

Pediatric blastic plasmacytoid dendritic cell neoplasms are molecularly defined by recurrent *MYB* rearrangements: clinical and molecular insights

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Supplementary Figure S1. Integrated clinicogenomic landscape of pediatric BPDCN (n=21).

Columns represent individual cases. Tracks depict specimen type used for molecular testing, assays performed, clinical involvement at diagnosis (skin, bone marrow [BM], lymph node [LN], and central nervous system [CNS]), treatment exposures, response and relapse, immunophenotype, structural variants (including *MYB*-region alterations), selected somatic variants, and copy-number alterations and tumor ploidy. Colors and symbols are defined in the key; “*” denotes venetoclax exposure and “&” denotes CD123-directed CAR T-cell therapy. Percentages are calculated using cases with available data, and denominators vary by feature.

Abbreviations: BM, bone marrow; CNS, central nervous system; CN-LOH, copy-neutral loss of heterozygosity; CNV, copy-number variation; HSCT, hematopoietic stem cell transplant

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Specimen for molecular test																						
RNA sequencing/RNA fusion panel																						
Whole-exome/genome sequencing																						
Targeted sequencing (DNA-based)																						
Clinical information		No./N (%)																				
Gender, Male	12 (57)																					
Initial skin involvement	16 (80)																					
Initial BM involvement	9 (56)																					
Initial LN involvement	8 (57)																					
CNS involvement	5 (45)																					
Remission during therapy	17 (100)																					
Relapse	2 (12)																					
ALL-type therapy	16 (94)			*		*&	*															
HSCT	2 (12)																					
Outcome, alive	15 (88)																					
Immunophenotype																						
CD56+	21 (100)																					
CD123+	21 (100)																					
TCF4+	6 (100)																					
Rearrangements (tested cases, n=12)																						
MYB::PLEKHO1	2 (17)																					
MYB::DCPS	4 (33)																					
MYB::ZFAT	1 (8)																					
MYB trunc	2 (17)																					
MYBL1::MTFR1	1 (8)																					
ETV6 translocation/trunc	1 (8)																					
HBS1L::UGCG	1 (8)																					
Mutations (tested cases: SNV/indels, n= 14; CNV, n= 7)																						
NRAS	6 (43)																					
KRAS	2 (14)																					
RB1	2 (14)																					
KMT2C/KMT2D	2 (14)																					
CDKN1C	1 (7)																					
NF1	1 (7)																					
IKZF1	1 (7), 3 (43)																					
TP53	1 (7), 1 (14)																					
ABL1 deletion	2 (28)																					
ETV6 deletion	2 (28)																					
CDKN2A	3 (43)																					
CDKN2B	3 (43)																					
JAK1/2 deletion	2 (28)																					
NOTCH1 deletion	2 (28)																					
TCF4 deletion	1 (14)																					
Tumor ploidy& cytogenetics (tested cases, n=7)																						
9q deletion/monosomy	6 (86)																					
12p deletion	6 (86)																					
13q deletion/monosomy	6 (86)																					
17p deletion	4 (57)																					
6q deletion	3 (43)																					
5q deletion/gain	2 (28)																					

Bone marrow
Soft tissue
Skin

0 Frequency (%) 100



Yes/Positive
No/Negative
Not available/Not tested
Inadequate RNA quality

Structural variants
SNV/indels
CNV

Complex karyotype
* Venetoclax therapy
& CD123 CAR-T cell therapy

Supplementary Table S1. Clinical, cytogenetic, and molecular findings in the pediatric blastic plasmacytoid dendritic cell neoplasm cohort (n = 21).

Case no.	Treatment	Follow-up, mo	Response; Outcome	Specimen; Molecular test method	Fusion; Variants (SNV/indel; CNV)	Coordinates/description	Tumor ploidy (CNV/CN-LOH); Karyotype
Case 1	ALL-type therapy	10	Remission; Alive	Skin; RNA-seq, WES	<i>MYB::PLEKHO1</i> t(1;6)(q21.2;q23.3); <i>KRAS</i> G12C	chr6:135196002::chr1:150158819	
				Bone marrow; RNA-seq, WES, WGS	Not detected		
Case 2	ALL-type therapy	12	Remission; Alive	Skin; RNA-seq, WES	<i>MYB::PLEKHO1</i> t(1;6)(q21.2;q23.3); <i>CNOT3</i> E70K, <i>NRAS</i> Q61P, <i>RB1</i> c.-197G>A, <i>TCF4</i> deletion (1 copy)	chr6:135517140::chr1:150131014	Loss: 5q23, chr. 9, 12p, chr.13, chr.Y; Gain: none; CN-LOH: none
Case 3	ALL-type therapy; Venetoclax	12	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	<i>MYB::DCPS</i> t(6;11)(q23.3;q24.2); Not detected		
Case 4	ALL-type therapy	50	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	<i>MYB</i> structural variant (truncated); <i>NRAS</i> Q61H	Structural variant involving <i>MYB</i> (C-terminal truncation of <i>MYB</i> after exon 9).	
Case 5	ALL-type therapy; Venetoclax; tagraxofusp	23	Remission/relapse; Alive with disease	Bone marrow; RNA-seq, WES, WGS	<i>MYB::DCPS</i> t(6;11)(q23.3;q24.2); <i>ETV6</i> trunc t(8;12)(q24.3;p13.2); <i>RB1</i> C712R, <i>TP53</i> P278S, <i>CDKN2A/CDKN2B</i> deletion (1 copy each), <i>NR3C1</i> del, <i>MUTYH</i> Ala385ProfsTer23 (germline)	chr6:135515600::chr11:126176465	Loss: 2q32.1-q37.3, 6q23.3-q27, 8p23.3-q13.1, 9q12-q31.3, 10p15.3-p11.22, 17p13.3-q11.2, 22q11.21-q13.33; Gain: 5q34-q35.3, 11q13.4-q24.2, 11q24.2-q25; CN-LOH: none; Karyotype: Complex; involving del(6)(q?23),del(12)(p?12),-17
Case 6	ALL-type therapy; Venetoclax	5	Remission; Alive, treatment abandoned	Skin; RNA-seq, WES	<i>HBS1L::UGCG</i> t(6;9)(q23.3;q31.3); <i>NRAS</i> G12S, <i>IKZF1</i> Q149*	chr6:135359170::chr9:114688664	
Case 7				Skin; RNA-seq, NGS (DNA-based)	<i>MYB::DCPS</i> t(6;11)(q23.3;q24.2); <i>NRAS</i> G12D, <i>KMT2D</i> Q5170*		
Case 8	ALL-type therapy	120	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	<i>MYB</i> structural variant (truncated); Not detected	Structural variant involving <i>MYB</i> (C-terminal truncation of <i>MYB</i> after exon 9).	
Case 9	ALL-type therapy	108	Remission; Alive	Bone marrow; RNA-seq	<i>MYB::ZFAT</i> t(6;8)(q23;q24)	chr6:135517140::chr8:135529901	46,XX,t(2;9)(q37;q13),add(3)(p25),add(12)(p11.2),del(13)(q12),del(14)(q13);46,XX(3)
Case 10				Skin; RNA-seq, NGS (DNA-based)	Not detected; Inadequate DNA quality		
Case 11	ALL-type therapy	72	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	Inadequate RNA quality; <i>KRAS</i> Q61R		69-79 (unbanded)[7/41], 84-90 (unbanded)[2/11], 46,XY[8/47]
Case 12	ALL-type therapy	144	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	Inadequate RNA quality; <i>CDKN1C</i> p.208_210del		
Case 13	ALL-type therapy	132	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	Inadequate RNA quality; <i>KMT2C</i> Q1186*		
Case 14	ALL-type therapy	84	Remission; Alive	Skin; RNA-seq; NGS (DNA-based)	Inadequate DNA& RNA quality		45,XY,-9,del(12)(p11.2),-13,del(17)(p11.2),+mar(20)
Case 15				Skin; RNA-seq; NGS (DNA-based)	Inadequate DNA& RNA quality		
Case 16	ALL-type therapy	168	Remission; Alive	Skin; RNA-seq; NGS (DNA-based)	Inadequate DNA& RNA quality		
Case 17	AML-type therapy	17	Remission/relapse; Died				
Case 18	ALL-type therapy	48	Remission; Alive				
Case 19	ALL-type therapy	8	Remission; Died (infection)	Bone marrow; NGS (DNA-based)			Loss: 1p (<i>JAK1</i>), 7p (<i>IKZF1</i>), 9q (<i>ABL1</i> & <i>NOTCH1</i>), 17p (<i>PRPF8</i> & <i>TP53</i>); Gain: Xq (<i>BRCC3</i>); Karyotype: 83~85,XXYY,-3,add(6)(q11),del(6)(q13q23),add(7)(p11.2),-8,-9,add(11)(p15),-12,-13,-13,-14,-15,-17,add(17)(p11.1),-18,+0~4mar[cp8]/46,XY[12]
Case 20	ALL-type therapy	17	Remission; Alive	Bone marrow; RNA fusion panel (Archer); NGS (DNA-based)	<i>MYB::DCPS</i> ; <i>NRAS</i> A146V, <i>NF1</i> H586fs		Loss: 7p (1 copy <i>IKZF1</i>), 9p (1 copy deletion <i>JAK2</i> , <i>CDKN2A</i> , <i>CDKN2B</i>); 9q (1 copy deletion <i>ABL1</i> , <i>NOTCH1</i>); 11q (1 copy deletion <i>ATM</i> , <i>KMT2A</i> , <i>CBL</i>), 12p (1 copy deletion <i>ETV6</i>); Karyotype: 43~44,XX,del(6)(q23q27),-9,del(11)(q21q23),der(12)t(12;14)(p13;q11.2),-13,-14,add(17)(p11.2),+0~1r[cp5]/46,XX[15]
Case 21				Nasal soft tissue; RNA fusion panel (Archer); NGS (DNA-based)	<i>MYBL1::MTFR1</i> ; <i>NRAS</i> G12A		Loss: 7p (<i>IKZF1</i>), 9p (<i>CDKN2A/CDKN2B/MTAP</i>), 3p, 9q, 12p, 13q, and 17p

Abbreviations: CN-LOH, copy-neutral loss of heterozygosity; CNV, copy-number variation; mo, months; NGS, next-generation sequencing; RNA-seq, RNA sequencing; SNV, single-nucleotide variant; WES, whole-exome sequencing; WGS, whole-genome sequencing. When multiple specimens were tested for a case, the results are listed on separate rows (case 1).

Supplementary Table S2. Clinical and molecular findings in pediatric patients (≤ 20 years old) investigated by molecular tests: literature review. Patients with *MYB* alteration (including cases with presumptive *MYB* alteration of 6q abnormality based on cytogenetics) are highlighted in pink.

References:

1. Karube K, Ohshima K, Tsuchiya T, et al. Non-B, non-T neoplasms with lymphoblast morphology: further clarification and classification. *Am J Surg Pathol*. 2003;27(10):1366-1374.
2. Rossi JG, Felice MS, Bernasconi AR, et al. Acute leukemia of dendritic cell lineage in childhood: incidence, biological characteristics and outcome. *Leuk Lymphoma*. 2006;47(4):715-725.
3. Jegalian AG, Buxbaum NP, Facchetti F, et al. Blastic plasmacytoid dendritic cell neoplasm in children: diagnostic features and clinical implications. *Haematologica*. 2010;95(11):1873-1879.
4. Sun W, Liu H, Kim Y, et al. First pediatric experience of SL-401, a CD123-targeted therapy, in patients with blastic plasmacytoid dendritic cell neoplasm: report of three cases. *J Hematol Oncol*. 2018;11(1):61.
5. Kohso A, Toyoda H, Morimoto M, et al. Acute Liver Failure in a 17-Year-Old Boy Caused by a Blastic Plasmacytoid Dendritic Cell Neoplasm With a Novel *MYB* Rearrangement. *Pediatr Blood Cancer*. 2025;72(3):e31542.
6. Kosasih HJ, Healey G, Brennan MS, et al. A novel *MYB::PAIP1* oncogenic fusion in pediatric blastic plasmacytoid dendritic cell neoplasm (BPDCN) is dependent on *BCL2* expression and is sensitive to venetoclax. *Hemasphere*. 2024;8(2):e1.
7. Suzuki K, Suzuki Y, Hama A, et al. Recurrent *MYB* rearrangement in blastic plasmacytoid dendritic cell neoplasm. *Leukemia*. 2017;31(7):1629-1633.
8. Li R, Kuang W, Yang H, et al. Single cell sequencing deciphering the heterogeneous landscape of blastic plasmacytoid dendritic cell neoplasm with novel *MYB-ZFAT* fusion gene. *Cancer Cell Int*. 2025;25(1):274.
9. Yigit N, Suarez LF, Roth LG, Orazi A, Tam W. CD4-Negative Variant of Cutaneous Blastic Plasmacytoid Dendritic Cell Neoplasm With a Novel *PBRM1* Mutation in an 11-Year-Old Girl. *Am J Clin Pathol*. 2017;147(5):453-460.
10. Diness BR, Risom L, Frandsen TL, et al. Putative new childhood leukemia cancer predisposition syndrome caused by germline bi-allelic missense mutations in *DDX41*. *Genes Chromosomes Cancer*. 2018;57(12):670-674.
11. Liao C, Hu NX, Song H, et al. Pediatric blastic plasmacytoid dendritic cell neoplasm: report of four cases and review of literature. *Int J Hematol*. 2021;113(5):751-759.
12. Yu B, Liu C, Qin P, Li Q, Li X. Blastic Plasmacytoid Dendritic Cell Neoplasm Presenting as a Mammary Gland Tumor in a Pediatric Patient: A Case Report. *Int J Surg Pathol*. 2024;32(5):1051-1057.
13. He J, Garcia MB, Connors JS, et al. Frontline Hyper-CVAD Plus Venetoclax for Pediatric Blastic Plasmacytoid Dendritic Cell Neoplasm. *J Pediatr Hematol Oncol*. 2023;45(8):e1001-e1004.

14. Sumarriva Lezama L, Chisholm KM, Carneal E, et al. An analysis of blastic plasmacytoid dendritic cell neoplasm with translocations involving the MYC locus identifies t(6;8)(p21;q24) as a recurrent cytogenetic abnormality. *Histopathology*. 2018;73(5):767-776.
15. Liu H, Li S. Pediatric blastic plasmacytoid dendritic cell neoplasm, acute leukemic variant. *Blood*. 2015;126(25):2764.
16. Fei F, Telatar M, Tomasian V, et al. Genetic characteristics of blastic plasmacytoid dendritic cell neoplasm: A single institution experience. *Oncotarget*. 2025;16:495-507.
17. Chen X, Wang J, Hao W, et al. Case Report: Early diagnostic precision matters: navigating therapeutic uncertainty in pediatric BPDCN illustrated by misdiagnosis sequelae and fleeting CAR-T response. *Front Pediatr*. 2026;13:1710591.

Supplementary Table S2 is provided as a separate Excel file.