Impact of Time to Chemotherapy Initiation on Overall Survival in Acute Myeloid Leukemia: A National Cancer Database Analysis

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BACKGROUND

Acute myeloid leukemia (AML) is traditionally a **hematologic emergency.**

Precision medicine has introduced clinical tension as induction is **deferred for genomic profiling** and targeted therapy selection.

The survival **impact of brief treatment delays** in treatment-eligible patients remains unclear.

We evaluated the association between **time to treatment initiation (TTT)** and overall survival, and identified a clinically relevant **treatment window** in a modern national cohort.

METHODS

Data Source: National Cancer Database (NCDB) 2016–2020.

Cohort: 31,617 adults (≥18 years) with acute myeloid leukemia (AML) who received chemotherapy.

Exclusion: Patients who died within 30 days of diagnosis were excluded to minimize early death bias and isolate a treatment-eligible population.

Analysis: Overall survival (OS) was evaluated using multivariable Cox proportional hazards models adjusted for demographic, clinical, socioeconomic, facility-level factors, and year of diagnosis.

Time to Treatment Initiation (TTT): Analyzed as a continuous variable, in categories (0–3, 4–7, 8–14, >14 days), and via restricted cubic splines to identify nonlinear thresholds.

Primary Endpoint: Overall Survival (OS).

CONCLUSIONS

Increasing treatment delay was **independently associated with progressively worse overall survival** after multivariable adjustment.

While genomic profiling provides essential information, **delays within routine diagnostic workflows** may carry unintended survival consequences.

These findings highlight the importance of **streamlining the path from diagnosis to induction** to optimize outcomes in AML.

These results reflect risks in stable, treatment-eligible populations and may not apply to those in hyperleukocytic or metabolic crisis requiring emergent intervention.

RESULTS

Key finding: Mortality risk begins to increase after approximately 3–5 days of delay

Spline modeling identified a clear inflection point at ~3–5 days, after which risk remains elevated.

RESTRICTED CUBIC SPLINE

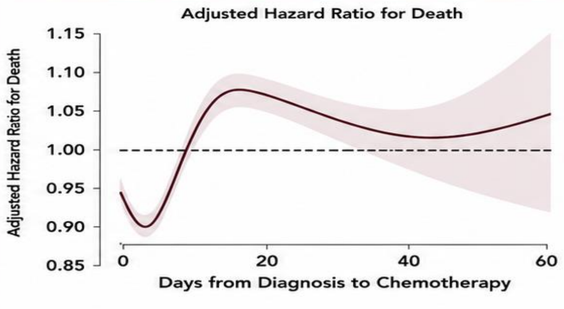

Figure 1. Restricted cubic spline analysis.
Adjusted hazard of death increased beginning at approximately 3–5 days after diagnosis and remained elevated thereafter. Shaded area = 95% confidence interval.

KAPLAN–MEIER SURVIVAL

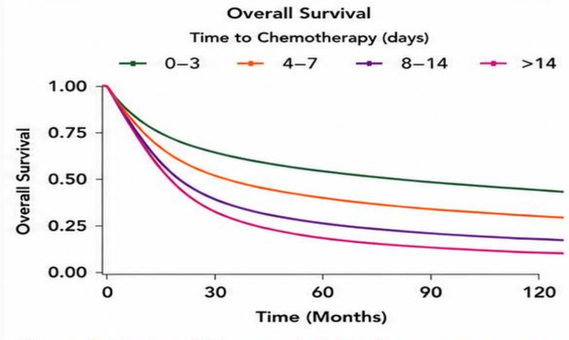

Figure 2. Kaplan–Meier survival by time to treatment.
Earlier chemotherapy initiation was associated with significantly improved overall survival (log-rank p<0.001).

KEY NUMERIC SUMMARY

Median TTT
6 days (IQR 3–11)

Continuous Model
HR 1.003
95% CI 1.002–1.004, p<0.001

Inflection Point
~3–5 days

Adjusted HR (vs 0–3 days)

4–7 days	**1.11**
8–14 days	**1.19**
>14 days	**1.16**

Cohort
31,617 adults
NCDB 2016–2020
Excluded deaths <30 days

CLINICAL IMPLICATIONS

1. TIMELY INITIATION MATTERS
Mortality risk begins to increase after approximately **3–5 days** of delay to induction chemotherapy among treatment-eligible AML patients.

2. EXPEDITE MOLECULAR PROFILING
Routine molecular and cytogenetic testing should be expedited whenever feasible to avoid delays in treatment initiation.

3. STREAMLINE DIAGNOSTIC WORKFLOWS
These findings support the need for streamlined diagnostic pathways and efficient care coordination to minimize time from diagnosis to treatment.

4. INFORM QUALITY IMPROVEMENT INITIATIVES
Healthcare systems should consider quality improvement initiatives aimed at reducing preventable delays to induction, with a target of **≤3 days** when possible.

Optimizing time to treatment is a **modifiable factor** that may improve outcomes for **patients with acute myeloid leukemia.**

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