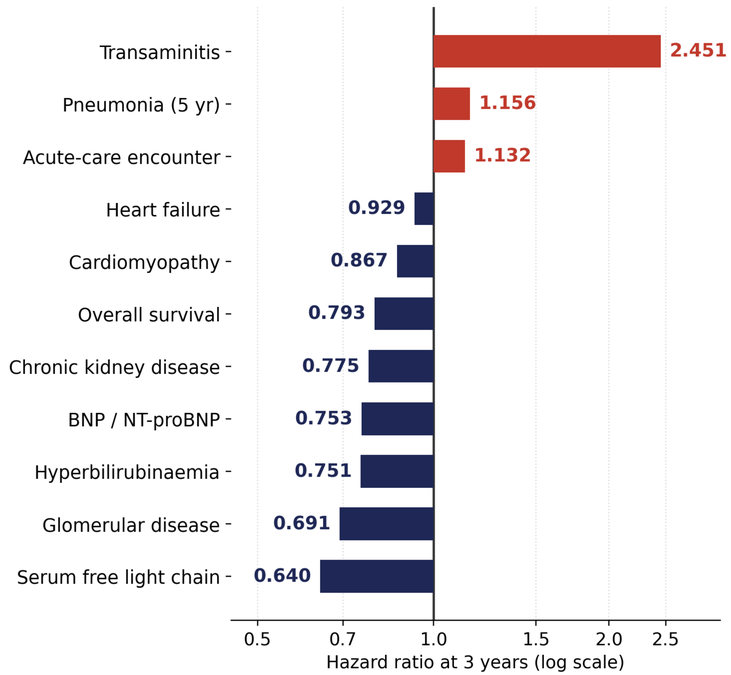


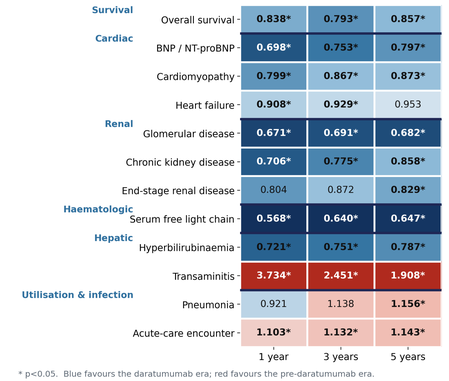
Figure 1. Cumulative mortality and hazard ratios for death, by era.

- Mortality fell by about one fifth at three years — the horizon at which both cohorts have the most complete follow-up.
- Roughly 22 patients need to be diagnosed in the daratumumab era for one additional survivor at three years.
- Proportional hazards held at every horizon; survival was the only domain in the study where it did.

Benefit and cost side by side



Results by organ system



* p<0.05. Blue favours the daratumumab era; red favours the pre-daratumumab era.

- Benefit appears in every organ system — BNP and cardiomyopathy in the heart, glomerular disease and CKD in the kidney, and the free light chain response marker.
- Glomerular disease is the most stable finding, down about a third at all three horizons; end-stage renal disease reaches significance only at five years.
- Transaminitis is the largest single effect in the study — 3.73-fold at one year, falling to 1.91-fold by five.

Conclusions

- Survival and cardiorenal outcomes improved measurably in the daratumumab era, in a population that includes trial-ineligible patients.
- The benefit is coherent across five organ systems: deeper free light chain response → lower BNP and less cardiomyopathy → less glomerular disease and CKD → better survival.
- The cost is concentrated and monitorable, supporting scheduled liver function monitoring during and after induction, and infection vigilance beyond three years.

Limitations

- Retrospective and non-randomised; exposure inferred from calendar era rather than confirmed prescriptions, which biases toward the null.
- Outcomes are diagnostic codes, not adjudicated events; censoring at the last recorded fact means out-of-network deaths are missed.
- Death is treated as censoring for organ endpoints, and the post-2021 window overlaps COVID-19 and rising coding intensity.