



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Clinical Pathology Characteristics of 221 Pediatric Anaplastic Large Cell Lymphoma-3 Years Follow up and Experience from China Net Childhood Lymphoma(CNCL)

Shuang Huang¹, Xiaomei Yang², Yanlong Duan¹, Ling Jin¹, Fu Li², Mincui Zheng³, Pan Wu³, Ying Liu⁴, Bo Hu⁴, Yunpeng Dai⁵, Guotao Guan⁵, Ansheng Liu⁶, Shuang Qin⁶, Lirong Sun⁷, Jian Jiang⁷, Wei Liu⁸, Jianwen Zhou⁸, Jian Wang⁹, Lijun Qu⁹, Leping Zhang¹⁰, Yueping Jia¹⁰, Xiaojun Yuan¹¹, Yushuang Dong¹¹, Baoxi Zhang¹², Lian Jiang¹³, ZhuJun Wang¹⁴, XiGe Wang¹⁵, Shuquan Zhuang¹⁶, Chunju Zhou¹⁷, Zifen Gao¹⁸, Jing Yang¹, Yonghong Zhang⁴

¹ Department of Pediatric Oncology, National Center for Children's Health, Beijing Children's Hospital, Capital Medical University, Beijing, China

² Department of Pediatric Hematology/Oncology, Shandong University Affiliated Hospital (Jinan Children's Hospital), Jinan, China

³ Department of Hematology, Hunan Children's Hospital, Changsha, China

⁴ Department of Pediatric Lymphoma, Beijing Gobroad Boren Hospital, Beijing, China

⁵ Department of Pediatrics Hematology and Endocrinology, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, China

⁶ Department of Hematologic Oncology, Xi'an Children's Hospital, Xi'an, China

⁷ Department of Pediatric Hematology and Oncology, Affiliated Hospital of Qingdao University, Qingdao, China

⁸ Department of Hematology & Oncology, Zhengzhou Children's Hospital, Zhengzhou, China

⁹ Department of Hematology and Oncology, Anhui Provincial Children's Hospital, Hefei, China

¹⁰ Department of Pediatrics, Peking University People's Hospital, Beijing, China

¹¹ Department of Pediatric Hematology and Oncology, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China

¹² Department of Pediatrics, The Second Hospital of Hebei Medical University, Shijiazhuang, China

¹³ Department of Pediatrics, The fourth Hospital of Hebei Medical University, Shijiazhuang, China

¹⁴ Department of Pediatrics, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

¹⁵ Department of Pediatrics, the Third Affiliated Hospital of Zhengzhou University, Zhengzhou, China

¹⁶ Department of Pediatric, Quanzhou First Hospital Affiliated to Fujian Medical University, Quanzhou, China

¹⁷ Department of Pathology, National Center for Children's Health, Beijing Children's Hospital, Capital Medical University, Beijing, China

¹⁸ Department of Pathology, Peking University Third Hospital, Beijing, China

Objective: To investigate the clinical-pathology characteristics, risk factors, necessary for VBL maintenance therapy, through summarize the clinical data of 221 cases of pediatric Anaplastic Large Cell Lymphoma (ALCL), treated with CNCL-ALCL-2017 witch is modify from BFM-ALCL-99 (\pm vincristine maintenance therapy) in China Net Childhood Lymphoma (CNCL).

Methods: Data were collected on 221 children with ALCL enrolled from CNCL at time between April 2017 to March 2023, including: numbers of cases enrolled in each single center, gender and age at the time of initial diagnosis, the first initial symptom, a delay diagnosis, the misdiagnosis disease, the site of involvement, the level of blood uric acid, the level of blood lactate dehydrogenase, the bone marrow and CNS status, tumor complication, complicated with HLH, staging and treatment subgroups, pathological subtypes, CD3 expression in tumor tissue, bone marrow and peripheral blood ALK gene expression at initial diagnosis (qPCR + FISH), and treatment outcomes, treatment strategy(vincristine maintenance or not), time from initial diagnose to relapse, second-line treatment regimen after relapse, and treatment outcomes after relapsed. Statistical analysis was conducted using SPSS 21.0 software.

Results: 221 cases were from 22 hospitals in China. Male = 144 cases, female = 71 cases, age range from 1-16 years (median age 8.9 years), duration from initial symptoms onset to diagnosis was 0.3-11 months (median time 1.0 months), delayed diagnosis was present in 51(23%) children (45 children were misdiagnosed with infectious diseases). Pathological subtypes

were: common sub type = 150(67.8%), small cell sub type = 19(8.5%), histiocytic variant subtype = 9(4%), ALK negative subtype = 12(5.4%).others = 31(14%). CD3 expression in tumor: negative = 119, positive = 91. ALK positive by qPCR in peripheral blood at the time of the initial diagnosis = 77, ALK positive by qPCR in bone marrow = 78, bulky disease= 21, mediastinal invasion = 84, CNS invasion = 17, skin invasion = 32. tumor related HLH = 25, normal LDH level at initial diagnosis = 133, 1-fold elevated = 45, 2-3-fold elevated = 39, 4-fold elevated = 2, >4-fold elevated = 2, stage I = 5, stage II = 24, stage III = 70, stage IV = 120 , leukemic stage = 2 . Grouping: group A = 1, group B = 21, group C = 191, group D = 8. Vincristine maintenance = 121. Median follow-up time was 35.4 months (0.5-74.9 months), OS at 3 years = 95.1±1.5% (95% CI = 90%-97.3%, Fig. 1), EFS at 3 years = 84.7±4.5% (95% CI = 79%-89.9%, Fig. 2), and there were a total of 23 patients with events, median time was 7 months. There were 10 patients died, 5 of them quit to the treatment, median time was 5 months, and 13 patients who had an event but still alive after second line treatment. Univariate results of the 3 years EFS are detailed in Table 1, with statistically significant including (<0.05): tumor related HLH before treatment, LDH levels higher than 4 times normal and MDD positive at the beginning of the disease, and treated without VBL. The event patients are 23 cases ,the detailed in Table 2, which showed that the earlier the event occurs, the higher the mortality rate.

Conclusion: Pediatric ALCL in China is mostly found in school-age boys, and it is easy to be diagnosed as infectious diseases at the time of initial diagnosis due to high fever and elevated CRP. 87% of patients were diagnosed as late stage or high-risk group. The application of the CNCL-ALCL-2017 protocol showed a 3-year OS 84.7% and 3-year EFS 95.1%, indicating that the efficacy was significantly better than that of various centers before the multi center cooperation. The overall survival time is significantly better than the event free survival time, indicating that most patients with progression and recurrence still have a chance of re remission after second line treatment. Adverse prognostic factors include a significant increase in LDH levels at initial diagnosis, initial onset of HLH, positive MDD before treatment, and no use of vinblastine maintenance therapy. Recurrent children: The median recurrence time is 7 months, and the prognosis of early progression and recurrence is worse than that of late recurrence.

Key words: Anaplastic large cell lymphoma, Pediatric, Clinical-pathology features, Prognosis

Disclosures No relevant conflicts of interest to declare.

Figure 1, OS at 3 years in 221 children with ALCL

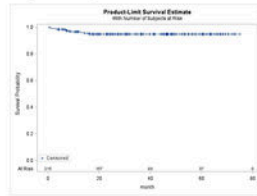


Figure 2, EFS of 221 children with ALCL at 3 years

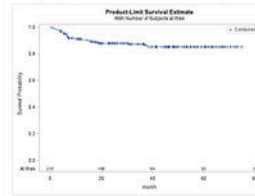


Table 1, results of univariate analysis of 221 cases of childhood mesenchymal large cell lymphoma

consideration	3 years EFS	P-value	consideration	3 years EFS	P-value
Pathological type			Mediastinal invasion		
Common type n=150	81.1±3.9%	0.65	None n=137	88.8±2.9%	0.58
Small cell type n=19	89.5±3.7%		With n=84	66.5±3.4%	
Histologic variant n=9	87.5±3.7%				
ALK negative n=12	81.8±5.6%				
CD3 expression					
Negative n=119	82.2±3.7%	0.14			
Positive n=92	85.7±4.2%				
Peripheral blood of ALK expression by qPCR detection			Central nervous system violations		
Negative n=69	92.9±2.8%	0.05	None n=204	83.3±5.3%	0.42
Positive n=77	75.1±6.8%		With n=17	94.1±5.7%	
Bone marrow of ALK gene expression by qPCR detection			Completed with HLH at the beginning of the disease		
Negative n=83	92.3±3.7%	0.07	None n=196	85.3±5.9%	0.018
Positive n=78	72.4±1.9%		With n=25	71.4±4.2%	
Peripheral blood of ALK gene by FISH detection			clinical staging		
Negative n=75	95.8±2.4%	0.06	I n=7	100%	0.64
Positive n=31	77.3±2.6%		II n=26	76.2±17.4%	
Bone marrow of ALK gene by FISH detection			III n=116	86.7±3.4%	
Negative n=56	85.8±5.9%	0.09	IV n=74	89±4%	
Positive n=31	77.3±2.6%		LDH level		
gene name			Normal n=131	84.9±7.2%	0.02
None n=200	84.2±3.3%	0.8	1-fold elevated n=45	92.9±4%	
With n=21	88.8±4.1%		2-fold elevated n=39	76.7±7.5%	
			3-fold elevated n=2	50±3.5%	
			>4-fold elevated n=2	50±3.4%	
			Therapeutic grouping		
			Group A n=1	100%	0.56
			Group B n=21	100%	
			Group C n=191	81.4±6.1%	
			Group D n=8	87.5±11.7%	
			Treated with VBL		
			Yes n=121	92±2.6%	0.03
			No n=100	67.3±15.4%	

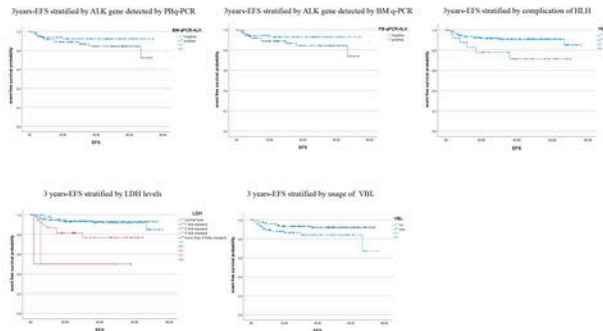


Table 2 Details of 23 events patients

serial number	Event Type	EFS (months)	OS (months)	Fluore/antibody therapy	is or isn't dead
1	Death from CNS progression on treatment	5	6	not have	dead
2	VELBL then progressed after 1 month of maintenance, and the original disease progressed and died 6 months after second-line treatment	8	15	VBL (primary diagnosis)PD-1 (post relapse)	dead
3	Always positive for ALK by PCR, CNS relapse during maintenance	15	70	VBL (primary diagnosis)Erlotinib (after relapse)	survive (a serious accident)
4	Death from tumor complications due to progression of primary disease during treatment	7	7	not have	dead
5	Tumor Progress in Therapy	7	67	VBL (post relapse)Crizotinib (after relapse)	survive (a serious accident)
6	Comprehensive tumor progression in maintenance therapy	9	64	VBL (primary diagnosis)Erlotinib (after relapse)	survive (a serious accident)
7	Progress in treatment Abandonment of treatment	2	3	not have	dead
8	Central nervous system relapse during maintenance	18	60	VBL (primary diagnosis)Erlotinib (after relapse)	survive (a serious accident)
9	Progression on therapy, death from tumor progression despite second-line therapy	4	10	VBL (initial diagnosis + post relapse)Crizotinib, erlotinib (sequential application after relapse)	dead
10	Death from tumor complications	1	1	All are applications	dead
11	Poor response to early treatment, poor tumor resection, CNS relapse	15	26	VBL (primary + relapse)Crizotinib (initial diagnosis)Erlotinib (relapse)	survive (a serious accident)
12	Tumor recurrence with elevated bone marrow ALK gene	12	44	VBL (post relapse)Centinib, Loratinib (sequential application after relapse)allogeneic hematopoietic stem cell transplantation	survive (a serious accident)
13	Progress in treatment	5	32	second-line chemotherapy	an unauthorized visit
14	Progress in maintenance therapy	36	60	VBL (first diagnosis, recurrence should be applied)Crizotinib (after relapse)	survive (a serious accident)
15	Death from tumor progression	3	3	not have	dead
16	Death from tumor progression after transplantation	6	12	not haveallogeneic hematopoietic stem cell transplantation	dead
17	Progress in treatment	3	30	not have	survive (a serious accident)
18	Relapse off medication (ALK reversion)	30	30	None (2023.7 recurrence)	survive (a serious accident)
19	Progress in treatment (tumor foci)	5	27	VBL (primary diagnosis)ALK antibody (post-progression)	survive (a serious accident)
20	Deaths progressing in treatment	9	9	not have	dead
21	Relapse (ALK transitions)	20	27	VBL (none)Crizotinib maintenance (after relapse)	survive (a serious accident)
22	early relapse	7	21.9	VBL (none)Crizotinib (after relapse)	survive (a serious accident)
23	recur (of a disease)	5	17	VBL (none at first diagnosis)Erlotinib, Loratinib, Allogeneic Stem Cell Transplantation	dead

Figure 1

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