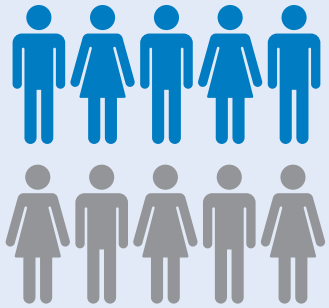
AFTER ACHIEVING COMPLETE REMISSION (CR) IN ADULT B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)[1-3]

Get deeper and test for minimal residual disease (MRD)

MRD IS ASSOCIATED WITH RELAPSE AND POORER SURVIVAL IN PATIENTS WITH ALL.[4]

Up to 50% of adult patients with ALL who achieve CR after chemotherapy may relapse[5,6]



Relapse after frontline therapy generally leads to poor long-term outcomes and fewer treatment options[7]

CR

MRD

Bone marrow microscopy cannot identify the presence of leukemic cells if there are fewer than 5% in the total cell population[1,2]

5%

Over a 10 year period, patients who achieved MRD negativity had a greater chance of survival vs patients who remained MRD(+)[4,*]

*According to a meta-analysis of 5 studies evaluating 806 adult patients with ALL.

Sensitivity of cancer cell detection in 3 testing methods

FLOW CYTOMETRY
1 in 10,000 normal cells[8]

POLYMERASE CHAIN REACTION
1 in 100,000 normal cells[8]

NEXT-GENERATION SEQUENCING
1 in 1,000,000 normal cells[9]

NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) for ALL recommend MRD testing at diagnosis, upon completion of initial induction therapy, and continued monitoring every 3–6 months for at least 5 years as clinically indicated.[3,†]

†While there is insufficient evidence to guide MRD monitoring for Ph-negative patients following completion of maintenance therapy, the approval of blinatumomab, and potentially future therapies for the MRD-positive[3] relapse, may warrant testing in this regard. Alternatively, for patients showing evidence of symptomatic relapse, the diagnostic workup should be repeated as per ALL-1 in the NCCN Guidelines for ALL.

"MRD is an essential component of patient evaluation over the course of sequential therapy."[3]

To learn more about MRD visit www.amgenoncology.com

To find an MRD testing facility see reverse side.

In both children and adults with ALL, MRD testing as early as induction therapy has been shown to have prognostic significance[3]

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REFERENCES:
1. Campana D. Minimal residual disease studies in acute leukemia. *Am J Clin Pathol.* 2004;122(suppl 1):S47-S57. **2.** 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. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Lymphoblastic Leukemia V.1.2019. ©National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed May 7, 2019. 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. **4.** 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. **5.** Hoelzer D. Monitoring and managing minimal residual disease in acute lymphoblastic leukemia. *Am Soc Clin Oncol Educ Book*. 2013;33:290-293. **6.** Jain N, Gurbuxani S, Rhee C, Stock W. Acute lymphoblastic leukemia in adults. In: Hoffman R, Benz EJ Jr, Silberstein LE, Heslop HE, Weitz JI, Anastasi J, eds. *Hematology: Basic Principles and Practice*. 6th ed. Philadelphia, PA: Elsevier; 2013:960-980. **7.** 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. **8.** Campana D. Minimal residual disease in acute lymphoblastic leukemia. *Semin Hematol.* 2009;46:100-106. **9.** Ladetto M, Brüggemann M, Monitillo L, et al. Next-generation sequencing and real-time quantitative PCR for minimal residual disease detection in B-cell disorders. *Leukemia*. 2014;28:1299-1307.

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
Seattle, WA	Adaptive Biotechnologies	NGS	https://www.adaptivebiotech.com	(855) 466-8667
Royal Oak, MI	Beaumont Health	Flow Cytometry	http://www.beaumontlaboratory.com	(800) 551-0488
Seattle, WA	CellNetix	Flow Cytometry, PCR	http://cellnetix.com/	(844) 344-4209
Cincinnati, OH	Cincinnati Children's Hospital	Flow Cytometry	https://www.cincinnatichildrens.org/service/c/cancer-blood/hcp/clinical-laboratories/immunopathology-lab	(513) 803-2567
Aurora, CO	ClinImmune Labs	Flow Cytometry	http://www.clinimmune.com/	(303) 724-7203
Durham, NC	Duke University (Molecular Diagnostics)	Flow Cytometry	https://clinlabs.duke.edu/molecular-diagnostics-laboratory	(919) 684-2698
Seattle, WA	Fred Hutchinson Cancer Research Center	Flow Cytometry, PCR	https://research.fhcrc.org/radich/en/MolecularOncology.html	(206) 667-6630
Carlsbad, CA	Genoptix	Flow Cytometry	https://www.genoptix.com	(800) 755-1605
Seattle, WA	Hematologics, Inc.	Flow Cytometry, NGS	http://www.hematologics.com/	(206) 223-2700
Baltimore, MD	Johns Hopkins Medicine (Pathology)	Flow Cytometry	http://pathology.jhu.edu/department/index.cfm	(410) 955-2405
Boston, MA	Massachusetts General Hospital (Pathology)	Flow Cytometry	http://www.massgeneral.org/pathology	(617) 643-0800
Rochester, MN	Mayo Clinic	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, NGS	https://neogenomics.com/	(866) 776-5907
Columbus, OH	Ohio State University (Division of Molecular Pathology)	Flow Cytometry, PCR	https://pathology.osu.edu/ext/divisions/Clinical/molpath/	(614) 292-2064
National	Quest Diagnostics	PCR	https://www.questdiagnostics.com	(866) 697-8378
Chapel Hill, NC	UNC Medical Center (McLendon Clinical Laboratories)	Flow Cytometry, PCR	https://www.uncmedicalcenter.org/mclendon-clinical-laboratories/	(919) 966-2361
Kansas City, KS	University of Kansas Cancer Center	Flow Cytometry	http://www.kucancercenter.org	(913) 588-1227
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, NGS	http://uwhematopathology.wixsite.com/hemepath	(206) 606-7060
Nashville, TN	Vanderbilt (Pathology Lab Services)	Flow Cytometry	https://ww2.mc.vanderbilt.edu/vpls	(800) 551-5227
New Haven, CT	Yale Cancer Center (Laboratory Medicine)	Flow Cytometry, PCR	https://www.yalecancercenter.org/	(203) 785-4095

This information is current as of April 2019. Amgen does not guarantee the accuracy of this information, and it is up to the individual physician to conduct his/her own research.
CDC, Centers for Disease Control and Prevention; CLIA, Clinical Laboratory Improvement Amendments; MRD, minimal residual disease; NGS, next-generation sequencing; PCR, polymerase chain reaction.

*https://wwwn.cdc.gov/clia/Resources/LabSearch.aspx

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Minimal residual disease (MRD) is the name given to small numbers of leukaemic cells (cancer cells from the bone marrow) that remain in the person during treatment, or after treatment when the patient is in remission (no symptoms or signs of disease). It is the major cause of relapse in cancer and leukemia. Up until a decade ago, none of the tests used to assess or detect cancer were sensitive enough to detect MRD. Now, however, very sensitive molecular biology tests are available, based on DNA, RNA yy Minimal residual disease (MRD) is a term used to describe the small number of cancer cells in the body after cancer treatment. An MRD positive test result means that disease was still detected after treatment. An MRD negative result means that no disease was detected after treatment. yy Doctors use MRD to measure the effectiveness of treatment and to predict which patients are at risk of relapse. It can also help doctors confirm and monitor remissions, and possibly identify an early return of the cancer. yy To test for MRD, doctors use samples from either a blood draw or a bone marrow as Ofatumumab for Residual Disease and Maintenance Following Chemotherapy or Chemoimmunotherapy in Patients With Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL). Actual Study Start Date : July 2011.Â Responses of (complete remission (CR) conversion to minimal residual disease (MRD) negative, partial remission (PR) conversion to nodular partial remission nPR or CR, and nPR conversion to complete remission (CR)) evaluated by physical examination, CBC, CT of chest, abdomen, pelvis, and bone marrow aspirate and biopsy with evaluation of residual disease (MRD) by 4-color flow cytometry.Â Positive serology for Hepatitis B virus (HB) defined as a positive test for HBsAg. Minimal Residual Disease or MRD is the term used to describe detectable signs of cancer in a patient who has had curative-intent treatment (usually surgery, radiotherapy, chemotherapy, immunotherapy, often in combination). It was initially used in haematological malignancies i.e. leukaemiaâ€™s and other cancers of the blood and lymphatic system. These â€œHemeâ€ cancers are caused by a massive over-production of tumour cells, which crucially all carry a specific genetic mutation e.g. the chromosomal translocation BRC-ABL1 (the Philadelphia chromosome. The MRD test relies on its detection to indicate Minimal residual disease (MRD) is common in patients with blood cancers, such as leukemia, lymphoma and multiple myeloma. But what does this mean for patients and their need for additional cancer treatment? Ghayas Issa, M.D., explains.Â If we canâ€™t detect minimal residual disease under the microscope, how do we test for it? We now have much more sensitive assays available to us that allow us to quantify MRD. These could include next generation genetic sequencing, where we can analyze bone marrow samples for genetic mutations. If there are mutations present, that means there is minimal residual disease, even though we canâ€™t see anything under the microscope.