Pilot study of modafinil for treatment of neurobehavioral dysfunction and fatigue in adult patients with brain tumors.

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Background: Patients with brain cancer develop neurobehavioral dysfunction and fatigue that compromise their performance of daily activities. We report results from evaluating the efficacy and safety of modafinil treatment for tumor/therapy sequelae in this medically fragile patient population.

Methods: Patients: 21-65 years old with primary malignant disease or nonmalignant cerebral tumors treated with neurosurgical resection, radiotherapy, and/or chemotherapy. Clinical Global Impression of Severity ratings of mild to severe attention/memory impairment and/or fatigue. Measures: Trail Making (TM) A and B, Symbol Digit Modalities (SDM), Verbal Fluency (VF), Hamilton Depression Scale (HAM-D), Fatigue Severity Scale (FSS), Visual Analogue Fatigue Scale (VAFS), Modified Fatigue Impact Scale (MFIS). Design: Double-blind dose-controlled randomization (200 or 400 mg/day modafinil in divided doses) 3 wks; Washout 1 wk; Open label extension 8 wks. Statistical analyses: Changes from baseline at scheduled visits (1, 3, 4, 8, 12 wks) using paired t-tests or Wilcoxon Signed Rank tests as appropriate.

Results: Thirty patients, 63% male, mean age (SD) = 45.3 (11.7) yrs were accrued from 6/03-10/05. Illness severity: moderate 3 (10%), marked 13 (43%), severe 14 (47%). Tumor histology: glioblastoma multiforme 8 (27%), anaplastic glioma 10 (33%), low grade glioma 10 (33%), meningioma 1 (3%), CNS lymphoma 1 (3%). Treatment: neurosurgical resection 93%, radiotherapy 87%, chemotherapy 70%. The table shows relationships of nine variables at baseline and 8 and 12 weeks after initiation of modafinil. Adverse events reported by >4 patients: headache 13 (42%); insomnia 8 (26%); dizziness 7 (23%); dry mouth 7 (23%); depressed consciousness 5 (16%); nausea 4 (13%).

Conclusions: Results show improvement across cognitive, mood, and fatigue outcome measures. Modafinil was generally well tolerated, with a low incidence of adverse events. Greatest improvements in outcomes were observed 8 wks after baseline.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline Mean (SD)</th>
<th>+8 Weeks Mean (SD)</th>
<th>p value</th>
<th>+12 Weeks Mean (SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TM-A</td>
<td>35.5 seconds (16.0)</td>
<td>29.7 seconds (21.7)</td>
<td>.01</td>
<td>28.8 seconds (16.3)</td>
<td>.002</td>
</tr>
<tr>
<td>TM-B</td>
<td>95.5 seconds (47.2)</td>
<td>68.0 seconds (36.5)</td>
<td>&lt;.0001</td>
<td>73.6 seconds (45.0)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>SDM-Oral</td>
<td>50.4 (15.3)</td>
<td>61.5 (22.7)</td>
<td>.0002</td>
<td>58.1 (21.6)</td>
<td>.006</td>
</tr>
<tr>
<td>SDM-Manual</td>
<td>44.3 (13.3)</td>
<td>54.2 (20.0)</td>
<td>&lt;.0001</td>
<td>50.7 (18.9)</td>
<td>.004</td>
</tr>
<tr>
<td>VF</td>
<td>32.5 (15.9)</td>
<td>42.3 (15.6)</td>
<td>&lt;.0001</td>
<td>39.2 (15.3)</td>
<td>.002</td>
</tr>
<tr>
<td>HAM-D</td>
<td>17.8 (9.0)</td>
<td>10.4 (6.5)</td>
<td>&lt;.0001</td>
<td>12.8 (8.5)</td>
<td>.007</td>
</tr>
<tr>
<td>FSS</td>
<td>5.2 (1.4)</td>
<td>3.6 (1.5)</td>
<td>&lt;.0001</td>
<td>3.5 (1.6)</td>
<td>.0003</td>
</tr>
<tr>
<td>MFIS</td>
<td>50.2 (17.0)</td>
<td>30.5 (16.7)</td>
<td>&lt;.0001</td>
<td>28.9 (21.0)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>VAFS</td>
<td>4.0 (2.4)</td>
<td>6.7 (2.6)</td>
<td>.0001</td>
<td>6.7 (3.0)</td>
<td>.0005</td>
</tr>
</tbody>
</table>

Associated Presentation(s):
1. Pilot study of modafinil for treatment of neurobehavioral dysfunction and fatigue in adult patients with brain tumors.

Meeting: 2006 ASCO Annual Meeting
Presenter: Thomas A Kaleita, PhD
Session: Central Nervous System Tumors (Oral Presentation)
glioma (LGG).

Meeting: 2006 ASCO Annual Meeting  Abstract No: 1500  First Author: E. G. Shaw
Category: Central Nervous System Tumors - CNS Tumors

2. Study design considerations for phase II trials of anaplastic gliomas and its impact on phase III survival studies.

Meeting: 2006 ASCO Annual Meeting  Abstract No: 1501  First Author: V. A. Levin
Category: Central Nervous System Tumors - CNS Tumors


Meeting: 2006 ASCO Annual Meeting  Abstract No: 1502  First Author: C. R. Miller
Category: Central Nervous System Tumors - CNS Tumors

Abstracts by T. A. Kaleita
1. Pilot study of modafinil for treatment of neurobehavioral dysfunction and fatigue in adult patients with brain tumors.

Meeting: 2006 ASCO Annual Meeting  Abstract No: 1503  First Author: T. A. Kaleita
Category: Central Nervous System Tumors - CNS Tumors

Presentations by T. A. Kaleita
1. Pilot study of modafinil for treatment of neurobehavioral dysfunction and fatigue in adult patients with brain tumors.

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PubMed Articles by T A Kaleita
PMID: 15072475 [PubMed - in process]

PMID: 11543979 [PubMed - in process]

PMID: 11822985 [PubMed - in process]