Minimal Residual Disease Report

Patient Name:		DOB:	
CLIA_0000206_mod		October 1, 1949	
Ordering Physician: Alizadeh, Arash	NPI No: 1295824423	Specimen Collection May 06, 2014	Accession No: 201012
Clinical Indication: Follicular lymphoma		Specimen Source: Peripheral Blood	Report Date: July 1, 2015

clonoSEQ ID Test Summary:

ID sample was tested on March 25, 2014 (Accession No. 200703). IGH-VDJ, IGK receptors were recommended for follow-up minimal residual disease (MRD) testing.

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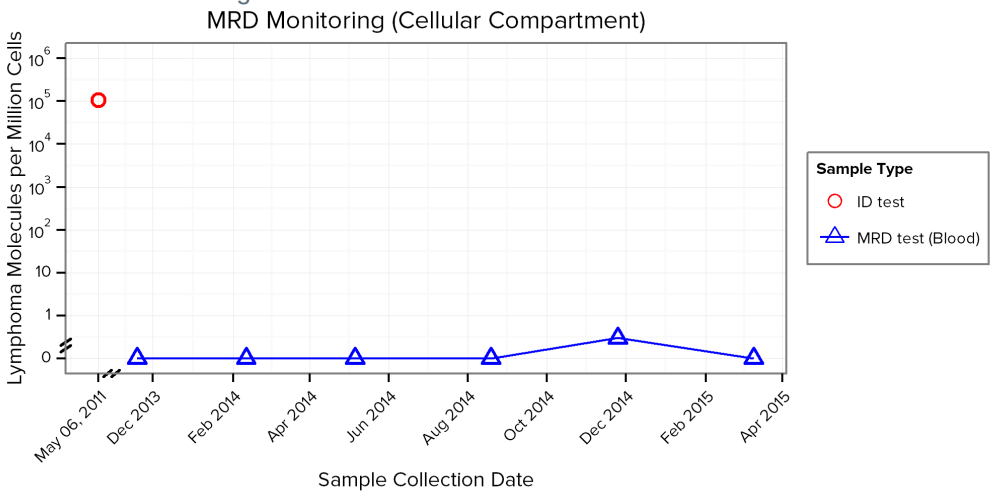
Test Results

Minimal Residual Disease (MRD) Status	Estimated Lymphoma Molecules per Million Cells
NEGATIVE	0.0

Interpretation

The sample is NEGATIVE for the presence of lymphoma gene rearrangements. Lymphoma gene rearrangements were previously identified in an ID sample (March 25, 2014, Accession No. 200703). The previously identified lymphoma gene rearrangements are NOT present in the current MRD sample, which is consistent with the sample being NEGATIVE for lymphoma cells. The results of this test should be interpreted in the complete clinical context, including the patient's clinical presentation and current treatment regimen.



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Patient: CLIA_0000206_mod | DOB: October 1, 1949 | Patient No: 32857

Detail Results

Receptor	Presence of Lymphoma Gene Rearrangements	Estimated Lymphoma Molecules per Million Cells
IGK	-	0.0
IGH-VDJ	-	0.0

Clinical Utility

Minimal residual disease (MRD) analysis by the immune receptor sequencing method is intended to detect cancer molecules in peripheral blood or bone marrow samples[1]. Higher MRD levels during therapy and post-treatment have been shown to have prognostic value in numerous disease

Method

DNA was extracted from Fresh Peripheral Blood. A set of multiplexed primers was used to amplify the full IGH-VDJ, IGK repertoires. Amplified products were sequenced deeply. The level of the lymphoma gene rearrangements previously identified in an ID sample (March 25, 2014, Accession No. 200703) was determined in the current MRD detection sample (May 06, 2014). Assay sensitivity is generally limited by the number of input cells. For example, if only 100,000 cells are present in the tested sample, then the assay lower limit of detection is typically 1 in 100,000 cells.

Quality Assessment: Assay results passed strict QC guidelines for amplification and sequencing depth and quality. The assay lower limit of detection for this sample is 0.21 molecules per million cells.

Immune Receptor Sequencing Method

Regions of the variable (V), diversity (D), and joining (J) gene segments are amplified using a two-stage PCR. In the first stage, multiplexed V and J primers are utilized. This is followed by a second stage that uses a single pair of primers to append sequences necessary for cluster formation and sample multiplexing. Amplified product is sequenced to obtain a high number of reads. Sequences are analyzed to determine similar sequences that form a clonotype, whose frequency can be determined by the number of member reads.

The immune receptor sequencing method is used for clonality assessment and MRD detection.

- ID test: Lymphoma gene rearrangements are identified in diagnostic samples. The following immune receptors are assayed in diagnostic samples: IGH-VDJ, IGH-DJ, IGK
- MRD test: Follow-up samples are monitored for the presence of lymphoma gene rearrangements. Positive receptors which demonstrate a lymphoma gene rearrangement in the clonoSEQ ID test are sequenced, and MRD levels are determined. The sensitivity of this technology enables detection of a single cancer molecule.

References

1. Faham et al. Blood, 2012, 120:5173-80.
2. Gawad et al. Blood, 2012, 120:4407-17.
3. Logan et al. Leukemia, 2013, 27:1659-65.
4. Armand et al. Br J Haematol, 2013, 163:123-6.
5. Martinez-Lopez et al. Blood, 2014, 123:3073-9.
6. Logan et al. Biol Blood Marrow Transplant, 2014, doi: 10.1016/j.bbmt.2014.04.018.
7. Ladetto et al. Leukemia, 2014, 28:1299-307.
8. Vij et al. Clin Lymphoma Myeloma Leuk, 2014, 14:131-139.

Eletronically Signed By:

Name	Date
sdfsd	July 1, 2015