AFTER ACHIEVING COMPLETE REMISSION (CR) IN B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

Get deeper and test for measurable (or minimal) residual disease (MRD)

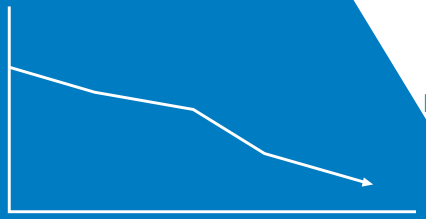
MRD IS ASSOCIATED WITH RELAPSE AND POORER SURVIVAL IN PATIENTS WITH ALL.[1]

Up to **50%** of adult patients

and

up to **20%** of pediatric patients

with ALL who achieve CR after chemotherapy may relapse[2,3]



Relapse after frontline therapy generally leads to poor long-term outcomes and fewer treatment options[4]

CR

MRD

Bone marrow microscopy cannot identify the presence of leukemic cells if there are fewer than 5% in the total cell population[5]

5%

Over a 10-year period, adult and pediatric patients who achieved MRD negativity had a greater chance of event-free survival vs patients who remained MRD(+)[1,*]

10 years

*According to a meta-analysis of 16 studies with 2,065 adult patients and a meta-analysis of 20 studies with 11,249 pediatric patients with ALL.[1]

Typical sensitivity of cancer cell detection in 3 testing methods[6]

FLOW CYTOMETRY
1 in 10,000 normal cells

POLYMERASE CHAIN REACTION
1 in 100,000 normal cells

NEXT-GENERATION SEQUENCING
1 in 1,000,000 normal cells

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend MRD testing throughout the treatment journey in adult and pediatric patients with ALL.[7,8,†]

"MRD is an essential component of patient evaluation over the course of sequential therapy."[7,8]

The NCCN Guidelines® recommend characterization of leukemic clones at diagnosis for subsequent MRD testing when using some techniques in adult and pediatric patients with ALL.[7,8]

In adult patients, the NCCN Guidelines recommend MRD testing upon completion of initial induction therapy, at the end of consolidation, and at additional time points guided by the regimen used. During surveillance, MRD assessment can be considered with a bone marrow aspirate as clinically indicated at a frequency of up to 3–6 months for at least 5 years.[7]

In pediatric patients, the NCCN Guidelines recommend MRD testing upon completion of initial induction therapy, at the end of consolidation, at additional time points guided by the regimen used, and at surveillance for suspected relapse.[8]

[†]AYA patients may be included in either pediatric or adult patient populations.[7,8]

MRD positivity at the time of HSCT is associated with an increased risk of relapse post-HSCT.[9] NCCN Guidelines for ALL recommend "eliminating MRD prior to allogeneic HCT," when possible.[7]

To learn more about MRD, visit https://www.amgenoncology.com/minimal-residual-disease.html

To find an MRD testing facility, see reverse side.

In both adult and pediatric patients with ALL, MRD testing as early as induction therapy has been shown to have prognostic significance[7,8]

AYA, adolescent and young adult; HCT, hematopoietic cell transplantation; HSCT, allogeneic hematopoietic stem cell transplantation; NCCN, National Comprehensive Cancer Network® (NCCN®).

REFERENCES:
1. Berry DA, Zhou S, Higley H, et al. Association of minimal residual disease with clinical outcome in pediatric and adult acute lymphoblastic leukemia: a meta-analysis. *JAMA Oncol*. 2017;3:e170580. **2.** Hoelzer D. Monitoring and managing minimal residual disease in acute lymphoblastic leukemia. *Am Soc Clin Oncol Educ Book*. 2013;33:290-293. **3.** Cooper SL, Brown PA. Treatment of pediatric acute lymphoblastic leukemia. *Pediatr Clin North Am*. 2015;62:61-73. **4.** Gökbuget N, Dombret H, Ribera JM, et al. International reference analysis of outcomes in adults with B-precursor Ph-negative relapsed/refractory acute lymphoblastic leukemia. *Haematologica*. 2016;101:1524-1533. **5.** Gökbuget N, Kneba M, Raff T, et al. Adult patients with acute lymphoblastic leukemia and molecular failure display a poor prognosis and are candidates for stem cell transplantation and targeted therapies. *Blood*. 2012;120:1868-1876. **6.** Dalle IA, Jabbour E, Short NJ. Evaluation and management of measurable residual disease in acute lymphoblastic leukemia. *Ther Adv Hematol*. 2020. doi:10.1177/2040620720910023. **7.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Lymphoblastic Leukemia V.1.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed October 24, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **8.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pediatric Acute Lymphoblastic Leukemia V.1.2023. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed November 22, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **9.** Campana D. Minimal residual disease in acute lymphoblastic leukemia. *Semin Hematol*. 2009;46:100-106.

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Facilities Conducting MRD Testing

The following is a list of facilities that are CLIA-certified and accept external MRD samples. CLIA certification was validated using the CDC website,* and acceptance of external samples was confirmed by reviewing facility websites and/or contacting facilities directly. Amgen neither recommends nor endorses, and may or may not have financial relationships with, any facility that appears on this list. This list is not intended to be a comprehensive list nor as a referral to any provider listed. If you would like to suggest a facility to be added to this list, please contact Amgen MedInfo at 800-77-AMGEN.

LOCATION	FACILITY NAME	MRD TEST	WEBSITE	PHONE NUMBER
National	Adaptive Biotechnologies	NGS	https://www.clonoseq.com	(888) 552-8988
Salt Lake City, UT	ARUP Laboratories	Flow Cytometry	https://www.aruplab.com	(800) 242-2787
Seattle, WA	CellNetix	Flow Cytometry, PCR [Ph(+) only]	https://cellnetix.com	(844) 344-4209
Los Angeles, CA	Children's Hospital Los Angeles (Pathology and Laboratory Medicine)	Flow Cytometry	https://www.chla.org/pathology-and-laboratory-medicine	(877) 543-9522
Cincinnati, OH	Cincinnati Children's Hospital (Immunopathology Laboratory)	Flow Cytometry	https://www.cincinnatichildrens.org/service/c/cancer-blood/hcp/clinical-laboratories/immunopathology-lab	(513) 803-2567
Durham, NC	Duke University Health System Clinical Laboratories	Flow Cytometry	https://clinlabs.duke.edu/molecular-diagnostics-laboratory	(919) 684-2698
Seattle, WA	Fred Hutchinson Cancer Research Center (Molecular Oncology Laboratory)	PCR [Ph(+) only]	https://research.fredhutch.org/molecular-oncology/en.html	(206) 667-2592
Seattle, WA	Hematologics, Inc.	Flow Cytometry	https://www.hematologics.com	(206) 223-2700
Baltimore, MD	Johns Hopkins Medicine (Pathology)	Flow Cytometry, PCR [Ph(+) only], NGS	https://pathology.jhu.edu/patient-care/testing	(410) 955-1921
Boston, MA	Massachusetts General Hospital (Pathology)	Flow Cytometry	https://mghlabtest.partners.org OR https://mghlabtest.partners.org/clinicians/directory-of-labs/	(617) 724-5227
Rochester, MN	Mayo Clinic Laboratories	Flow Cytometry	https://www.mayocliniclabs.com	(800) 533-1710
Houston, TX	MD Anderson Cancer Center (Molecular Diagnostics Laboratory)	Flow Cytometry, PCR	https://www.mdanderson.org/research/research-resources/core-facilities/molecular-diagnostics-lab.html	(713) 794-4780
National	NeoGenomics	Flow Cytometry, PCR [Ph(+) only]	https://neogenomics.com	(866) 776-5907
Columbus, OH	The Ohio State University Wexner Medical Center James Molecular Laboratory	PCR [Ph(+) only]	https://pathology.osu.edu/divisions/Clinical/molpath/ordering.html	(614) 293-0665
National	Quest Diagnostics	PCR [Ph(+) only]	https://www.questdiagnostics.com	(866) 697-8378
Grand Rapids, MI	Spectrum Health Advanced Technology Laboratories	Flow Cytometry	https://www.spectrumhealth.org/for-health-professionals/advanced-technology-laboratories	(866) 989-7999
Chapel Hill, NC	UNC Medical Center (McLendon Clinical Laboratories)	Flow Cytometry	https://www.uncmedicalcenter.org/mclendon-clinical-laboratories/directory	(984) 974-8320
Iowa City, IA	University of Iowa Health Care (Carver College of Medicine)	Flow Cytometry	https://medicine.uiowa.edu/uidl/faculty-services/10-color-flow-cytometry	(866) 844-2522
Kansas City, KS	University of Kansas Health System (Pathology and Laboratory Medicine)	Flow Cytometry	https://www.kansashealthsystem.com/care/specialties/pathology	(913) 588-1227
Ann Arbor, MI	University of Michigan (Department of Pathology)	Flow Cytometry	https://www.pathology.med.umich.edu/handbook/#/details/5337	(800) 862-7284
Dallas, TX	UT Southwestern Medical Center (Department of Pathology)	Flow Cytometry	https://www.utsouthwestern.edu/education/medical-school/departments/pathology/	(214) 648-4088
Seattle, WA	University of Washington (Hematopathology)	Flow Cytometry, PCR [Ph(+) only], NGS	https://dlmp.uw.edu/patient-care/hematopathology	(206) 606-7060
New Haven, CT	Yale School of Medicine (Laboratory Medicine)	Flow Cytometry, PCR [Ph(+) only]	https://medicine.yale.edu/labmed/sections/flowcytometry/	(203) 688-2450

This information is current as of October 2022. Amgen does not guarantee the accuracy of this information, and it is up to the individual physician to conduct their own research.
CDC, Centers for Disease Control and Prevention; CLIA, Clinical Laboratory Improvement Amendments; MRD, measurable or minimal residual disease; NGS, next-generation sequencing; PCR, polymerase chain reaction; Ph(+), Philadelphia chromosome–positive.

*https://www.cdc.gov/clia/LabSearch.html

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