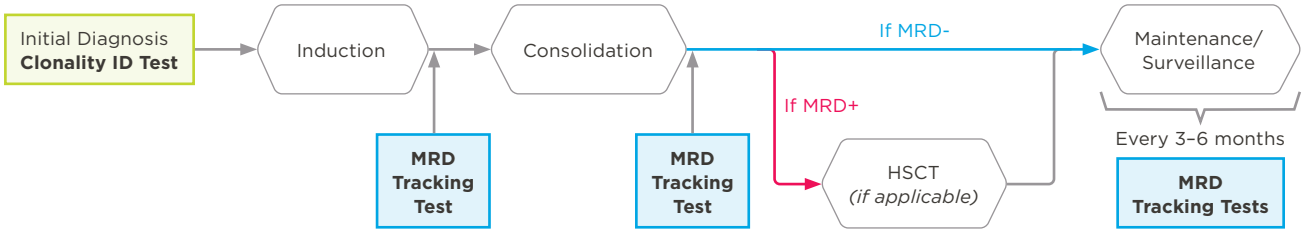
CLONOSEQ MRD TESTING IN ADULT ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): A POTENTIAL CLINICAL PATHWAY

Based on available evidence, the following clinical strategy reflects a potential approach for integrating clonoSEQ® MRD testing into the management of patients with adult ALL:

Key Takeaways

- Clinical practice guidelines suggest performing a Clonality (ID) assessment at time of diagnosis to establish tumor-specific DNA sequences to track; use a fresh or archived bone marrow or blood sample collected prior to initiation of treatment.[1]
- Evaluation of MRD status should be considered after induction, after consolidation, and at further time points during maintenance and follow-up.[2,3,4,5,6]
- In general, MRD positivity at the end of induction/consolidation predicts high relapse rates and should prompt an evaluation for allogeneic hematopoietic stem cell transplantation (HSCT).[1,4,7]
- Prospective MRD monitoring is recommended for MRD-negative patients in 3 to 6-month intervals during maintenance therapy and follow-up.[1,3,6,8]

Adult ALL MRD Patient Pathways
(based on Clinical Practice Guidelines and the GMALL 06/99 and 07/03 trials)[1,3]



Supporting Data, Guidelines and References

The study design above reflects guideline-recommended MRD timepoints and incorporates assessment timelines from the 06/99 and 07/03 trials of the German Multicenter Study Group for Adult Acute Lymphoblastic Leukemia (GMALL).[3] In addition to guidance for testing during treatment, data generated from these trials and related studies support the use of serial MRD monitoring in adult ALL post-transplant and during surveillance.

MRD Assessment Timepoints

- Per NCCN guidelines, it is recommended that the initial MRD measurement be performed on completion of induction therapy; additional time points for MRD evaluation should be guided by the treatment protocol or regimen used.[1]

- In line with GMALL 06/99 and 07/03, consider MRD evaluation after induction (day 71), after consolidation (week 16), and in 3-to-6-month intervals during maintenance therapy and follow-up.[2,3,4]
  - *Note: these testing recommendations are presented within the context of the specific 6-drug regimen utilized in GMALL 06/99 and 07/03. Precise timepoints for MRD testing when using other regimens will require modification accordingly.*
- Consider HSCT for those patients deemed MRD-positive after consolidation.[4,7]

Summary of supporting data:

- Studies in adults with ALL have shown a strong correlation between MRD positivity and risk for relapse.[1,2,5,6,9,10,11]
- Existing evidence suggests high value of MRD monitoring for identifying subgroups of patients who may benefit from further intensified therapies or alternative treatments.
  - Data supports unique risk stratification via MRD assessment after induction, then again after consolidation.[2,3,4,5]
  - Post-consolidation MRD status is a risk factor for poorer outcomes in adults with ALL and may stratify high-risk patients who might benefit from HSCT.[4,7]
- Serial monitoring of MRD positivity may be useful in patients with molecular relapse and low-level disease after induction and consolidation, and patients with persistent MRD negativity have been shown to have a favorable OS rate after HSCT.[1,6,8,12]
- MRD negativity via NGS (10^{-6}) has been shown to predict relapse in adult patients receiving allo-HSCT, and may confer additional prognostic information compared to MRD status by less sensitive measures (e.g., MFC) at identical time points.[12,13,14]
- Studies have shown a high correlation between MRD results assessed in the bone marrow and peripheral blood in the context of adult ALL; thus, blood* may be a potential sample source for MRD assessment under certain circumstances.[12,15,16]

Summary of guidelines:

- Guidelines recommend MRD following induction therapy, with the optimal sample for MRD assessment being the first pull or early pull of the bone marrow aspirate.[1]
- For patients with unavailable MRD status at start of consolidation, consider retesting for MRD at first available opportunity.[1]
- When possible, therapy aimed at eliminating MRD prior to allogeneic HSCT is preferred.[1]

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*Blood-based clonoSEQ testing in ALL is available as a CLIA-validated LDT and has not been cleared or approved by the FDA.

clonoSEQ® is available as an FDA-cleared *in vitro* diagnostic (IVD) test service provided by Adaptive Biotechnologies to detect minimal residual disease (MRD) in bone marrow from patients with multiple myeloma or B-cell acute lymphoblastic leukemia (B-ALL) and blood or bone marrow from patients with chronic lymphocytic leukemia (CLL). Additionally, clonoSEQ is available for use in other lymphoid cancers and specimen types as a CLIA validated laboratory developed test (LDT). For important information about the FDA-cleared uses of clonoSEQ including test limitations, please visit clonoSEQ.com/technical-summary.

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