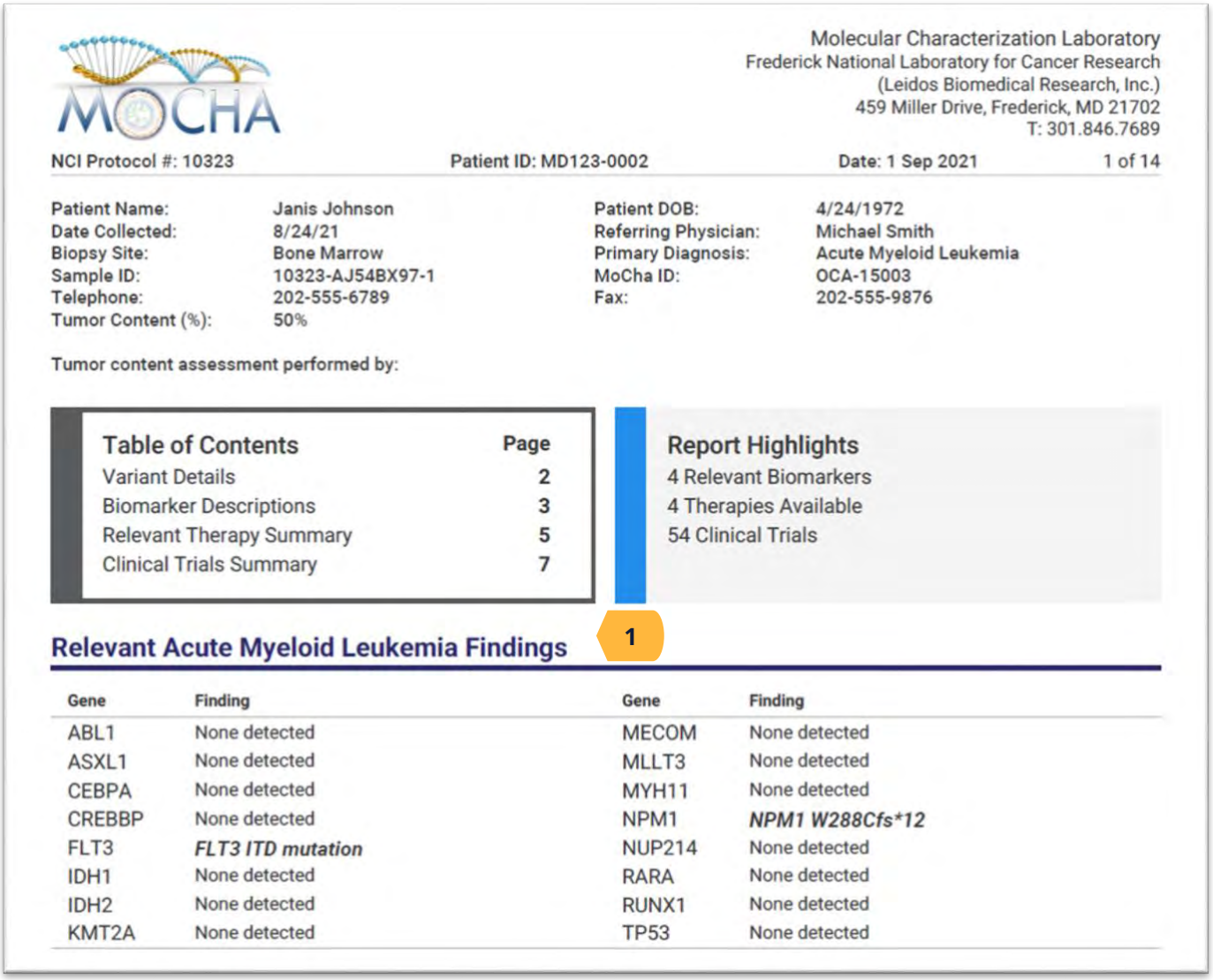
Guide to the MoCha Acute Myeloid Leukemia Biomarker Report



MOCHA

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NCI Protocol #: 10323 | Patient ID: MD123-0002 | Date: 1 Sep 2021 | 1 of 14

Patient Name:	Janis Johnson	Patient DOB:	4/24/1972
Date Collected:	8/24/21	Referring Physician:	Michael Smith
Biopsy Site:	Bone Marrow	Primary Diagnosis:	Acute Myeloid Leukemia
Sample ID:	10323-AJ54BX97-1	MoCha ID:	OCA-15003
Telephone:	202-555-6789	Fax:	202-555-9876
Tumor Content (%):	50%		

Tumor content assessment performed by:

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1

Relevant Acute Myeloid Leukemia Findings

Gene	Finding	Gene	Finding
ABL1	None detected	MECOM	None detected
ASXL1	None detected	MLLT3	None detected
CEBPA	None detected	MYH11	None detected
CREBBP	None detected	NPM1	***NPM1 W288Cfs*12***
FLT3	***FLT3 ITD mutation***	NUP214	None detected
IDH1	None detected	RARA	None detected
IDH2	None detected	RUNX1	None detected
KMT2A	None detected	TP53	None detected

1. Relevant Findings

This table lists key acute myeloid leukemia genes tested for. If a gene tested for was found, the description and location of any gene mutations are included.

Relevant Biomarkers 2

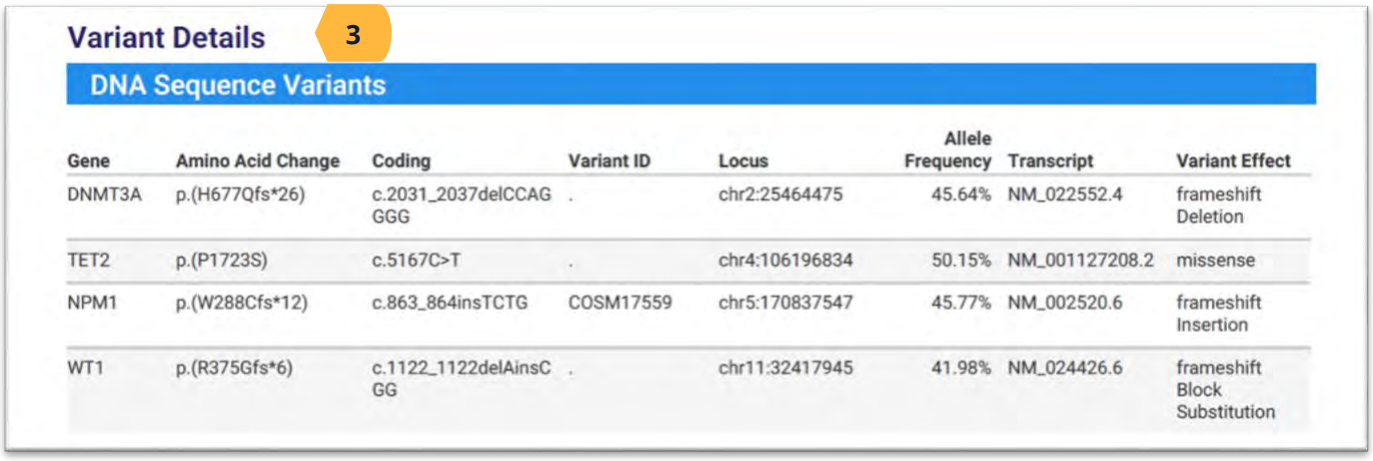
Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*FLT3 ITD mutation*	**gilteritinib** [1] **midostaurin + chemotherapy** [1] sorafenib + chemotherapy venetoclax + chemotherapy	None	45

Prognostic significance: ELN 2017: Favorable to Intermediate
Diagnostic significance: None

Public data sources included in relevant therapies: FDA[1], NCCN
Public data sources included in prognostic and diagnostic significance: NCCN
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

2. Relevant Biomarkers

This table lists therapies (treatments) based on the cancer type and specific biomarkers found in the cancer. The list includes therapies for this cancer type as well as for other types of cancers that have the same biomarkers. Different cancer types that share biomarkers may respond to the same biomarker-targeted therapies.



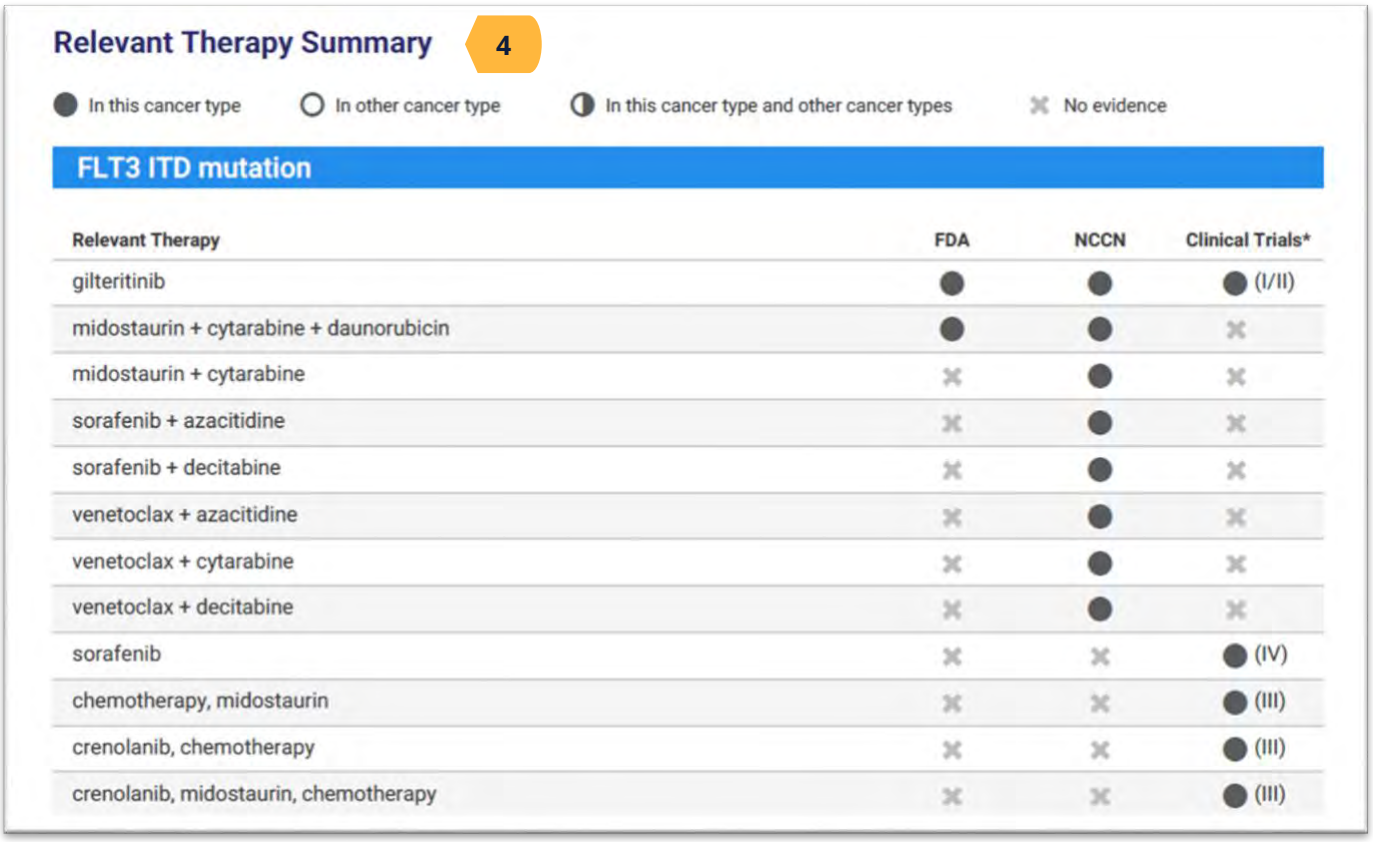
Variant Details 3

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
DNMT3A	p.(H677Qfs*26)	c.2031_2037delCCAGGGG	.	chr2:25464475	45.64%	NM_022552.4	frameshift Deletion
TET2	p.(P1723S)	c.5167C>T	.	chr4:106196834	50.15%	NM_001127208.2	missense
NPM1	p.(W288Cfs*12)	c.863_864insTCTG	COSM17559	chr5:170837547	45.77%	NM_002520.6	frameshift Insertion
WT1	p.(R375Gfs*6)	c.1122_1122delAinsCGG	.	chr11:32417945	41.98%	NM_024426.6	frameshift Block Substitution

3. Variant Details

The biomarker report lists genes that are known to be related to cancer in some way. It also lists changes (variants) in those genes found in the cancer. Doctors may find this information useful when recommending treatment. There are still some changes in cancer genes that are not understood yet. They may be included in the report if they were detected, since they have been found in many cancers. This is another reason why research on these biomarkers is important.



Relevant Therapy Summary 4

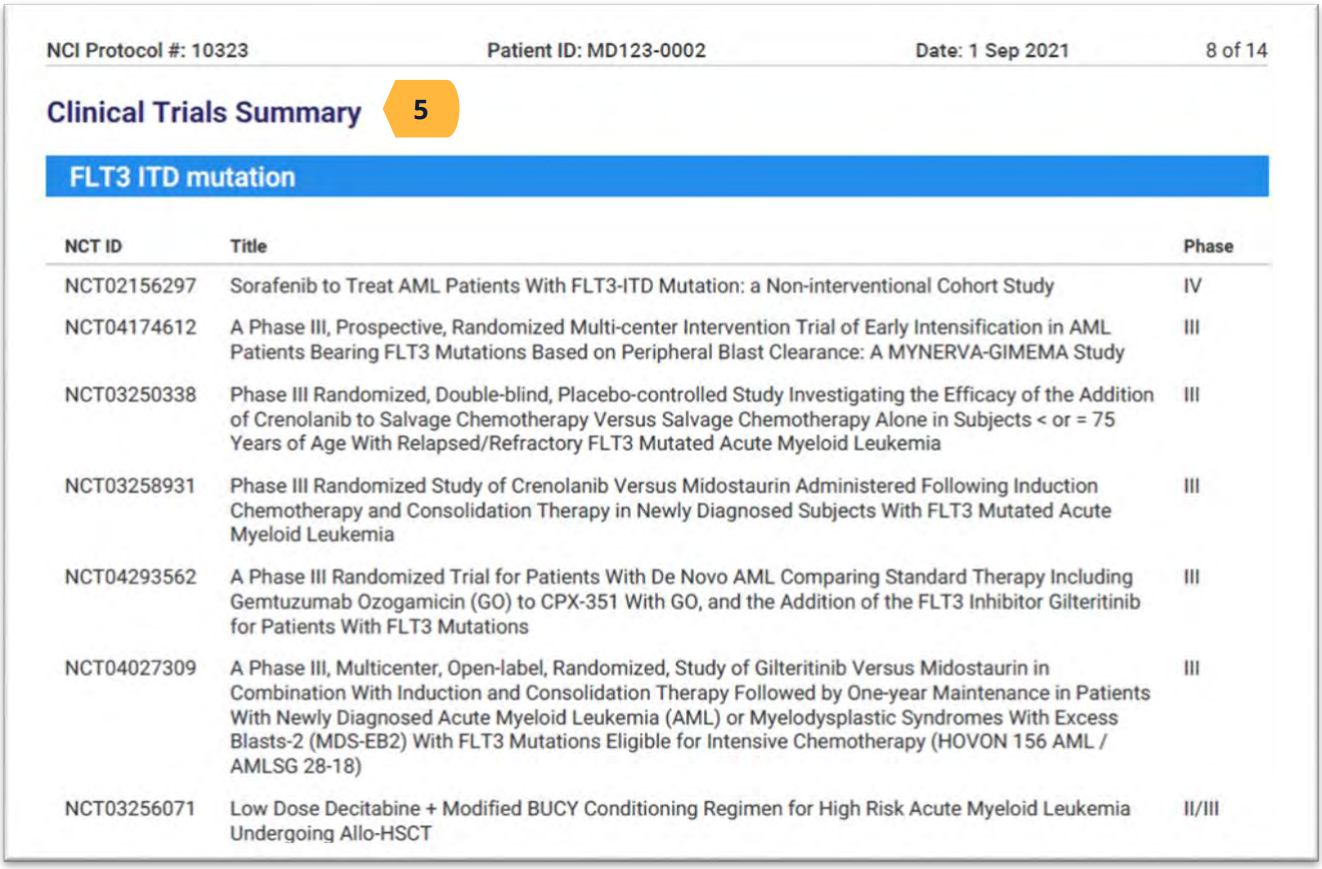
● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

FLT3 ITD mutation

Relevant Therapy	FDA	NCCN	Clinical Trials*
gilteritinib	●	●	● (I/II)
midostaurin + cytarabine + daunorubicin	●	●	✖
midostaurin + cytarabine	✖	●	✖
sorafenib + azacitidine	✖	●	✖
sorafenib + decitabine	✖	●	✖
venetoclax + azacitidine	✖	●	✖
venetoclax + cytarabine	✖	●	✖
venetoclax + decitabine	✖	●	✖
sorafenib	✖	✖	● (IV)
chemotherapy, midostaurin	✖	✖	● (III)
crenolanib, chemotherapy	✖	✖	● (III)
crenolanib, midostaurin, chemotherapy	✖	✖	● (III)

4. Relevant Therapy Summary

The Food and Drug and Administration (FDA) and National Comprehensive Cancer Network (NCCN) publish therapy guidelines for specific cancer types. This table lists their recommended therapies based on the biomarkers found in the cancer. The table also shows whether there may be clinical trials available. A clinical trial is a type of research study that tests potential new therapies.



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Clinical Trials Summary 5

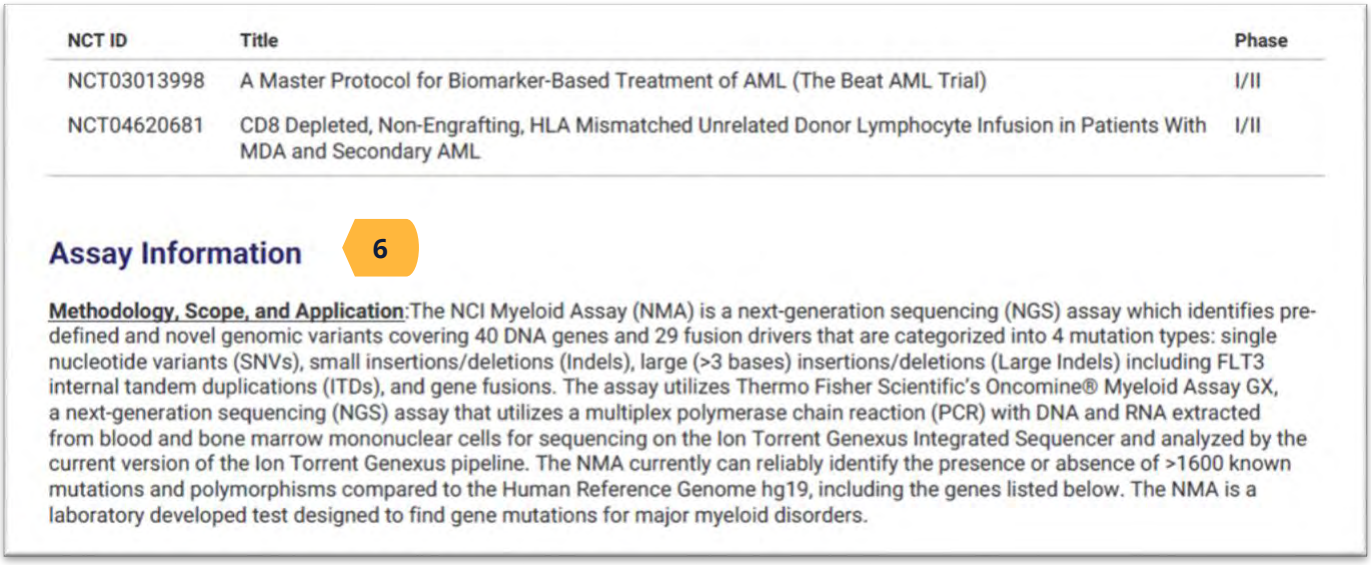
FLT3 ITD mutation

NCT ID	Title	Phase
NCT02156297	Sorafenib to Treat AML Patients With FLT3-ITD Mutation: a Non-interventional Cohort Study	IV
NCT04174612	A Phase III, Prospective, Randomized Multi-center Intervention Trial of Early Intensification in AML Patients Bearing FLT3 Mutations Based on Peripheral Blast Clearance: A MYNERVA-GIMEMA Study	III
NCT03250338	Phase III Randomized, Double-blind, Placebo-controlled Study Investigating the Efficacy of the Addition of Crenolanib to Salvage Chemotherapy Versus Salvage Chemotherapy Alone in Subjects < or = 75 Years of Age With Relapsed/Refractory FLT3 Mutated Acute Myeloid Leukemia	III
NCT03258931	Phase III Randomized Study of Crenolanib Versus Midostaurin Administered Following Induction Chemotherapy and Consolidation Therapy in Newly Diagnosed Subjects With FLT3 Mutated Acute Myeloid Leukemia	III
NCT04293562	A Phase III Randomized Trial for Patients With De Novo AML Comparing Standard Therapy Including Gemtuzumab Ozogamicin (GO) to CPX-351 With GO, and the Addition of the FLT3 Inhibitor Gilteritinib for Patients With FLT3 Mutations	III
NCT04027309	A Phase III, Multicenter, Open-label, Randomized, Study of Gilteritinib Versus Midostaurin in Combination With Induction and Consolidation Therapy Followed by One-year Maintenance in Patients With Newly Diagnosed Acute Myeloid Leukemia (AML) or Myelodysplastic Syndromes With Excess Blasts-2 (MDS-EB2) With FLT3 Mutations Eligible for Intensive Chemotherapy (HOVON 156 AML / AMLSG 28-18)	III
NCT03256071	Low Dose Decitabine + Modified BUCY Conditioning Regimen for High Risk Acute Myeloid Leukemia Undergoing Allo-HSCT	II/III

5. Clinical Trials Summary

This table lists clinical trials that may be available for a specific type of cancer, based on gene mutations and or biomarkers found in the cancer. A clinical trial is a type of research study that tests potential new therapies.

More information on each clinical trial, such as where the clinical trial is being done, can be found at ClinicalTrials.gov.



NCT ID	Title	Phase
NCT03013998	A Master Protocol for Biomarker-Based Treatment of AML (The Beat AML Trial)	I/II
NCT04620681	CD8 Depleted, Non-Engrafting, HLA Mismatched Unrelated Donor Lymphocyte Infusion in Patients With MDA and Secondary AML	I/II

Assay Information 6

Methodology, Scope, and Application:The NCI Myeloid Assay (NMA) is a next-generation sequencing (NGS) assay which identifies pre-defined and novel genomic variants covering 40 DNA genes and 29 fusion drivers that are categorized into 4 mutation types: single nucleotide variants (SNVs), small insertions/deletions (Indels), large (>3 bases) insertions/deletions (Large Indels) including FLT3 internal tandem duplications (ITDs), and gene fusions. The assay utilizes Thermo Fisher Scientific's Oncomine® Myeloid Assay GX, a next-generation sequencing (NGS) assay that utilizes a multiplex polymerase chain reaction (PCR) with DNA and RNA extracted from blood and bone marrow mononuclear cells for sequencing on the Ion Torrent Genexus Integrated Sequencer and analyzed by the current version of the Ion Torrent Genexus pipeline. The NMA currently can reliably identify the presence or absence of >1600 known mutations and polymorphisms compared to the Human Reference Genome hg19, including the genes listed below. The NMA is a laboratory developed test designed to find gene mutations for major myeloid disorders.

6. Assay Information

The biomarker test looks for three types of biomarkers:

- Single Nucleotide Variants and Indels – which are variations of a gene
- Copy Number Variants – which is the number of times a gene is repeated
- Gene fusions – when two separate genes combine together.

Get more information on the genetics of cancer.