Results from patient-derived xenograft models support co-administration of allopurinol and 6-mercaptopurine to reduce hepatotoxicity and improve event-free survival in pediatric acute lymphoblastic leukemia

Authors

Yixiao Mo,[1*] Qi Zhang,[1*] Miao Wang,[1,2*] Jihui Chen,[3*] Wenting Hu,[1] Changcheng Chen,[1] Yanjing Tang,[1] Zhuo Wang,[1] Jingjing Wang,[4] Xiaoxiao Chen[1] and Shuhong Shen[1]

[1]Department of Hematology/Oncology, Shanghai Children's Medical Center, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; [2]Department of Pediatrics, Henan Provincial People's Hospital, People's Hospital of Zhengzhou University, People's Hospital of Henan University, Zhengzhou, Henan, China; [3]Department of Clinical Pharmacy, Xinhua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China and [4]Crown Bioscience, Inc., San Diego, CA, USA

*YM, QZ, MW and JC contributed equally as first authors.

Correspondence:
S. SHEN - shenshuhong@scmc.com.cn
X. CHEN - cxxsunny9@aliyun.com

https://doi.org/10.3324/haematol.2024.286882

Received: October 29, 2024.
Accepted: January 7, 2025.
Early view: January 16 2025.

Supplemental Table 1. Characteristics of enrolled patients

Characteristic	Total n = 752	No ALLO Combination n = 603	ALLO combination n = 149	P value
Male sex, n (%)	489 (65.0)	392 (65.0)	97 (65.1)	1
Age[a], n (%)				0.03
<1	21 (2.8)	17 (2.8)	4 (2.7)	
1 to <5	404 (53.7)	313 (51.9)	91 (61.1)	
5 to <10	227 (30.2)	182 (30.2)	45 (30.2)	
≥10	100 (13.3)	91 (15.1)	9 (6.0)	
Risk stratification, n (%)				<0.001
Low risk	415 (55.2)	312 (51.7)	103 (69.1)	
Intermediate risk	337 (44.8)	291 (48.3)	46 (30.9)	
Immunophenotype, n (%)				0.006
B	670 (89.1)	528 (87.6)	142 (95.3)	
T	82 (10.9)	75 (12.4)	7 (4.7)	
Cytogenetic subtypes, n (%)				0.32
Hyperdiploidy	254 (33.8)	195 (32.3)	59 (39.6)	
TEL::AML1	137 (18.2)	106 (17.6)	31 (20.8)	
MLL-rearranged	29 (3.9)	22 (3.6)	7 (4.7)	
TCF3::PBX1	37 (4.9)	31 (5.1)	6 (4.0)	
BCR::ABL1	28 (3.7)	26 (4.3)	2 (1.3)	
MRD D19, n (%)				0.08
<0.01%	365 (48.5)	282 (46.8)	83 (55.7)	
0.01% to <0.1%	130 (17.3)	103 (17.1)	27 (18.1)	
0.1% to <1%	128 (17.0)	103 (17.1)	25 (16.7)	
≥1%	112 (14.9)	99 (16.4)	13 (8.7)	
MRD D46, n (%)				0.07
<0.01%	649 (86.3)	511 (84.7)	138 (92.6)	
0.01% to <0.1%	48 (6.4)	43 (7.1)	5 (3.4)	
≥0.1%	24 (3.2)	22 (3.6)	2 (1.3)	

[a]Data at diagnosis.

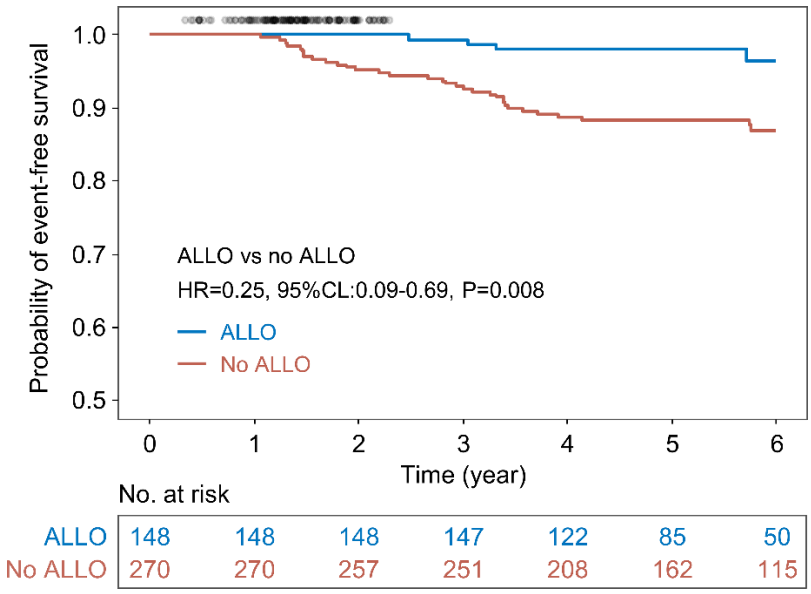
Abbreviations: ALLO, allopurinol; MRD, minimal residual disease.

Supplemental Table 2. Characteristics of enrolled patients after Propensity Score Matching

Characteristic	No ALLO Combination n = 270	ALLO combination n = 148	P value
Male sex, n (%)	176 (65.2)	96 (64.9)	0.95
Age[a], n (%)			0.91
<1	10 (3.7)	4 (2.7)	
1 to <5	156 (57.8)	90 (60.8)	
5 to <10	86 (31.9)	45 (30.2)	
≥10	18 (6.7)	9 (6.0)	
Risk stratification, n (%)			0.88
Low risk	188 (69.6)	102 (68.9)	
Intermediate risk	82 (30.4)	46 (30.9)	
Immunophenotype, n (%)			0.75
B	259 (95.9)	141 (95.3)	
T	11 (4.1)	7 (4.7)	
Cytogenetic subtypes, n (%)			0.86
Hyperdiploidy	96 (35.6)	58 (39.2)	
TEL::AML1	58 (21.5)	31 (20.8)	
MLL-rearranged	12 (4.4)	7 (4.7)	
TCF3::PBX1	14 (5.2)	6 (4.0)	
BCR::ABL1	7 (2.6)	2 (1.3)	
MRD D19, n (%)			0.81
<0.01%	141 (52.2)	83 (55.7)	
0.01% to <0.1%	49 (18.1)	27 (18.1)	
0.1% to <1%	53 (19.6)	24 (16.2)	
≥1%	21 (7.8)	13 (8.7)	

[a]Data at diagnosis.

Abbreviations: ALLO, allopurinol; MRD, minimal residual disease.



Supplemental Figure 1. Kaplan-Meier curves for event-free survival in allopurinol (ALLO) group and no allopurinol group. Propensity score matching was performed to balance baseline characteristics between the two groups. Black dots represent the time points when allopurinol treatment started. Hazard ratio (HR) with 95% confidence intervals (CI) and P values were estimated using the time-dependent Cox regression analysis.