MUTATIONAL SPECTRUM AND CLINICAL OUTCOMES OF TP53-MUTATED B-ALL IN ADULTS: A RETROSPECTIVE ANALYSIS

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INTRODUCTION

- TP53 mutations are markers of poor prognosis in many hematologic cancers.
- Their relevance in adult B-ALL remains poorly defined.
- We aimed to characterize the mutational spectrum and clinical outcomes in TP53-mutated adult B-ALL.

METHODS

- Population: 290 adults with B-ALL (9-year period, single institution).
- Genomic profiling: DNA/RNA targeted NGS.
- Kaplan-Meier and log-rank tests used for survival analysis.
- Endpoints:
  a. OS : time from diagnosis to death/last day of follow-up.
  b. EFS : Time from diagnosis to MRD-positive status, relapse, treatment change or, last day of follow-up.

RESULTS

- 57 patients (19.6%) TP53 mutations : Median age: 65 years (23–84).
- 74 total alterations, 81% missense.
- 13 patients had >1 TP53 variant.Concurrent mutations: RAS pathway (n=13), CDKN2A/B loss (n=12), epigenetic modifiers (n=17). [Figure 1]
- ICC subtypes: low hypodiploid (n=10), BCR::ABL1+ (n=3), KMT2A rearranged (n=3), MYC-rearranged (n=2), Ph-like (n=1), ETV6::RUNX1 (n=1). 36 did not fit into a defined ICC category.
- Post-induction: 51% remained MRD-positive (22/43 evaluable).
- Median OS: 18.5 mo (95% CI: 8.4–45.5) in TP53-mutated vs 84.4 mo (95% CI: 49.8–NA) in wild-type; p < 0.0001. [Figure 2 and 3]
- Median EFS: 6.1 mo (95% CI: 4.9–8.3) in TP53-mutated vs 12.5 mo (95% CI: 10.6–15.2) in wild-type; p = 0.0096.
- No significant OS differences by sex, MRD status, or ICC category.

Figure 1: Distribution of Concurrent Mutations in TP53 ALL

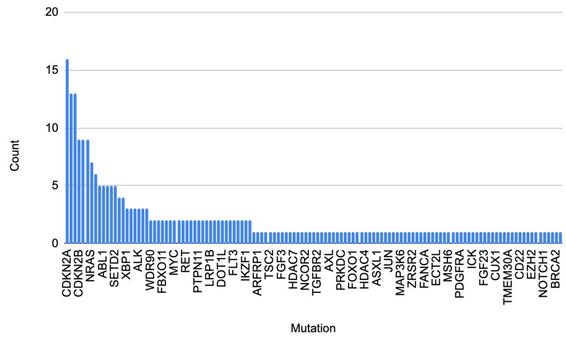


Figure 2: Overall Survival by TP53 Status

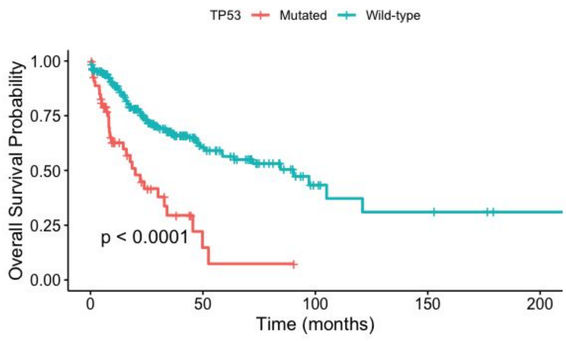
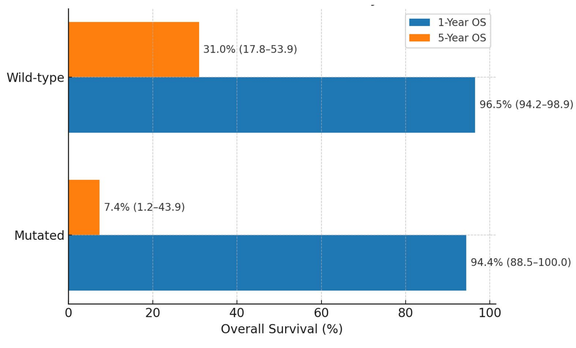


Figure 3: 1-Year and 5-Year Overall Survival by TP53 Status



CONCLUSION

- TP53 mutations occur in ~20% of adult B-ALL and associated with high MRD positivity and poor outcomes.
- This study supports recognition of TP53-mutated B-ALL as a distinct subgroup.
- Tailored therapy and prospective risk stratification is needed.