

| Patient | Specimen Information | Ordered By |
|---|---------------------------------|------------|
| Name: Beverly Weber | Primary Tumor Site: Leukemia | |
| Date of Birth: 1976-11-09 | Specimen Site: Peripheral blood | |
| Sex: Female | Specimen ID: 3577 | |
| Case Number: 8623 | Specimen Collected: 2023-11-03 | |
| Diagnosis: Chronic myeloid leukemia (CML) | Test Initiated: 2023-11-04 | |

| Biomarker | Method | Analyte | Result | Therapy association | | Biomarker level |
|-----------|--------|-----------|---------------------|---------------------|--|-----------------|
| ER | IHC | protein | Positive 3+, 100% | BENEFIT | abemaciclib, palbociclib, ribociclib, endocrine, therapy, everolimus | level 2 |
| PR | IHC | protein | Positive 2+, 95% | BENEFIT | abemaciclib, palbociclib, ribociclib, endocrine therapy | level 2 |
| TMB | seq | DNA tumor | 14 m/Mb High | BENEFIT | pembrolizumab | level 2 |
| ERBB2 | IHC | Protien | Negative 0 | LACK OF BENEFIT | trastuzumab, ado-trastuzumab emtansine, pertuzumab, fam-trastuzumab deruxtecan-nxki, lapatinib, neratinib, tucatinib | level 1 |

Cancer-Type Relevant Biomarkers

| BioMarker | Method | Analyte | Result |
|-----------|--------|-----------|---------------------|
| JAK2 | Seq | RNA-Tumor | Fusion not detected |
| DDR2 | Seq | DNA-Tumor | Stable |
| ER | IHC | Protien | Negative 2+, 16% |
| AR | IHC | Protien | Positive 3+, 84% |
| PR | IHC | Protien | Positive 3+, 62% |

| BioMarker | Method | Analyte | Result |
|-----------|--------|-----------|-----------------------|
| AR | IHC | Protien | Negative 3+, 58% |
| MUTYH | Seq | RNA-Tumor | Mutation not detected |
| CSF3R | Seq | RNA-Tumor | Fusion not detected |
| STAT5B | Seq | DNA-Tumor | Fusion not detected |
| MTOR | Seq | DNA-Tumor | Stable |

Genomic Signatures

| BioMarker | Method | Analyte | Result |
|--------------------------------------|--------|-----------|---|
| Microsatellite instability | Seq | DNA tumor | Equivocal |
| Tumor mutational burden | Seq | DNA tumor | 14 mutations/Mb High |
| Genomic loss of heterozygosity (LOH) | Seq | DNA tumor | High - 27% of tested genmoic segments exhibit LOH |

Genes Tested with Pathogenic Alterations or likely Pathogenic Alterations

| Gene | Method | Analyte | Variant Interpretation | Protien Alteration | Exon | DNA Alteration | Allele Frequency % |
|--------|--------|-----------|------------------------|--------------------|------|---------------------|--------------------|
| NTRK1 | Seq | DNA tumor | Likely Benign | p.R139H | 15 | c.416G>A | 10.26 |
| DDR2 | Seq | DNA tumor | Pathogenic | p.N159Y | 2 | . | 27.25 |
| MAP2K2 | Seq | DNA tumor | Pathogenic | p.W515L | 3 | c.1543_1544delinsAA | 4.69 |
| PDGFRA | Seq | DNA tumor | Likely Pathogenic | p.Q338H | 16 | c.1014G>C | 17.65 |
| ABL1 | Seq | DNA tumor | Likely Pathogenic | p.I1307K | 2 | c.3920T>A | 12.07 |
| CSF3R | Seq | DNA tumor | Likely Pathogenic | p.K656E | 12 | c.1966A>G | 8.82 |

Gene Variants of Unknown Significance

| Gene | Method | Analyte | Variant Interpretation | Protien Alteration | Exon | DNA Alteration | Allele Frequency % |
|--------|--------|-----------|-----------------------------------|--------------------|------|----------------|--------------------|
| MYO1G | Seq | DNA tumor | Variant of uncertain significance | p.M1R | 11 | c.2T>G | 4.74 |
| PDGFRA | Seq | DNA tumor | Variant of uncertain significance | p.N515H | 6 | 1 | 17.18 |
| ALDH2 | Seq | DNA tumor | Variant of uncertain significance | p.G12X | 2 | c.35G>T | 19.76 |
| BRCA1 | Seq | DNA tumor | Variant of uncertain significance | p.C481X | 8 | c | 9.36 |
| JAK3 | Seq | DNA tumor | Variant of uncertain significance | p.G503A | 12 | c.1508G>C | 3.86 |
| MYO1G | Seq | DNA tumor | Variant of uncertain significance | p.K666X | 14 | c | 1.64 |

Immunohistochemistry Results

| Biomarker | Result |
|-----------|-------------------|
| MSH6 | Negative 1+, 53% |
| PR | Positive 3+, 98% |
| ER | Negative 2+, 32% |

Genes Tested with Indeterminate Results by Tumor DNA Sequencing

CDKN2A CALR ABL1

Specimen Information

Specimen ID: 3577

Specimen Collected: 2023-11-03

Specimen Recieved: 2023-11-04

Testing Initiated: 2023-11-04

Gross Description: 3577

Pathological Diagnosis:

Left breast, central, 12:00, suspicious mass, 12-gauge core needle biopsy: Infiltrating moderately-differentiated mammary carcinoma, grade 2, Nottingham score 6 (architectural grade 3, nuclear grade 2, mitotic figures 1).

Dissection Information:

Molecular testing of this specimen was performed after harvesting of targeted tissues with an approved manual microdissection technique. Candidate slides were examined under a microscope and areas containing tumor cells (and separately normal cells, when necessary for testing) were circled. A laboratory technician harvested targeted tissues for extraction from the marked areas using a dissection microscope.

Clinical Trials Connector

| CHEMOTHERAPY CLINICAL TRIALS | | | | |
|------------------------------|-----------|--------|-----------|---|
| Drug class | Biomarker | Method | Analyte | Investigational agents |
| Anti hormonal therapy | ER | IHC | protein | anastrozole, letrozole, exemestane, fulvestrant, tamoxifen, goserelin, leuprolide |
| Anti hormonal therapy | PR | IHC | protein | anastrozole, letrozole, exemestane, fulvestrant, tamoxifen, goserelin, leuprolide |
| Anti inflammatory agents | PIK3CA | NGS | DNA tumor | aspirin |

| TARGETED THERAPY CLINICAL TRIALS | | | | |
|----------------------------------|-----------|--------|-----------|--|
| Drug class | Biomarker | Method | Analyte | Investigational agents |
| Akt inhibitors | ARID1A | NGS | DNA tumor | AZD5363, MK-2206, ipataserib |
| immunomodulatory agents | TMB | NGS | DNA tumor | avelumab, atezolizumab, durvalumab, ipilimumab, nivolumab, pembrolizumab |
| PARP inhibitors | NBN | NGS | DNA tumor | BGB-290, BMN-673, olaparib, rucaparib, talazoparib |
| Akt/mTor inhibitors | PIK3CA | NGS | DNA tumor | AZD5363, BYL719, MK-2206, ipataserib, everolimus, temsirolimus |