



Mastering MRD for Prognosis and Treatment in ALL: KEY TAKEAWAYS

- In ALL, 30% to 50% of patients have residual leukemic cells that contribute to eventual relapse
 - Pediatric and adult patients who are MRD-positive consistently experience worse outcomes than those who are MRD-negative
- MRD should be measured at multiple times in ALL, including at diagnosis, after induction, after consolidation, before transplantation, and at regular intervals during maintenance and surveillance
- Multiple techniques are available to evaluate MRD, each with advantages and limitations.
- Awareness of these limitations is important when choosing the correct method to enable precise MRD measurement
- For patients who are MRD-positive, the goal is to eradicate MRD with MRD-specific therapy—specifically blinatumomab—before stem cell transplant

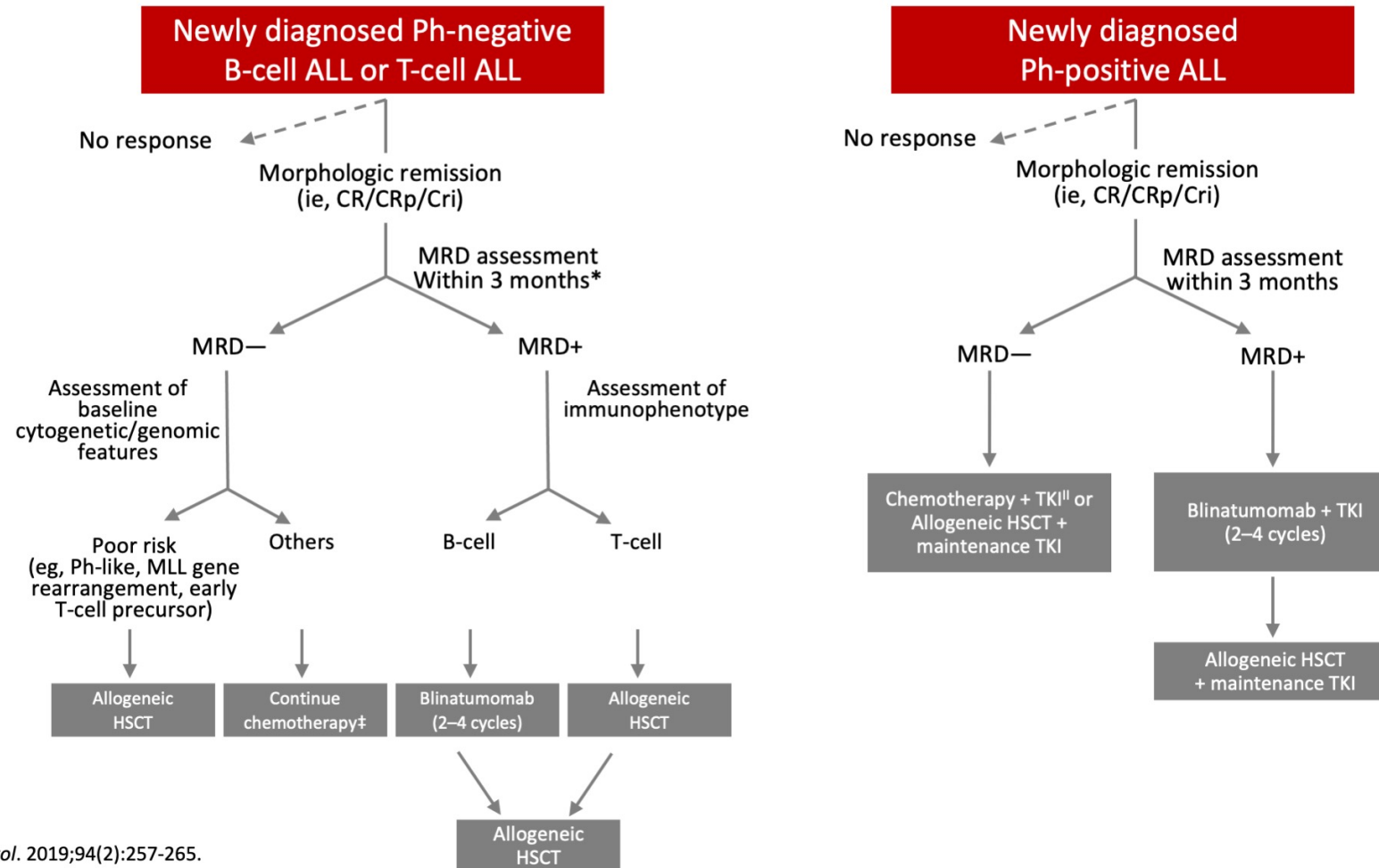
Comparison of MRD Assays^{1,2}

MRD Method	Sensitivity	Advantages	Disadvantages
Multiparameter Flow Cytometry (FCM)	10^{-4} (0.01%)	<ul style="list-style-type: none"> • Fast • Cost effective • Widely available platform • Clinically proven platform 	<ul style="list-style-type: none"> • Subjective interpretation • Immunophenotype may change during treatment • Inadequate standardization • Immunotherapy treatment can complicate interpretation
RQ-PCR for IgH/TCR gene rearrangements	$10^{-4} - 10^{-5}$ (0.01%-0.001%)	<ul style="list-style-type: none"> • Well-standardized • More sensitive than FCM 	<ul style="list-style-type: none"> • Technically labor intensive • Requires technical expertise • Expensive
qRT-PCR for gene fusions	$10^{-4} - 10^{-5}$ (0.01%-0.001%)	<ul style="list-style-type: none"> • More sensitive than FCM • Technically simpler 	<ul style="list-style-type: none"> • Need for baseline specimen • Limited standardization • Not all ALL cases have a gene rearrangement – immature T-ALL
Next generation sequencing	10^{-6} (0.0001%)	<ul style="list-style-type: none"> • Very sensitive • Relatively fast 	<ul style="list-style-type: none"> • Not standardized yet • Requires bioinformatics • Limited clinical validation • Expensive



An MRD-Guided Treatment Algorithm

A 2019 consensus of North American hematologic oncologists defined treatment algorithms for Ph+/Ph- B-ALL and T-ALL based on MRD status¹



Images adapted from Short NJ, et al. *Am J Hematol.* 2019;94(2):257-265.

TKI, tyrosine kinase inhibitor.

1. Short NJ, et al. *Am J Hematol.* 2019;94(2):257-265.