**MGMT Promoter Methylation Detection**

**Indications for Ordering**

*MGMT* promoter methylation status is a prognostic biomarker in patients with high-grade gliomas and is useful in treatment decisions.

**Test Description**

**Test methodology**

Genomic DNA is isolated from microscopically guided dissection of tumor tissue. Bisulfite conversion and subsequent polymerase chain reaction (PCR) amplification of region of interest is followed by enzymatic cleavage at thymine residues. The resulting fragments, which differ in molecular mass based on CpG site methylation status, are analyzed by MassARRAY matrix-assisted laser desorption/ionization (MALDI) time-of-flight (TOF) mass spectrometry to determine CpG methylation status. Methylation status of *MGMT* promoter CpG sites 72-83 and 86-89 is evaluated. Total methylation is calculated as an average across listed CpG sites.

**Tests to Consider**

**Primary test**

*MGMT* Promoter Methylation Detection 2009310

- Prognostic biomarker in patients with high-grade gliomas and is useful in treatment decisions

**Related tests**

IDH1 and IDH2 Mutation Analysis, exon 4 2006444

- Prognostic testing for individuals with glioma

EGFR Gene Amplification by FISH 3001310

- Aids in prognostic testing and therapeutic decisions for neoplasms in which amplification has been demonstrated

**Disease Overview**

**High-grade gliomas**

- *MGMT* promoter methylation status is an essential part of molecular diagnostics for all patients with high-grade gliomas (grade III and IV)
- *MGMT* promoter methylation is strongly associated with IDH1/2 mutations
- *MGMT* promoter methylation confers a survival advantage in glioblastoma
- *MGMT* promoter methylation status is useful in treatment decisions for elderly patients

- Patients with glioblastoma that are not *MGMT* promoter methylated derive less clinical benefit from treatment with temozolomide compared to those whose tumors are methylated
- For specific ordering and treatment recommendations please refer to NCCN Clinical Practice Guidelines in Oncology, Central Nervous System Cancers [www.nccn.org]

**Genetics**

*Gene: MGMT (O6-methylguanine-DNA methyltransferase)*

*Area of interest: promoter region*

*Function: DNA repair*

**Test Interpretation**

**Sensitivity/specificity**

- Analytical sensitivity: 5% methylation
- Analytical specificity: 100%

**Results**

- Detected: *MGMT* promoter methylation was detected
  - Total methylation equal to or greater than 30%
- Low-level: Low level *MGMT* promoter methylation was detected
  - Total methylation of 10-29%
- Not detected: *MGMT* promoter methylation was not detected
  - Total methylation of 0-9%

**Limitations**

- Methylation at CpG sites other than those listed in test methodology section will not be detected
- Total methylation is calculated as an average across multiple CpG sites; methylation status of individual sites may vary from nonmethylated to highly methylated
- Bisulfite conversion is not 100% efficient and some unmethylated C's may not be converted to T's
- This method involves PCR:
  - Rare polymorphisms under primers may affect assay results
  - Rare polymorphisms at CpG locations or at the amplicon cleavage cut sites may affect assay results
- Results of this test must always be interpreted within the clinical context and other relevant data and should not be used alone for a diagnosis of malignancy
References