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POSTER ABSTRACTS

637.MYELODYSPLASTIC SYNDROMES - CLINICAL AND EPIDEMIOLOGICAL

Clinical Impact of the New Bone Marrow Blasts Cutoff Defined By the International Classification Consortium (ICC) in Myeloid Neoplasms with Mutated *TP53* gene

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Introduction: The recent ICC introduced a novel category denominated "myeloid neoplasms with mutated *TP53*" (MN-*TP53*) that includes: 1) myelodysplastic syndromes (MDS- *TP53*) in cases with multi-hit *TP53* or mutated *TP53* with complex karyotype, and blasts <10%; 2) MDS/acute myeloid leukemia (MDS/AML- *TP53*) in those with *TP53* mutations and blasts between 10-19% and 3) AML- *TP53* in patients with *TP53* mutations and blasts ≥ 20%. In all the aforementioned groups, a variant allele frequency (VAF) >10% of *TP53 gene* is required for inclusion. As opposite to ICC, the WHO 2022 classification does not recognize this mutated group as a distinct entity, maintaining the 20% blast count as the boundary between MDS and AML, with no intermediate category. The objective of this study was to assess, in a multicentric series, whether the 10% blast cutoff has clinical implications in the MN- *TP53* category.
Methods: All patients diagnosed with MDS and AML with MN- *TP53* criteria according to ICC between 2009-2023 were included from four Spanish centers. *TP53* gene status was assessed by Next-Generation Sequencing.
Results: A total of 107 patients were included: 25 (23.4%) MDS- *TP53*, 17 (15.9%) MDS/AML- *TP53*, and 65 (60.7%) AML- *TP53*. The median age at diagnosis was 70 years (interquartile range, IQR: 65-78) and 54 (50.5%) were male. Among all patients, 83 (77.6%) presented a complex karyotype. After a median follow-up of 6.2 months, 84 patients (78.5%) died, resulting in a median overall survival (OS) of 7.9 months.
The median OS for the MDS- *TP53*, MDS/AML- *TP53* and AML- *TP53* groups was 12.9, 14.3 and 5.4 months, respectively (p=0.025) (Figure 1). Paired comparisons showed similar OS between MDS- *TP53* and MDS/AML- *TP53* groups (p=0.5) but shorter OS in AML- *TP53* group when confronted with MDS/AML- *TP53* (p=0.03) or AML- *TP53* with MDS- *TP53* (p=0.052).
In addition to potential outcome dissimilarities, clinical characteristics at baseline were also compared (Table 1). Again, there were no differences between the MDS- *TP53* and MDS/AML- *TP53* groups at diagnosis. Intensity of chemotherapy treatment and frequency of allogenic hematopoietic stem cell transplant (alloHSCT) were also analyzed. One important difference between MDS- *TP53* and MDS/AML- *TP53* was that 4% and 29% of cases underwent alloHSCT, respectively. To assess the potential impact of allotransplant in this cohort, the survival analysis was repeated censoring the OS at the infusion date. The OS between groups MDS- *TP53* and MDS/AML remained comparable (p=0,98).
Conclusions: In our cohort, patients with MDS- *TP53* and MDS/AML- *TP53* exhibit similar clinical behavior, in contrast to AML-*TP53*, suggesting that the newly proposed 10% blasts cutoff is not adding clinical value to the management of these entities.

Disclosures Tormo: *AbbVie:* Honoraria; *Pfizer:* Honoraria; *MSD:* Honoraria; *BMS:* Honoraria; *Astellas:* Honoraria. **Salamero:** *Pfizer:* Consultancy, Honoraria; *Jazz:* Consultancy, Honoraria; *BMS:* Consultancy, Honoraria; *Astellas:* Consultancy, Honoraria; *Abbvie:* Consultancy, Honoraria. **Tazon:** *Bristol Myer Squibb:* Honoraria. **Bosch:** *Novartis:* Consultancy, Honoraria; *AbbVie:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria; *Gilead:* Consultancy, Honoraria; *Mundipharma:* Consultancy, Honoraria; *Lilly:* Consultancy; *Roche:* Honoraria; *BeiGene:* Consultancy; *AstraZeneca:* Consultancy, Honoraria; *Takeda:* Consultancy, Honoraria; *Karyospharm:* Other; *Celgene:* Consultancy, Honoraria; *Roche:* Consultancy, Honoraria. **Jerez:** *GILEAD:* Research Funding; *Astrazeneca:* Research Funding; *Novartis:* Consultancy; *BMS:* Consultancy.

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Variable	Total (n=107)	MDS-*TP53* (n=25)	MDS/AML-*TP53* (n=17)	AML-*TP53* (n=65)	MDS-*TP53* vs MDS/AML-*TP53*	AML-*TP53* vs MDS-*TP53*+ MDS/AML-*TP53*
Age. years (median. IQR)	70 (65-78)	74 (67-84)	66 (61-77)	70 (66-76)	*p=0.09*	*p=0.3*
Gender. male. %	50.5	52	47	50.1	*p=0.75*	*p=0.94*
Hb. g/dL (median. IQR)	8.8 (7.8-9.7)	8.8 (8.2-9.7)	9.2 (8.3-9.8)	8.5 (7.6-9.7)	*p=0.93*	*p=0.46*
Neutrophils. x10^6/uL (median. RIQ)	1.1 (0.4-2.7)	1.5 (1-2.8)	0.7 (0.5-2.7)	1 (0.3-2.6)	*p=0.79*	*p=0.18*
Platelets. x10^6/uL (median. IQR)	53 (26-88)	75 (51-103)	52 (30-125)	41 (20-80)	*p=0.89*	***p=0.006***
Complex karyotype. %	85.6	95.8	82.4	82.1	*p=0.15*	*p=0.26*
Intensive CXT. %	23.4	0	17.6	33.8	*p=0.09*	***p=0.005***
AlloHSCT. %	14	4	29	13.8	***p=0.02***	*p=0.95*

Table 1. Main clinical characteristics of the subgroups.

Hb: hemoglobine; AlloHSCT: Allogeneic Hematopoietic Stem Cell Transplant; CXT: Chemotherapy; MDS-*TP53*: myelodysplastic syndrome with *TP53* mutated; AML-*TP53*: akute myeloid leukemia with *TP53* mutated; IQR: interquartile range.

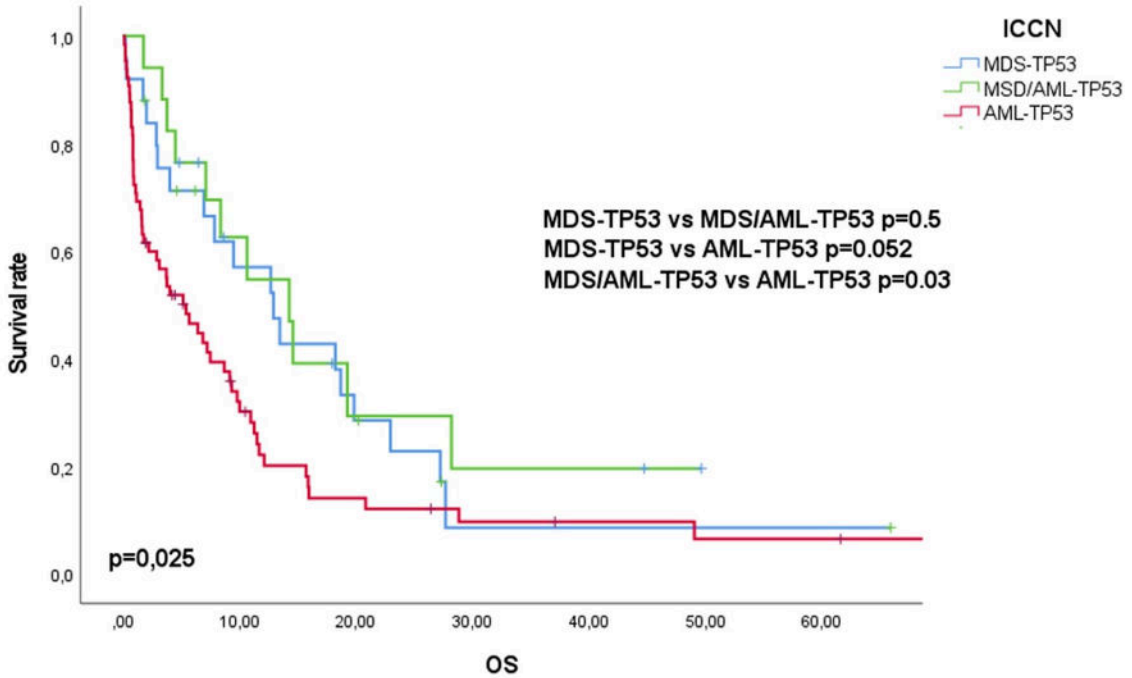

Figure 1. Survival analysis (non-censored)

Figure 1