Classification of diffuse Gliomas
Combined Immunohistochemistry on IDH1 R132H and ATRX substitutes molecular testing.
The routine practical approach for diagnosing astrocytomas and oligodendrogliomas begins with performing IHC for ATRX and IDH1 R132H expression. Stepwise analysis of molecular parameters with initial IHC for ATRX and IDH1 R132H followed by 1p/19q analysis and then by IDH sequencing significantly reduces the number of molecular tests required for unequivocal diagnosis (Reuss et al., 2015).

### IDH1 R132H

The 2016 CNS WHO classification recommends IDH1 R132H IHC as a backbone for differential diagnosis of glioma. IDH1 R132H IHC is widely applied as a favorable prognostic marker.

### ATRX

ATRX mutations in gliomas result in the loss of nuclear ATRX expression, which can be diagnosed by IHC. Loss of ATRX expression is close to being mutually exclusive to 1p/19q codeletion.

### p53

p53 can be selected as a marker since prominent staining is mutually exclusive to 1p/19q deletion, suggesting the usefulness of ATRX and p53 IHC should 1p/19q analysis not be possible.

### Ki-67

High Ki-67 labeling index is high in IDH wild type gliomas and lower in IDH1 mutant glioma. The mitotic index is associated with outcome in IDH wild type tumors.

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**Biomarker**

<table>
<thead>
<tr>
<th>IDH1/2</th>
<th>1p/19q</th>
<th>ATRX</th>
<th>hTERT-Promotor mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>mutated</td>
<td>co-deleted</td>
<td>nuclear expression</td>
<td>common</td>
</tr>
</tbody>
</table>

**Typical histological finding and prognosis**

<table>
<thead>
<tr>
<th>Histology</th>
<th>WHO grading</th>
<th>Median Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>oligodendrogial</td>
<td>II or III</td>
<td>&gt;15 years</td>
</tr>
<tr>
<td>astrocytic</td>
<td>II or III (rare IV)</td>
<td>8-12 years</td>
</tr>
<tr>
<td>astrocytic</td>
<td>IV (rare II or III)</td>
<td>&lt;2-3 years</td>
</tr>
</tbody>
</table>

**Diffuse glioma with IDH mutation and 1p/19q-codeletion (oligodendroglioma)**

**Diffuse glioma with IDH mutation**

**Diffuse glioma without IDH mutation**

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References: