**IDH1 and IDH2 Mutation Analysis, Exon 4**

### Indications for Ordering

Use to determine the risk group
- Newly diagnosed cytogenetically normal acute myeloid leukemia (CN-AML)
- Individuals with gliomas

### Test Description

Polymerase chain reaction followed by Sanger sequencing

### Tests to Consider

**Primary tests**

- **IDH1 and IDH2 Mutation Analysis, Exon 4 2006444**
  - Detect IDH1 and IDH2 mutations in whole blood or bone marrow
  - May have prognostic significance in patients with hematologic malignancies, depending on the clinical and genetic context

- **IDH1 and IDH2 Mutation Analysis, Exon 4, Formalin-Fixed, Paraffin-Embedded (FFPE) Tissue 2014188**
  - IDH1/IDH2 mutational status is a prognostic marker in individuals with low- and high-grade gliomas
  - Aid in distinguishing a primary from a secondary glioblastoma

**Related tests**

- Initial prognostication for patients with CN-AML
  - **NPM1 Mutation Detection by RT-PCR, Quantitative 3000066**
  - **CEBPA Mutation Detection 2004247**
  - **LeukoStrat CDx FLT3 Mutation Detection by PCR 2014683**
  - **Myeloid Malignancies Mutation Panel by Next Generation Sequencing 2011117**

- Secondary prognostication for patients with CN-AML
  - **WT1 Mutation Detection by Sequencing 2005766**

### Disease Overview

#### Diagnostic/treatment issues

**AML**
- 50% of AML cases are cytogenetically normal
  - Patients are considered to be at intermediate risk
- Mutation testing may help to prognosticate CN-AML
  - Presence of mutations may alter therapeutic decisions
  - Significance of IDH1/IDH2 mutations appears to be context specific
    - Unfavorable prognosis if IDH1/IDH2 mutations appear with NPM1 mutations and in the absence of FLT3-ITD mutations
- SNP rs11554137 is associated with unfavorable prognosis

**Gliomas**
- IDH1 (rarely IDH2) mutations occur in >70% of WHO grade I and II astrocytomas and oligodendrogliomas, as well as glioblastomas that have developed from these lower grade lesions
- IDH1 and IDH2 mutations are associated with favorable outcome in all WHO grade gliomas
- SNP rs11554137 is associated with unfavorable prognosis

### Genetics

**Genes** – IDH1 and IDH2

### Test Interpretation

**Analytical sensitivity** – 40% mutated cells

**Results**
- Positive – mutation detected
  - SNP rs11554137 will be reported
- Negative – no mutation detected

**Limitations**
- Negative test result does not exclude
  - Mutations below the limit of detection
  - Presence of gene mutations other than those detected by the test
- This marker should be interpreted within the group of CN-AML prognostic markers