# *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