Phase I/Randomized Phase II Trial of Either Dasatinib or Placebo Combined with Standard Chemo-Radiotherapy for Newly Diagnosed Glioblastoma Multiforme (GBM).

**Purpose of Study:**
1) To establish a maximum tolerable dose of dasatinib combined with radiation and temozolomide in this patient population.

2) To determine the efficacy of dasatinib in combination with RT and concomitant and adjuvant TMZ in patients with newly diagnosed glioblastoma multiforme, and compare it with the standard of care approach in the treatment of these patients consisting of RT and TMZ, followed by adjuvant TMZ (Stupp regimen).

- Translational (Phase II only)
1) To determine the relationship between tumor biomarkers and clinical outcome of patients treated with the dasatinib/RT/TMZ combination.

2) As part of ongoing research for NCCTG CNS studies, we are banking paraffin-embedded tissue blocks/slides and blood products for future studies.

- QOL (Phase II only)
1) Assess the impact of the addition of dasatinib to RT/TMZ on quality of life (QOL) using both FACT-Br (50 items) and EORTC QLQ C15-PAL plus BN20 (35 items).

2) To compare the results of the two most commonly used QOL tools, FACT-Br (50 items) and EORTC QLQ C15-PAL plus BN20 (35 items) in newly diagnosed GBM patients.

**Study Chairs:** Nadia Nicole Laack M.D.  
Francois J. Geoffroy M.D.  
Clinton H. Leinweber M.D.

**QC Specialist:** Butch K. Kvittem CCRP

**Statistician:** Wenting Wu Ph.D.

**Nurse Resource:** Wanda L. DeKrey R.N., OCN

**Status:** 06/05/2009 Activated

**Projected Number of Patients:** 223

**Excluded:** None

**Final Accrual:** NA

**Stratification Factors:** (For Phase II Only) Age: >70 vs. <=

**Schema:** Reg  
Phase I  
Dasatinib + RT + Temozolomide  
Dasatinib + Temozolomide  
Phase II  
Group A: Placebo + RT + Temozolomide
**Treating Schedule:**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Agent</th>
<th>Dose</th>
<th>Route</th>
<th>Days</th>
<th>Freq</th>
</tr>
</thead>
<tbody>
<tr>
<td>*</td>
<td>Dasatinib</td>
<td>Assigned by Rand-</td>
<td>Oral</td>
<td>Daily starting on</td>
<td>Daily during RT, 28-42 day rest period, then daily til prog.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ommization Center</td>
<td></td>
<td>same day as RT</td>
<td></td>
</tr>
<tr>
<td>*</td>
<td>Temozolomide</td>
<td>75 mg/m2/d</td>
<td>Oral</td>
<td>7 days/week for 6</td>
<td>Daily during RT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>weeks during RT</td>
<td></td>
</tr>
<tr>
<td>*</td>
<td>Temozolomide</td>
<td>150 mg/m2/d</td>
<td>Oral</td>
<td>Days 1-5, Week 1</td>
<td>Cycle 3 which starts after the post-RT 28-42 day rest period</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*</td>
<td>Temozolomide</td>
<td>200 mg/m2/d</td>
<td>Oral</td>
<td>Days 1-5, Week 1</td>
<td>Every 28 days for 5 cycles (cycles 4-8)</td>
</tr>
</tbody>
</table>

**Study Design:** This trial includes a phase I dose-escalation study (Study 1) and a double-blind randomized phase II trial (Study 2) for patients with newly diagnosed glioblastoma multiforme (GBM). Study 1 will be a phase I cohort of 3 dose-escalation trial of dasatinib in combination with radiation and concomitant TMZ. Study 2 will be a randomized phase II trial with two arms. Patients will be randomized at the time of registration at a ratio of 1:2 respectively to either: standard therapy arm (continuous daily placebo prior, during and after standard RT/TMZ followed by TMZ alone), or the experimental arm (continuous daily dasatinib prior, during and after standard RT/TMZ followed by TMZ).

**Accrual:** This study was activated on June 5, 2009. At the time of this report, August 4, 2009, one patient has been enrolled to the phase I portion of this study.

**Patient Characteristics:** Patient Characteristics for the patient enrolled is not available at this time.

**Adverse Events:** Adverse event data will be reported as it becomes available. At the time of this report no patients are evaluable for adverse events.

**Study Status:** This study has been temporarily closed as of August 10, 2009 while the first cohort of patients is evaluated for adverse events.
Accrual Table:

<table>
<thead>
<tr>
<th>Randomizing Membership</th>
<th>Total Entered</th>
<th>Past 6 Months</th>
<th>Past 12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Florida</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total Membership Accrual</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>