

# Incidence and outcomes of treatment-associated hepatotoxicity during pediatric acute lymphoblastic leukemia induction therapy: a Reducing Ethnic Disparities in Acute Leukemia (REDIAL) Consortium report

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Ashley N. Chavana,<sup>1</sup> Emily J. Mason,<sup>1,2</sup> John P. Woodhouse,<sup>1,2</sup> Olga A. Taylor,<sup>1,2</sup> M. Monica Gramatges,<sup>1,2</sup> Joanna S. Yi,<sup>1,2</sup> Sandi Pruitt,<sup>3,4</sup> M. Brooke Bernhardt,<sup>5</sup> Kathleen Ludwig,<sup>6</sup> Laura Klesse,<sup>4,6</sup> Kenneth Heym,<sup>7</sup> Timothy Griffin,<sup>1,2</sup> Marley Roberts,<sup>1</sup> Rodrigo Erana,<sup>8</sup> Juan Carlos Bernini,<sup>8</sup> Hong Zhu,<sup>9</sup> Philip J. Lupo,<sup>1,2</sup> Karen R. Rabin,<sup>1,2</sup> Michael E. Scheurer,<sup>1,2</sup> Steven D. Mittelman,<sup>10</sup> Van Huynh,<sup>11</sup> Etan Orgel<sup>12#</sup> and Austin L. Brown<sup>1,2#</sup>

<sup>1</sup>Baylor College of Medicine, Department of Pediatrics, Division of Hematology/Oncology, Houston, TX; <sup>2</sup>Texas Children's Cancer and Hematology Centers, Houston, TX; <sup>3</sup>University of Texas Southwestern Medical Center, Peter O'Donnell Jr. School of Public Health, Dallas, TX; <sup>4</sup>Harold C. Simmons Comprehensive Cancer Center, Dallas, TX; <sup>5</sup>St. Jude Children's Research Hospital, Department of Pharmacy and Pharmaceutical Sciences, Memphis, TN; <sup>6</sup>University of Texas

Southwestern Medical Center, Department of Pediatrics, Dallas, TX; <sup>7</sup>Cook Children's Medical Center, Department of Hematology/Oncology, Fort Worth, TX; <sup>8</sup>Vannie E. Cook Children Cancer and Hematology Clinics, McAllen, TX; <sup>9</sup>University of Virginia School of Medicine, Division of Biostatistics, Charlottesville, VA; <sup>10</sup>University of California, Los Angeles, David Geffen School of Medicine, Division of Pediatric Endocrinology, Los Angeles, CA; <sup>11</sup>Children's Hospital of Orange County, University of California Irvine College of Medicine, Orange, CA and <sup>12</sup>Children's Hospital Los Angeles, Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA

*#EO and ALB contributed equally as senior authors.*

Correspondence:

A. L. BROWN - [austin.brown@bcm.edu](mailto:austin.brown@bcm.edu)

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## SUPPLEMENTAL FIGURES AND TABLES

Table S1. Clinical and demographic characteristics of the study cohort overall and stratifying on self-reported ethnicity

	Self-Reported Ethnicity			P-value <sup>1</sup>
	Overall N=1,865	Hispanic, all races N=1,099	Non-Hispanic, all races N=746	
Median age at diagnosis, yrs (range)	6.0 (1.0-22.3)	6.4 (1.0-22.3)	5.5 (1.0-21.5)	0.003
Age Group, n(%)				0.020
1-9 years	1,308 (70.2)	747 (68.0)	544 (73.0)	
≥10 years	556 (29.8)	352 (32.0)	201 (27.0)	
Biologic Sex, n(%)				0.110
Male	1,053 (56.5)	638 (58.1)	405 (54.3)	
Female	812 (43.5)	461 (41.9)	341 (45.7)	
Race, n(%)				<0.001
White	1,431 (76.7)	924 (84.1)	505 (67.7)	
Black	113 (6.1)	6 (0.6)	107 (14.3)	
Other	254 (13.6)	120 (10.9)	133 (17.8)	
Unknown	67 (3.6)	49 (4.5)	1 (0.1)	
Diagnosis and NCI Risk Group, n(%)				0.631
Standard Risk B-ALL	1,013 (54.4)	588 (54.8)	397 (56.5)	
High Risk B-ALL/T-ALL	849 (45.6)	484 (45.2)	305 (43.5)	
BMI Category at Diagnosis, n(%)				<0.001
Underweight/Normal Weight	1,089 (65.7)	600 (60.7)	477 (73.5)	
Overweight/Obese	568 (34.3)	389 (39.3)	172 (26.5)	
CTCAE AST Grade, n(%)				0.580
Grade <3	1,129 (91.6)	700 (91.9)	412 (90.9)	
Grade ≥3	104 (8.4)	62 (8.1)	41 (9.1)	
CTCAE ALT Grade, n(%)				0.001
Grade <3	1,180 (76.2)	676 (73.2)	489 (80.7)	
Grade ≥3	368 (23.8)	247 (26.8)	117 (19.3)	
CTCAE Total Bilirubin Grade, n(%)				0.036
Grade <3	985 (93.1)	614 (92.0)	356 (95.4)	
Grade ≥3	73 (6.9)	53 (8.0)	17 (4.6)	
Conjugated Bilirubin, n(%)				0.003
≤3 mg/dL	1,544 (97.0)	934 (96.1)	594 (98.7)	
>3 mg/dL	48 (3.0)	38 (3.9)	8 (1.3)	

<sup>1</sup> p-value based on t-test for continuous variables and chi-squared or Fisher's exact test for categorical variables

Abbreviations: acute lymphoblastic leukemia, ALL; National Cancer Institute, NCI; body mass index, BMI

Conjugated bilirubin data incomplete or unavailable on n=273 individuals during induction therapy

Table S2. Multivariable logistic regression models<sup>1</sup> for clinical factors associated with treatment-associated hepatotoxicity during induction therapy

	Grade ≥3 AST		Grade ≥3 ALT		Grade ≥3 Total Bilirubin		C. Bilirubin >3 mg/dL	
	OR (95% CI)	P-val	OR (95% CI)	P-val	OR (95% CI)	P-val	OR (95% CI)	P-val
Age at diagnosis, years	0.95 (0.88-1.03)	0.23	1.02 (0.97-1.07)	0.43	1.21 (1.09-1.33)	<0.01	1.07 (0.56-4.88)	0.29
Gender		0.50		0.10		0.71		0.89
Male	Ref		Ref		Ref		Ref	
Female	1.16 (0.74-1.82)		1.24 (0.96-1.60)		0.90 (0.53-1.55)		0.96 (0.50-1.82)	
Ethnicity		0.20		0.09		0.13		0.09
Non-Hispanic	Ref		Ref		Ref		Ref	
Hispanic	0.73 (0.46-1.18)		1.27 (0.96-1.67)		1.66 (0.86-3.19)		2.10 (0.90-4.91)	
Race								
White	Ref		Ref		Ref		Ref	
Black	0.38 (0.08-1.66)	0.20	0.24 (0.10-0.63)	<0.01	1.35 (0.28-6.61)	0.71	0.53 (0.06-4.46)	0.56
Other	1.26 (0.72-2.20)	0.42	1.43 (1.02-2.01)	0.04	1.30 (0.62-2.71)	0.49	1.15 (0.48-2.77)	0.75
Unknown	0.47 (0.06-3.62)	0.47	0.74 (0.33-1.64)	0.46	1.92 (0.48-7.73)	0.36	2.21 (0.59-8.37)	0.24
Diagnosis & NCI Risk Group		0.02		0.03		0.74		0.36
B-ALL Standard Risk	Ref		Ref		Ref		Ref	
B-ALL High Risk/T-ALL	1.94 (1.09-3.47)		0.68 (0.48-0.96)		1.17 (0.48-2.84)		1.66 (0.56-4.88)	
BMI Category at Diagnosis		0.65		0.72		0.90		0.27
Under/Normal Weight	Ref		Ref		Ref		Ref	
Overweight/Obese	0.81 (0.33-2.01)		1.09 (0.67-1.79)		1.09 (0.26-4.66)		0.37 (0.06-2.19)	
Age by BMI Interaction	1.10 (1.01-1.21)	0.03	1.04 (0.99-1.10)	0.09	0.99 (0.89-1.10)	0.83	1.16 (1.01-1.33)	0.04

<sup>1</sup>Logistic regression models adjusted for all variables included in the table

Abbreviations: aspartate aminotransferase, AST; alanine aminotransferase, ALT; odds ratio, OR; confidence interval, CI; National Cancer Institute, NCI; acute lymphoblastic leukemia, ALL; body mass index, BMI

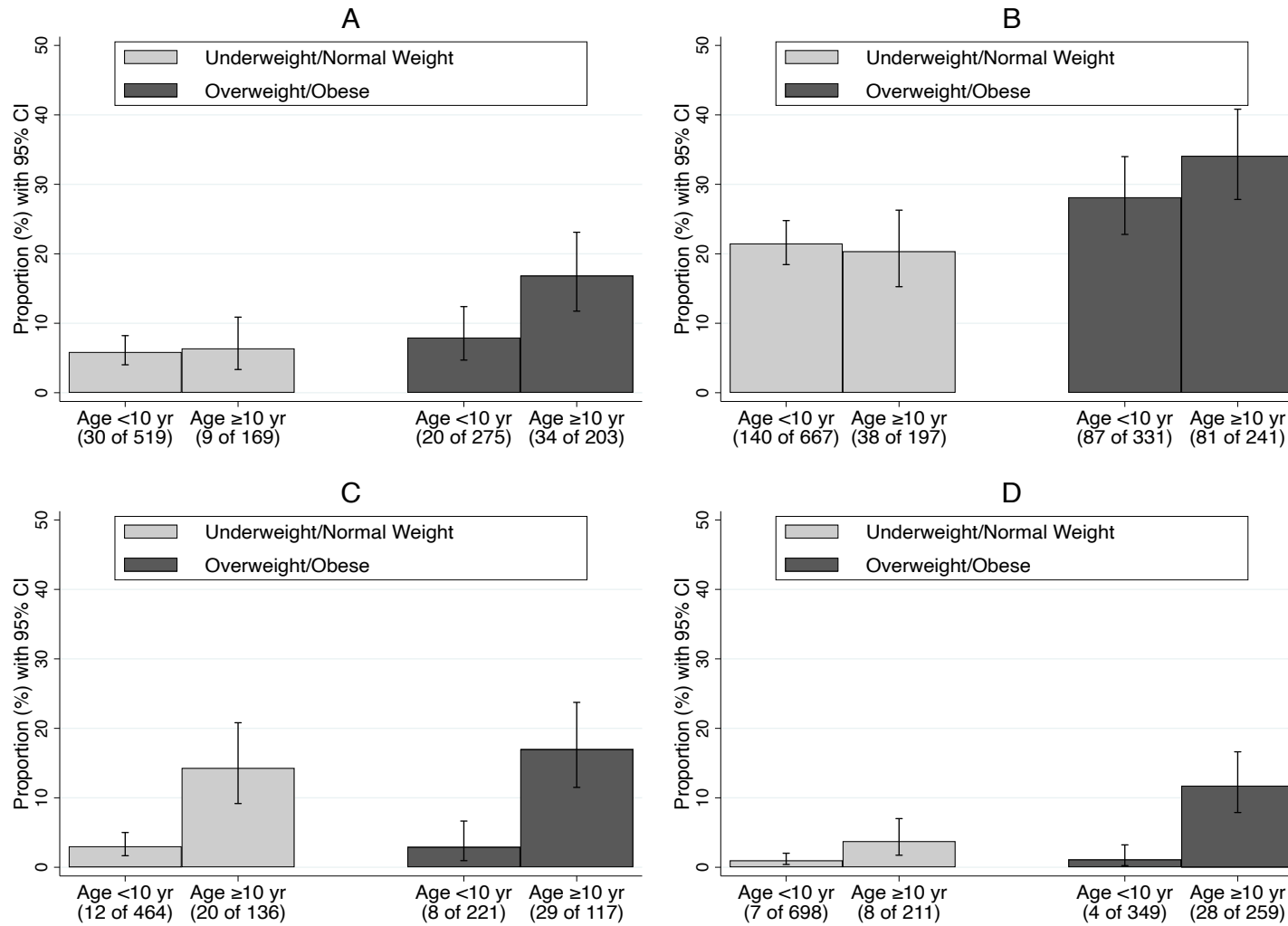


Figure S1. Incidence of CTCAE grade  $\geq 3$  aspartate aminotransferase (A), alanine aminotransferase (B), total bilirubin (C), and conjugated bilirubin  $>3$  mg/dL (D) during the induction phase of pediatric ALL therapy stratified by age group at ALL diagnosis and body mass index group.