An Open, Multi-Center, Phase II Clinical Trial to Evaluate Efficacy and Safety of Taxol® (Paclitaxel), UFT, and Leucovorin in Patients with Advanced Gastric Cancer

Clinical Study Report

Bristol-Myers Squibb (Taiwan) Ltd.
4F, No. 156, Jiankang Rd.,
Taipei 105, Taiwan R.O.C.
An Open, Multi-Center, Phase II Clinical Trial to Evaluate Efficacy and Safety of Taxol® (Paclitaxel), UFT, and Leucovorin in Patients with Advanced Gastric Cancer

Indication:   Gastric cancer
Protocol Number:   CA139-369
Study Phase:   II
Total Number of Study Centers:  7
Number of Subjects to be Enrolled:  55
Randomized:   N/A
Evaluable:  48
Report Date:   10-July-2005
Sponsor:   Bristol-Myers Squibb (Taiwan) Ltd.
4F, No. 156, Jiankang Rd.,
Taipei 105, Taiwan R.O.C.
## SYNOPSIS

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<tr>
<th>Name of Sponsor/Company:</th>
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<tbody>
<tr>
<td>Name of Finished Product:</td>
<td>Taxol®</td>
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<tr>
<td>Name of Active Ingredient:</td>
<td>Paclitaxel</td>
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<tr>
<td>Title of Study:</td>
<td>An Open, Multi-Center, Phase II Clinical Trial to Evaluate Efficacy and Safety of Taxol® (Paclitaxel), UFT, and Leucovorin in Patients with Advanced Gastric Cancer</td>
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**Objective**

**Primary:** To evaluate the response rate of weekly Taxol combination chemotherapy with UFT and Leucovorin in patients with advanced gastric cancer

**Secondary:**
- To determine time-to-progression of weekly Taxol combination chemotherapy with UFT and Leucovorin in patients with advanced gastric cancer
- To evaluate the safety of weekly Taxol combination chemotherapy with UFT and Leucovorin in patients with advanced gastric cancer

**Methodology:** An Open, Multi-Center, Phase II Clinical Trial
| Number of Patients: | Enrolled: 55  
Randomized: N/A  
Evaluable: 48 |
|-------------------|------------------|
| Diagnosis and Main Criteria for Inclusion: | - Patients with histologically confirmed gastric adenocarcinoma, defined as locally advanced, unresectable, metastatic or recurrent disease;  
- Patients with at least one measurable lesion;  
Patients with no prior chemotherapy and radiotherapy for metastatic disease (patients who had received and completed prior adjuvant chemotherapy at least 6 months prior to study enrollment might be enrolled into the study, prior taxane chemotherapy should be excluded). |
| Test Product: | Paclitaxel  
Dose: 100mg/m2  
Route: i.v., 1hr  
UFT  
Dose: 300mg/m2/day  
Route: p.o. in 3 divided doses  
Leucovorin  
Dose: 90mg/day  
Route: p.o. in 3 divided doses |
| Name of Sponsor/Company: | Bristol-Myers Squibb (Taiwan) Ltd. |
| Name of Finished Product: | Taxol® |
| Name of Active Ingredient: | Paclitaxel |
### Duration of Treatment:

The duration of treatment was based on tumor reassessment performed every two cycles. Patients with progressive diseases (PD) were taken off the study immediately. For patients with a complete response (CR), a minimum of 6 cycles were administered. However, if the CR was documented after the completion of 6 cycles, two additional cycles were added. For those who showed a partial response (PR), patients continued treatment until an unacceptable toxicity or disease progression was shown, or patients refused to continue the study treatment. For those who presented a stable disease (SD), patients continued treatment for a maximum of 6 cycles. Treatment was discontinued if unacceptable toxicity occurred.

### Criteria for Evaluation:

#### Efficacy:

All patients who received a minimum of two treatment cycles and had at least one tumor reassessment were considered evaluable for response. In addition, patients with early progressive disease were considered evaluable for response. The tumor response rate was defined as the total number of responders, complete and partial, divided by the number of response-evaluable patients.

Time to progression was calculated for all patients from the day of the first dose until the date that PD or death was first reported, whichever came first. Patients who died without a prior report of disease progression were considered to have progressed on the day of their death. Patients who did not progress were censored on the date of their last tumor assessment.

#### Safety:

All patients who received at least one dose of study medication were included in safety evaluable population. The primary safety endpoint was adverse events (AEs).
<p>| Statistical Methods: | The primary efficacy measure for this trial was the tumor response rate with 95% confidence intervals computed for response-evaluable patients. The secondary efficacy measure was time to progression. Kaplan-Meier estimates were calculated for time to progression and the median, along with two-sided 95% confidence intervals, were reported. |</p>
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### Summary and Conclusion

#### Efficacy Results:

Between February 2003 through February 2005, 55 patients with advanced gastric cancer were enrolled. 60.0% were male and 81.8% had an ECOG status of 1. The median age was 64 years. 48 patients were evaluable for response. 24 responded to treatment - 2 CRs and 22 PRs - for an objective response rate (ORR) of 50.0% (95% C.I., 35.2% to 64.8%). There were 20 cases of SD (41.7%) and 4 cases of PD (8.3%). After taking into account the group sequential nature of Simon two-stage design, the confidence interval was 35.5% to 65.8%. Median survival was 298.0 days (95% C.I., 260 to 321 days) and the median time to progression was 133 days (95% C.I., 121 to 194 days).

#### Safety Results:

The adverse events experienced by at least 20% of patients were leukopenia (72.7%), alopecia (72.7%), neutropenia (70.9%), hypoaesthesia (52.7%), anemia (50.9%), diarrhea (49.1%), anorexia (43.6%), nausea (32.7%), fatigue (30.9%), insomnia (30.9%), constipation (27.3%), vomiting (27.3%), abdominal pain (21.8%), cough (21.8%), weight loss (20.0%) and pyrexia (20.0%).

There were statistically significances between baseline and the end of study in the measure of RBC, hematocrit, neutrophil, lymphocyte, glucose, BUN, creatinine and bilirubin for laboratory tests.

#### Conclusion:

This trial demonstrated an objective tumor response rate of
50% with a 95% confidence interval of 35.5% to 65.8%. The combination of weekly paclitaxel (Taxol®) and daily UFT and leucovorin is an active regimen with acceptable toxicity for the treatment of advanced gastric cancer.

| Date of the Report: | July 10, 2005 |