NCCTG Status Report for Study 982052 - April 2002

Phase II Trial of Oral Topotecan and Paclitaxel With G-CSF (Filgrastim) Support in Patients With Previously Untreated Extensive-Stage Small Cell Lung Cancer

**Purpose of Study:**
1) To evaluate complete and partial responses and toxicity of this regimen for this study population.
2) To obtain preliminary estimates of survival for this regimen.

**Study Chairs:**
James R. Jett M.D.
Bradley S Lair M.D.

**Statistician:**
Shauna L Hillman M.S.

**Data Monitor:**
Jennifer L. Frank

**Nurse Resource:**
Tammy Fischer R.N.

**Status:**
11/12/1999 Activated
11/22/2000 Perm. Closed

**Projected Number of Patients:**
37

**Excluded:**
None

**Final Accrual:**
38

**Stratification:**
None

**Schema:**
Register
TOPA + TAXOL + G-CSF

**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>Topa</td>
<td>1.75 mg/m2/day</td>
<td>Orally</td>
<td>1-5</td>
<td>Every 4 wks</td>
</tr>
<tr>
<td></td>
<td>Taxol</td>
<td>175 mg/m2/day</td>
<td>IV over 3 hrs in 500 ML D5W (after topotecan)</td>
<td>5</td>
<td>Every 4 wks</td>
</tr>
<tr>
<td></td>
<td>G-CSF</td>
<td>5 mcg/kg</td>
<td>Subcutaneous</td>
<td>*</td>
<td>Every 4 wks</td>
</tr>
</tbody>
</table>

*Start 24-48 hrs after last dose of chemotherapy and daily for 10 days unless ANC of >=10,000/mcg after the nadir then stop sooner.

**Study Design:** This study was designed as a single-stage Phase II trial to evaluate the response and toxicity of oral topotecan and paclitaxel with G-CSF support in patients with previously untreated extensive-stage small cell lung cancer. A total of 37 evaluable patients will be accrued on this trial. The regimen will be considered for further testing if at least 24 of the 37 patients have a confirmed tumor response. An interim analysis will be performed when the 23rd eligible patient has been followed for 3 cycles allowing for early termination of the trial if insufficient response or excessive toxicity are observed.
**Accrual:** This study has completed accruing patients. A total of 38 patients have been enrolled. See NCCTG spring 2001 book for the final accrual information.

**Study Status:** Final data on accrual, patient characteristics, and adverse events appeared in the NCCTG spring 2001 book. An abstract summarizing the results of the study has been submitted for the 2002 ASCO meetings. The text is given below.
New therapies for ED-SCLC are desperately needed. Topotecan has good activity against SCLC, but is associated with significant myelosuppression. Oral topotecan is as active as IV topotecan, but less toxic.

Goal: To evaluate the response rate and toxicity of oral topotecan (T) and IV paclitaxel (P) in ED-SCLC patients and follow patients for survival.

Methods: Patients were ≥18 years with no prior chemotherapy, histologic proof of diagnosis, measurable or evaluable disease, extensive stage, PS of 0, 1 or 2 and adequate hematologic and blood chemistry parameters. Patients received oral T (1.75 mg/m²/dx5) and IV paclitaxel (175 mg/m²/3 hours/day 5) and G-CSF beginning day 6 every 28 days.

Results: From December 1999 until November 2000, 38 eligible patients were enrolled. All patients were evaluable. There were 14 females and 24 males. The median age was 64 years (range 43-85). PS was 0, 1 in 82% and 2 in 18%. Sixteen (42%) patients received all six cycles of therapy and 61% received 4 or more cycles. Myelosuppression was the main toxicity. Grade 3/4 neutropenia was observed in 40% of patients and thrombocytopenia in 16%. There were 2 treatment-related deaths (sepsis). The most frequent grade 3 or 4 non-hematologic toxicities were: nausea (18%), fatigue (13%), diarrhea (13%), anorexia (11%), and dehydration (11%). The major response rate was 45% (95% CI 29-65%) with 3 CR and 14 PR. Thirty-three patients have developed progressive disease and 27 have died. The median follow-up for patients still alive is 354 days. The median time to progression is 5 months and the median overall survival is 8.6 months. The one-year survival is 43% (95% CI: 30-63%). Survival data will be updated for ASCO.

Conclusion: Oral topotecan and paclitaxel has activity against ED-SCLC, but probably does not represent any improvement over standard therapy. Toxicity was generally mild. We plan to explore other combinations of chemotherapy that includes oral topotecan.