Differential Impact of Allogeneic Stem Cell Transplantation by TP53 Mutational Status in High-Risk Myeloid Neoplasms With Complex or Monosomal Karyotype

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BACKGROUND

- High-risk myeloid neoplasms defined by complex karyotype (CK), monosomal karyotype (MK), or TP53 mutation carry a dismal prognosis, with median overall survival (OS) under 12 months.
- TP53 allelic state (single-hit vs multi-hit) refines prognosis in MDS and AML, but its impact on transplant outcomes is less well defined.
- Whether allogeneic stem cell transplantation (allo-SCT) confers uniform benefit regardless of TP53 mutational status remains uncertain.

OBJECTIVE

To evaluate whether the benefit of allo-SCT in high-risk myeloid neoplasms with CK/MK is modified by TP53 mutational and allelic status.

METHODS

- **Design:** retrospective, single-center cohort (Einstein Hospital Israelita, São Paulo, 2012–2024).
- **Population:** 49 evaluable patients (25 AML, 24 MDS) with CK, MK, or TP53 mutation by NGS.
- **TP53 double-hit:** ≥2 TP53 mutations, or 1 mutation plus del(17p)/structural 17p abnormality.
- **Outcome:** OS from diagnosis (Kaplan–Meier, log-rank). Median follow-up 22.9 months.
- **Cox regression:** multivariable model with disease type + TP53 status + allo-SCT (n=46, 28 events; Schoenfeld p=0.85).
- **Subgroup analysis:** by TP53 status; sensitivity analyses for age and untested TP53.

TABLE 1. BASELINE CHARACTERISTICS

Characteristic	n = 49
Age at diagnosis, years, median (IQR)	73 (68–80)
Sex, female / male	19 (39%) / 30 (61%)
Diagnosis, AML / MDS	25 / 24
Complex karyotype (CK)	40 (82%)
Monosomal karyotype (MK)	31 (63%)
TP53 mutated (rest: WT or not tested)	30 (61%)
Double-hit, among TP53-mutated	23 (77%)
Allo-SCT performed (3 unknown)	12 (26%)
Death (event)	30 (61%)
Median OS, months (KM)	12.7

RESULTS

- **Median OS 12.7 months** overall; AML 6.4 vs MDS 13.1 months (p=0.059). OS did not differ by TP53 status (HR 1.31, p=0.48; Fig. 3).
- **Allo-SCT (n=12, 26%) was associated with longer OS: median 32.9 vs 8.4 months (log-rank p=0.050; Fig. 1). Benefit was concentrated in CK/MK patients without TP53 mutation: 41.3 vs 6.3 months (Fig. 2); no significant benefit in TP53-mutated or double-hit patients (Fig. 4).**
- **Multivariable Cox:** MDS (HR 0.34, 95% CI 0.15–0.80, p=0.014) and allo-SCT (HR 0.30, 0.11–0.83, p=0.019) were independent predictors of OS; TP53 mutation was not (HR 1.03, p=0.93).
- **Age-adjusted sensitivity analysis** attenuated the allo-SCT effect (HR 0.64, p=0.55), indicating partial confounding by age.

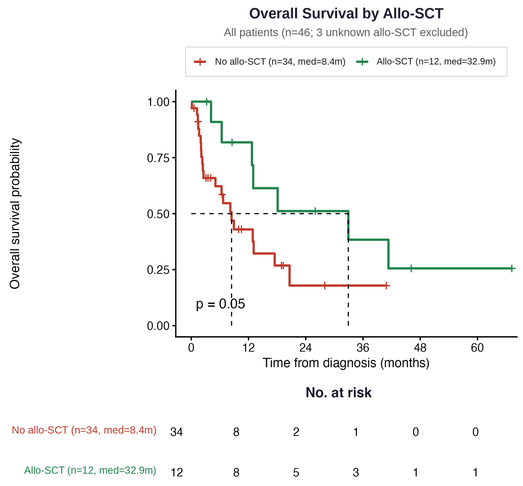

Figure 1. OS by allo-SCT, all patients (n=46; 3 with unknown allo-SCT status excluded).

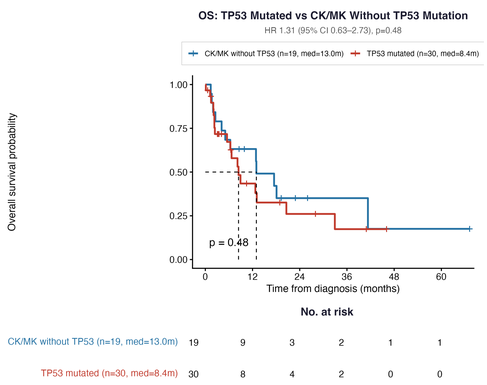

Figure 3. OS by risk group (n=49). Baseline prognosis did not differ between TP53-mutated and CK/MK without TP53 patients.

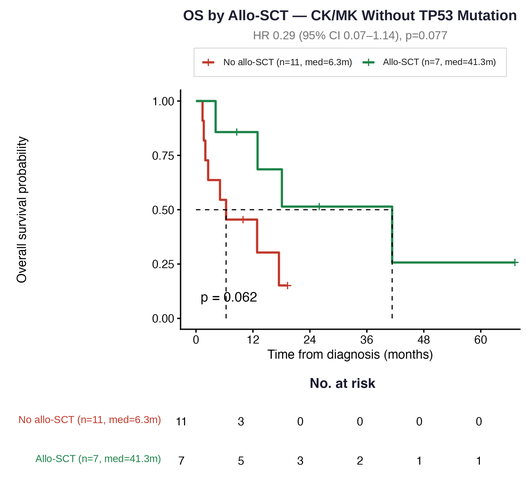

Figure 2. OS by allo-SCT in CK/MK patients without TP53 mutation (n=18; 1 with unknown allo-SCT status excluded): HR 0.29 (95% CI 0.07–1.14), p=0.077.

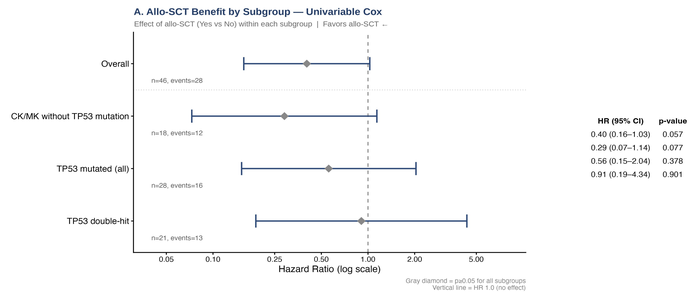

Figure 4. allo-SCT effect (yes vs no) within each subgroup, univariable Cox. Benefit is concentrated in CK/MK without TP53 mutation (HR 0.29); no significant benefit in TP53-mutated (HR 0.56) or double-hit (HR 0.91; only 2 transplanted) patients.

KEY FINDING

Allo-SCT benefit was confined to CK/MK patients **without** TP53 mutation: **41.3 vs 6.3 months**. No significant benefit in TP53-mutated patients.

CONCLUSIONS

- **Allo-SCT benefit is heterogeneous** in high-risk myeloid neoplasms with CK/MK.
- **CK/MK patients without TP53 mutation** derive the greatest benefit (median OS 41.3 vs 6.3 months).
- **TP53-mutated patients** showed no significant transplant benefit, either overall or in the double-hit subset.
- These findings support incorporating TP53 mutational status into allo-SCT decision-making for high-risk myeloid neoplasms.
- **Limitations:** single center, small sample, retrospective design and partial age confounding. Results are hypothesis-generating and warrant validation in larger cohorts.

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ACKNOWLEDGEMENTS & CONTACT

The authors thank the Hematology and Bone Marrow Transplant teams at Einstein Hospital Israelita.

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The authors declare no conflicts of interest. allo-SCT = allogeneic stem cell transplantation.