CLONOSEQ MRD TESTING IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: 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 pediatric 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 marrow or blood sample collected prior to initiation of treatment[1]
- Guidelines suggest assessing MRD following induction therapy[1]
  - If patient is MRD-positive post-induction, consider intensified consolidation with additional therapy, blinatumomab or tisagenlecleucel[1]
- Guidelines suggest assessing MRD following consolidation therapy[1]
- In patients undergoing transplant, consider MRD monitoring at the following post-transplant timepoints:[2]
  - Day 30
  - Day 100
  - Month 8
- Regardless of whether a patient undergoes transplant, continue to measure MRD during post-treatment surveillance (every 6-12 months)[1,2]
- Consider interim MRD assessments in peripheral blood (e.g., between bone marrow assessments) if more frequent monitoring is desired[3–6]

Supporting Data, Guidelines and References

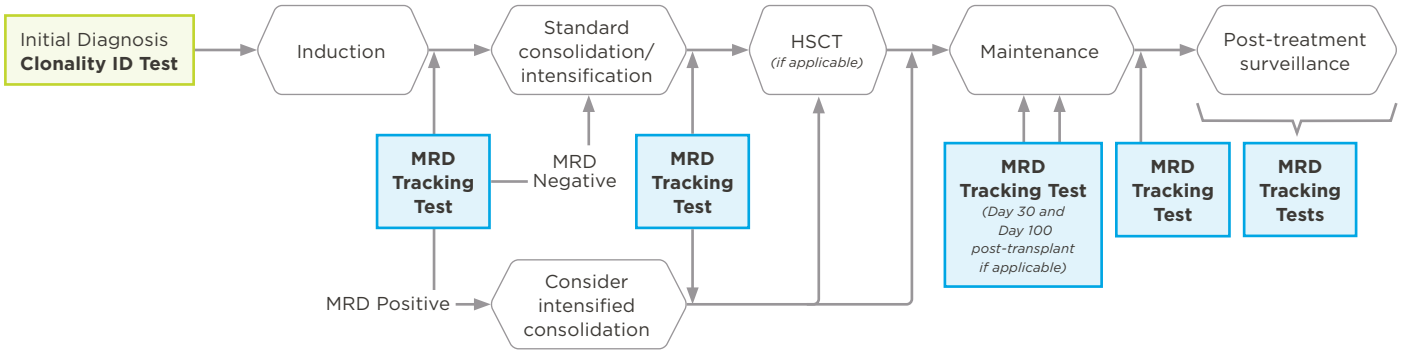
The study design below reflects guideline recommended MRD timepoints and incorporates MRD timepoints from COG ASCT0431.[1,2] The data generated from the Children's Oncology Group ASCT0431 study (NCT00382109) support the importance of serial MRD monitoring in ALL post-transplant and during surveillance.[2]

MRD assessment time points:

- Per NCCN guidelines, NGS MRD monitoring in bone marrow is to be performed at baseline, post-induction, post-consolidation, and during surveillance.[1]
  - If MRD-positive post-induction, consider intensified consolidation with additional chemotherapy, blinatumomab, or tisagenlecleucel.[1]
- Per COG ASCT0431, consider MRD assessment at day 30, day 100, and 8-12 months post-transplant.[2]
- Peripheral blood MRD monitoring may also be considered under certain circumstances (e.g., between bone marrow assessments per the clinician's discretion).[3-6]

* Adaptive Biotechnologies does not recommend or endorse any particular course of treatment

Pediatric ALL MRD Patient Pathways
(based on Clinical Practice Guidelines and COG ASCT 0431)[1,2]



Summary of supporting data:

- MRD is shown to be highly prognostic of patient outcomes.[2,7-9]
- The COG ASCT0431 study showed that MRD post-induction and at multiple timepoints post-transplant was prognostic for relapse and survival.[2]
- Studies have shown a high correlation between MRD results assessed in the bone marrow and peripheral blood; thus, blood may be a potential sample source for MRD assessment under certain circumstances.[3-6]

Summary of guidelines:

- NCCN clinical practice guidelines recommend assessing MRD post-induction, post-consolidation, and at other timepoints guided by the regimen used. Guidelines also recommend MRD monitoring during post-treatment surveillance.[1]

1. NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia. Version 2.2021.
2. Pulsipher M, et al. *Blood*. 2015;125(22):3501-8.
3. Sala Torra, et al. *Biol Blood Marrow Transplant*. 2017;23(4):691-696.
4. Logan AC, et al. *Biol Blood Marrow Transplant*. 2014;20(9):1307-13.
5. Muffly LS, et al. ASH 2020; Abstract 975.
6. Pulsipher M, et al. ASH 2018; Abstract 1551.
7. Wood B, et al. *Blood*. 2018; 131(12):1350-1359.
8. Wu D, et al. *Sci Transl Med*. 2012;4(134):134ra63.
9. Berry DA, et al. *JAMA Oncology*. 2017;3(7):e170580.

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.

PM-US-cSEQ-0618