Bevacizumab, a monoclonal antibody to the Vascular Endothelial Growth Factor (VEGF) and Irinotecan for treatment of recurrent primary malignant brain tumors in adults

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Background
The prognosis of recurrent malignant brain tumors/gliomas is poor, and no efficacious therapy exists in patients previously treated with radiotherapy and standard chemotherapy.

Angiogenesis is a requirement for growth of malignant brain tumors.

Vascular endothelial growth factor (VEGF) is abundantly produced in gliomas and is a prognostic factor with more VEGF expression correlating with a poor prognosis.

Bevacizumab is a monoclonal antibody which binds to VEGF, thereby inhibiting activation of the VEGF receptor (VEGFR).

Irinotecan is a topoisomerase inhibitor, with limited effect when used as monotherapy for gliomas.

Promising results from Duke Comprehensive Cancer Center, NC, with bevacizumab and Irinotecan for patients with recurrent gliomas, induced similar effect when used as monotherapy for gliomas tested as a part of a primary setting.

Results
Sex
- 17 female & 33 male
Age
- Median 46 years (26 – 67)
Performance status (WHO)
- PS 0: 20
- PS 1: 19
- PS 2: 11

Number of interventions before enrollment
- 2 (2 patients)
- 3 (16 patients)
- 4 (16 patients)
- >5 (16 patients)

Time from primary diagnosis until enrollment:
- Median: 36.7 months (5 – 183)

Tumor Types
- 25 Glioblastoma Multiforme
- 13 Grade III Astrocytoma
- 5 Grade III Oligodendroglioma
- 1 Malignant Ependymoma
- 1 Malignant Proclactinoma
- 3 Brainstem Glioma
- 1 Anaplastic Medulloblastoma

Table 2: Progression Free Survival at 6 months (PFS-6)

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Number of patients</th>
<th>PFS-6</th>
<th>PFS-6 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glioblastoma Multiforme</td>
<td>15</td>
<td>6</td>
<td>40.0 %</td>
</tr>
<tr>
<td>Grade III Gliomas</td>
<td>17</td>
<td>6</td>
<td>35.6 %</td>
</tr>
<tr>
<td>Others</td>
<td>4</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
<td>12</td>
<td>33.3 %</td>
</tr>
</tbody>
</table>

Table 1: Distribution of responses according to tumor type

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>CR</th>
<th>PR</th>
<th>SD</th>
<th>PD</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glioblastoma Multiforme</td>
<td>4</td>
<td>2</td>
<td>10</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Grade III Astrocytoma</td>
<td>-</td>
<td>2</td>
<td>8</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>Grade III Oligodendroglioma</td>
<td>1</td>
<td>-</td>
<td>3</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Others</td>
<td>-</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
<td>6</td>
<td>25</td>
<td>6</td>
<td>42</td>
</tr>
</tbody>
</table>

Table 3: Overall Toxicity (WHO)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Overall Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-II</td>
<td>4 - 56 %</td>
</tr>
<tr>
<td>III</td>
<td>2 - 6 %</td>
</tr>
<tr>
<td>V</td>
<td>2%</td>
</tr>
</tbody>
</table>

Table 4: Progression Free Survival at 6 months (PFS-6)

Toxicity
Manageable side effects
- 1 patient with trombosis
- 3 patients with hypertension

Unmanageable side effects
- 1 patient with diarrhea (Grade V)
- 1 patient with cerebral hemorrhage
- 1 patient with cardiac arrhythmia

Received cardiac bypass 2 years prior to therapy