Prognostic Impact of Early NGS MRD Dynamics And Cytomolecular Risk in Newly Diagnosed Ph- B-cell ALL

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Introduction

- Major prognostic factors in ALL: Baseline cytomolecular features and MRD dynamics.
- Unclear if early MRD response using high-sensitivity next-generation sequencing (NGS) MRD can overcome the adverse prognosis of high-risk (HR) cytomolecular features.

Methods

- Retrospective study
- 110 patients with newly diagnosed Philadelphia-chromosome negative (Ph-) B-cell ALL who underwent MRD assessment with NGS for IG/TR rearrangements (sensitivity: $1x10^{-6}$) within first 6 months
- HR Ph- ALL defined as: poor-risk cytogenetics (i.e. low hypodiploidy/near triploidy, complex cytogenetics, or KMT2A rearrangement), Ph-like ALL, and/or a *TP53* mutation.

Population

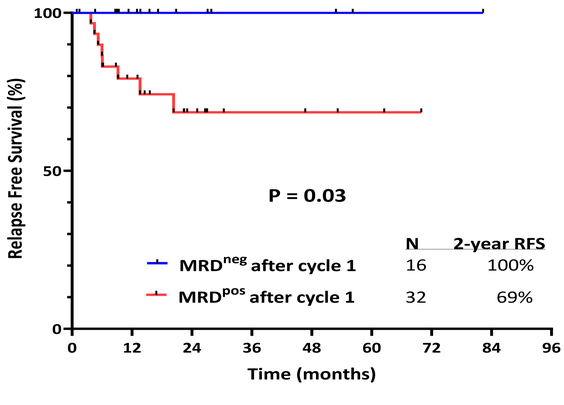
Characteristic	Value (N=110) N (%) / median [range]
Age (years)	46 [18-87]
Treatment Type	
Hyper-CVAD-based (no INO or Blina)	3 (3)
Hyper-CVAD + Blina ± INO	64 (58)
Mini-hyper-CVD + INO ± Blina	43 (39)
Cytogenetics	
Diploid	30 (27)
High hyperdiploidy	3 (3)
Low hypodiploidy / near triploidy	11 (10)
KMT2A rearranged	6 (5)
Complex	8 (7)
Miscellaneous	31 (28)
Insufficient metaphases	20 (19)
TP53-mutated	28/109 (25)
Poor-risk cytomolecular feature(s)	59 (54)

Results

Rates of NGS negativity by subgroup & timepoint

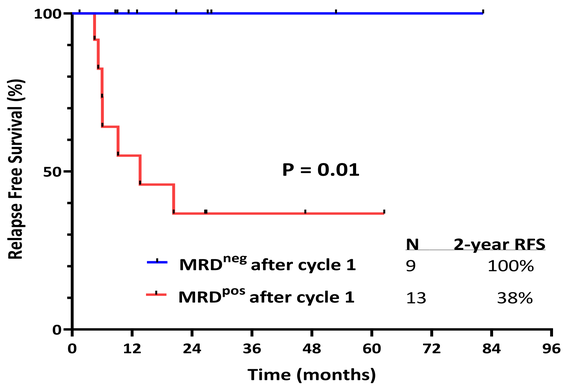
	After cycle 1	At 3 months	At 6 months
All patients	16/53 (30)	51/81 (63)	42/51 (82)
High-risk	9/25 (36)	26/42 (62)	23/27 (85)
Standard-risk	7/28 (25)	25/39 (64)	19/24 (79)

RFS by NGS MRD status after cycle 1 (entire cohort)

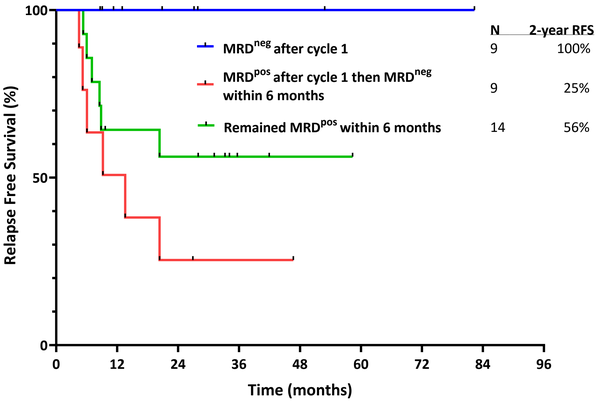


Results

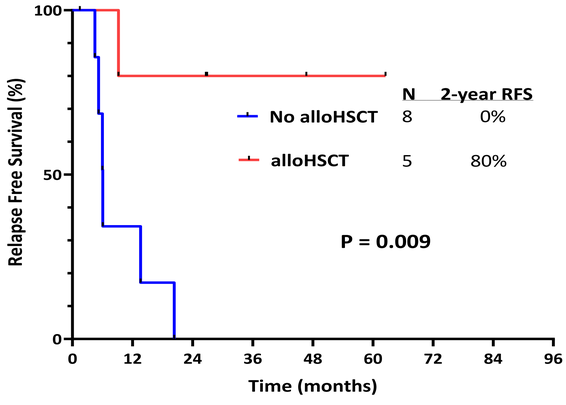
RFS in HR group by NGS MRD status after cycle 1



RFS in HR group by NGS MRD dynamics



Landmark analysis of RFS in HR pts with NGS MRD+ after C1 by HSCT



Conclusion

- Early NGS MRD negativity associated with durable remissions in Ph- B-ALL, regardless of baseline cytomolecular features
- Later MRD clearance not protective in HR patients.
- AlloSCT may improve outcomes of patients with HR ALL with suboptimal early MRD dynamics.

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