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POSTER ABSTRACTS

612.ACUTE LYMPHOBLASTIC LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

The Different Impacts of an MRD-Guided Protocol on Relapse of Childhood Acute Lymphoblastic Leukemia: The Report of Taiwan Pediatric Oncology Group (TPOG)-ALL-2013

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Taiwan Pediatric Oncology Group (TPOG)-ALL-2013 protocol (TPOG-2013), modifying from St. Jude Total Therapy XV Study and Total Therapy XVI Study, was launched since January 2013. This is the first nationwide minimal residual disease (MRD)-directed protocol for treatment of childhood acute lymphoblastic leukemia (ALL) in Taiwan. According to TPOG-2013, two MRD measurements were scheduled on days 15-19 of induction (MRD1 time point, TP1) and days 35-42, end of induction (MRD2 time point, TP2) to make the definitive risk stratification to guide subsequent therapy.

As of April 30, 2023, 814 newly diagnosed ALLs treated with TPOG-2013 and followed up \geq 3 years were enrolled in the study. The outcomes were compared with those of TPOG-ALL-2002 protocol (TPOG-2002) (N=1350, between January 2002 and December 2012), which did not integrate the MRD monitoring. The 5-year event-free survival and overall survival were significantly improved from 76% (95% CI, 74-78) and 81% (80-84) of TPOG-2002 to 86% (83-88) and 89% (87-92) of TPOG-2013, respectively (P< 0.0001).

For further analysis of TPOG-2013, 585 (72%) patients with exact adherence (EA) to both TPs were assigned as MRD EA group; 225 patients who were non-adherence (NA) to either one of TPs as MRD NA group; and four patients were excluded for the comparative outcome analysis. For B-cell precursor (BCP) ALL, the 5-year cumulative incidence of relapse (CIR) significantly decreased from TPOG-2002 (N=1194) to TPOG-2013 MRD EA (N=527) (P < 0.0001). However, there was no significant improvement of CIR between TPOG-2002 and MRD NA (N=202) (P = 0.21) (Figure 1). In MRD EA of BCP-ALL, compared with TPOG-2002, patients with *ETV6::RUNX1* or *BCR::ABL1* appeared to have significantly lower CIR. Patients without the common genetic subtypes , denoted as "negative" group, also had significant inferior CIR. And the trend of CIR decrease did not attain significant difference in high hyperdiploidy. In contrast, patients with *TCG3::PBX1* or infant with *KMT2A*-rearrangement did not show CIR improvement (Table 1). In T-ALL, compared with TPOG-2002 (N=156), there was a significant decrease of CIR in TPOG-2013 MRD EA (N=23)(P = 0.86).

There was a longer duration to relapse in MRD EA of BCP-ALL. However, a delay of relapse was only demonstrated in patients with *BCR::ABL1*, which could be addressed by the introduction of MRD-monitoring and TKI inhibitor in TPOG-2013 (Table 1). Further, in term of early relapse before 1.5 year of remission, there was no significant difference in MRD EA of BCP-ALL, compared with TPOG-2002.

In conclusion, this study demonstrated diffident impacts on relapse according to genetic subtypes and MRD adherence. In the negative group of BCP-ALL without the discovery of novel genetic alternations, the relapse could be much decreased with the MRD-directed treatment protocol.

Disclosures No relevant conflicts of interest to declare.



Figure 1. The Cumulative Incidence of Relapse in B-cell Precursor ALL. EA, exact adherence; NA, non-adherence

Table 1.

	5- year Cumulative incidence of relapse					Time to relapse				
	TPOG-ALL-2002		TPOG-ALL-2013			TPOG-ALL-2002		TPOG-ALL-2013		
	No.	Median (95% CI)	No.	Median (95% CI)	P	No.	Median (95% CI), Year	No.	Median (95% CI), Year	Р
Total	1350	21.6% (19.3-23.8)	814	11.4% (9.1-13.7)	<0.0001	308	2.0 (1.6-2.3)	90	2.1 (1.9-2.8)	0.9
2002 vs 2013 MRD EA										_
BCP-ALL	1194	21.7% (18.7-23.5)	527	8.5% (5.9-11.1)	<0.0001	251	1.4 (1.2-1.9)	43	2.9 (2.1-3.9)	0.002
High hyperdiploidy	161	16.4% (10.2-22.2)	92	8.7% (2.2-14.7)	0.08	24	2.8 (2.2-3.5)	7	3.1 (NE)	0.37
ETV6::RUNX1	113	12.1% (5.7-18.1)	102	4.2% (0.1-8.2)	0.006	17	2.4 (0.9-5.2)	4	3.0 (NE)	0.95
TCF3::PBX1	64	18.1% (7.8-27.3)	35	11.6% (0.2-21.7)	0.41	11	0.8 (NE)	4	1.2 (NE)	0.98
BCR::ABL1	36	55.4% (31.4-71.0)	20	22.0% (0-42.6)	0.049	16	1.0 (0.1-2.2)	5	4.0 (NE)	0.01
Infant KMT2A-R	24	61.6% (31.5-78.4)	6	0	0.1	12	0.3 (NE)	0	NA	NA
Negative*	319	23.0% (18.0-27.7)	253	8.9% (4.9-2.7)	<0.0001	75	2.0 (1.1-2.5)	21	3.5 (2.1-4.5)	0.25
T-ALL	156	33.9% (25.6-41.3)	58	16.0% (5.1-25.7)	0.01	54	1.3 (1.0-2.0)	8	1.7 (NE)	0.69

*Patients without the listed common genetic subtypes. BCP, B-cell precursor; *KMT2A*-R, *KMT2A*-rearrangement; NA, not applicable; NE, not estimable

Figure 1

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