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POSTER ABSTRACTS

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

TP53 Mutational Status in Myelodysplastic Neoplasm and Acute Myeloid Leukemia: Impact of Reclassification By Who 2022 and ICC Criteria - a Korean Multi-Center Study

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Introduction: The WHO 2022 classification (WHO 2022) introduced the category of myelodysplastic neoplasm (MDS) with biallelic *TP53* inactivation (MDS-bi *TP53*), while the international consensus classification (ICC) included the categories of MDS, MDS/acute myeloid leukemia (AML), and AML with mutated *TP53*. Particularly in MDS, multi-hit *TP53* mutations are clinically important, but there were differences in the criteria defining multi-hit *TP53* mutations between the WHO 2022 and ICC classifications. In this study, we investigated the *TP53* mutational status in Korean adult patients with MDS and AML and evaluated the impact of *TP53* mutation-related criteria of WHO 2022 and ICC on the reclassification of MDS.
Methods: This study included patients aged 18 years or older who were diagnosed with MDS and AML from January 2017 to December 2022 at six institutions. The results of bone marrow examination, chromosome analysis, *TP53* fluorescence *in situ* hybridization, and targeted next-generation sequencing including *TP53* were analyzed in 1264 patients with MDS and 2112 patients with AML. Multi-hit *TP53* mutation was defined based on WHO 2022 and ICC criteria as having any of the following: one *TP53* mutation with variant allele frequency (VAF) $\geq$ 50%, one *TP53* mutation with VAF $\geq$ 10% with 17p deletion, one *TP53* mutation with VAF $\geq$ 10% with complex karyotype (only for ICC), two *TP53* mutations with VAF $\geq$ 10% (only for ICC), or two *TP53* mutations (only for WHO 2022).
Results: *TP53* mutations were observed in 9.3% (118/1264) and 9.1% (192/2112) of patients with MDS and AML, respectively. Among these, 90% of patients had a single *TP53* mutation and multiple *TP53* mutations were observed in 10% of patients. There was no difference according to MDS or AML (P=0.478), and 91% of patients with a single *TP53* mutation had a VAF of $\geq$ 10%. Median VAFs of *TP53* mutations were 42.7% and 44.4% in MDS and AML, respectively (P=0.899), and complex karyotype was observed in 76.1% (236/310) of all patients with *TP53* mutations without differences between MDS and AML (P=0.534). In contrast, 17p deletion was identified in 40.3% of AML patients, significantly higher than in MDS (27.4%, P=0.02). Within MDS, 17p deletion was observed in 46.7% in MDS with 10-19% blasts (MDS-H), significantly higher than in MDS with 0-9% blasts (MDS-L, 20.7%, P=0.008), but similar to AML (P=0.514). When each *TP53* mutation-related criterion based on WHO 2022 and ICC criteria were applied to MDS, 55.7% (49/88) and 75% (66/88) of MDS-L met the criteria for multi-hit *TP53* mutation and were classified as MDS-bi *TP53* (WHO 2022) and MDS with mutated *TP53* (ICC), respectively. Notably, more patients were classified into this category based on ICC criteria (P<0.001), all due to the complex karyotype-related criterion included only in the ICC. Among MDS-H, 63.3% (19/30) of patients were classified as MDS-bi *TP53* (WHO 2022) based on multi-hit *TP53* mutation criteria, whereas 86.7% (26/30) of patients were classified as MDS/AML with mutated *TP53* (ICC) based on the single

TP53 mutation criterion with VAF ≥ 10%. Overall, 57.6% (68/118) and 78% (92/118) of patients with MDS and *TP53* mutations were reclassified into the *TP53* mutation-related MDS or MDS/AML subgroup according to WHO 2022 and ICC, respectively. **Conclusions:** *TP53* mutation status was not different between MDS and AML, but 17p deletion was observed at approximately 40% in MDS-H and AML, much higher than in MDS-L. Multi-hit *TP53* mutation based on WHO 2022 and ICC was present at a relatively high frequency at 60-80% in MDS and AML with *TP53* mutations. In particular, when ICC criteria were applied to MDS, 20% more patients were reclassified into *TP53* mutation-related MDS or MDS/AML subgroup than when WHO 2022 criteria were applied.

Disclosures No relevant conflicts of interest to declare.

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Table 1. Clinical, molecular and cytogenetic characteristics of patients with MDS and AML with *TP53* mutations

	MDS				AML (N=192)	*P* (MDS vs. AML)
	MDS-L (N=88)	MDS-H (N=30)	*P* (MDS-L vs. MDS-H)	Total (N=118)		
Age, years (range)	65.5 (27-92)	64 (27-77)	*0.551*	65.5(27-92)	65 (22-90)	0.790
Male, N (%)	52 (59.1)	21 (70)	0.480	73 (61.9)	111 (57.8)	0.480
TP53 mutation, N (%)						
Single	81/88 (92)	27/30 (90)	0.713	108/118 (91.5)	171/192 (89.1)	0.478
VAF ≥ 10%	74/88 (84.1)	26/30 (86.7)		100/118 (84.7)	154/192 (80.2)	
Multiple (≥ 2)	7/88 (8)	3/30 (10)		10/118 (8.5)	21/192 (10.9)	
TP53 mutation, VAF, %						
Median	39.4	44.3	0.197	42.7	44.4	0.899
Range	0.3-93.5	5-93.2		0.3-93.5	1-97.4	
17p deletion, N (%)	18/87 (20.7)	14/30 (46.7)	0.008	32/117 (27.4)	75/186 (40.3)	0.020
Chromosome study	17/85 (20)	13/30 (43.3)	0.015	30/115 (26.1)	72/186 (38.7)	0.023
TP53 FISH	12/63 (19)	8/18 (44.4)	0.059	20/81 (24.7)	21/48 (43.8)	0.026
Complex karyotype, N (%)	64/85 (75.3)	24/30 (80)	0.597	88/115 (76.5)	148/186 (79.6)	0.534
Multi-hit *TP53* mutation, N (%), according to the ICC	66/88 (75)	24/30 (80)	0.573	90/118 (76.3)	155/192 (80.7)	0.352
One *TP53* mutation with VAF ≥ 50%	36/88 (40.9)	12/30 (40)	0.93	48/118 (40.7)	83/192 (43.2)	0.659
One *TP53* mutation with VAF ≥ 10% with 17p deletion	18/87 (20.7)	13/30 (43.3)	0.019	31/117 (26.5)	71/186 (38.2)	0.035
One *TP53* mutation with VAF ≥ 10% with complex karyotype	63/86 (73.3)	23/30 (76.7)	0.711	86/116 (74.1)	142/188 (75.5)	0.785
Two *TP53* mutations with VAF ≥ 10%	6/88 (6.8)	3/30 (10)	0.691	9/118 (7.6)	15/192 (7.8)	0.953
Multi-hit *TP53* mutation, N (%), according to the WHO 2022	49/88 (55.7)	19/30 (63.3)	0.462	68/118 (57.6)	129/192 (67.2)	0.091

MDS, myelodysplastic neoplasm; AML, acute myeloid leukemia; MDS-L, MDS with 0–9% blasts; MDS-H, MDS with 10–19% blasts; VAF, variant allele frequency; FISH, fluorescence *in situ* hybridization; ICC, international consensus classification; WHO 2022, WHO 2022 classification

Figure 1