

IMPACT OF EXTREME TOXICITY AND DELAYS IN THERAPY ON SURVIVAL IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: A REPORT FROM THE LEARN CONSORTIUM

Ross Mangum¹, Ross Mangum², Tiffany M Chambers³, Andria Stevens², Robert C Lynch⁴, Evanette Burrows⁵, Tamara P Miller⁶, Kelly D Getz⁷, Richard Aplenc⁷, Philip J Lupo³, Maria M Gramatges⁸, Michael E Scheurer³, Karen R Rabin⁸

¹ Baylor College of Medicine, Department of Pediatrics, Hematology/Oncology

² Texas Children's Hospital, Pediatrics, Hematology/Oncology

³ Texas Children's Hospital, Pediatrics, Epidemiology

⁴ Texas Children's Hospital, Pediatrics, Neonatology

⁵ Children's Hospital of Philadelphia, Pediatrics, Biomedical and Health Informatics

⁶ Children's Healthcare of Atlanta, Pediatrics, Hematology/Oncology

⁷ Children's Hospital of Philadelphia, Pediatrics, Hematology/Oncology

⁸ Texas Children's Hospital, Pediatrics, Hematology/Oncology

Background: Intensified therapy for pediatric acute lymphoblastic leukemia (ALL) has improved survival but increased risk of complications and treatment delays. The prognostic impact of delays prior to maintenance remains unclear.

Materials/Methods: To determine the impact of treatment delays on relapse-free survival (RFS) and overall survival (OS), we performed a retrospective review of patients diagnosed with ALL at two large academic centers in the Leukemia Electronic Abstraction of Records Network (LEARN).

Results: Among 536 total patients, 31 experienced extreme toxicities necessitating major therapy modification, and were analyzed separately. The remaining 505 patients were divided into quartiles based on cumulative days of delay to start of maintenance. Patients in the highest quartile were more likely to be older, Hispanic or Asian, and treated on a high-intensity regimen. Overall, patients in the upper quartile did not have poorer 5-year RFS or OS compared with the other three quartiles, but those who received standard-intensity treatment had a significantly poorer RFS (70.9% vs 91.0%, $p=0.0452$). The 31 patients with extreme toxicities were more likely to be older, Hispanic or black, treated on a high-intensity regimen, and have T-ALL. This group had an inferior 5-year RFS (3.0 vs. 4.8 years; $p<0.001$) and OS (3.3 vs. 4.9 years; $p<0.001$) compared with the remainder of the cohort.

Conclusions: Our data suggest that delays in ALL treatment prior to the start of maintenance impact survival for those patients in the upper quartile for delays despite receiving standard-intensity treatment, and those who experience extreme toxicities resulting in major therapy modification.