Efficacy and safety of nanoliposomal irinotecan (nal-IRI, MM-398, PEPO2, BAX-2398) in patients with metastatic pancreatic cancer in Asia: A subgroup analysis of the phase 3 NAPOLI-1 Study


1Oncology, National Health Research Institutes - National Institute of Cancer Research, Taiwan, Taiwan, 2Oncology, Taipei Veteran’s General Hospital, Taipei, Taiwan, 3Medical Oncology, China Medical University Hospital, Taichung, Taiwan, 4Institute of Clinical Medicine, NCKU, Tainan, Taiwan, 5Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, 6Division of Hematology-Oncology, Chang Gung Memorial Hospital-Linkou, Taoyuan, Taiwan, 7Oncology, Korea University Guro Hospital, Seoul, Republic of Korea, 8Oncology, Chang Gung Memorial Hospital-Kaohsiung, Kaohsiung, Taiwan, 9Medical Affairs, Oncology, Shire, Basel, Switzerland, 10Medicine, Merrimack Pharmaceuticals, Inc., Cambridge, MA, USA, 11Biostatistics, Merrimack Pharmaceuticals, Inc., Cambridge, MA, USA, 12Drug Development, Pharmadigm, Taipei, Taiwan, 13Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea

Background: The global Phase 3 trial, NAPOLI-1, demonstrated that nal-IRI + 5-fluorouracil and leucovorin (5-FU/LV) significantly improved overall OS, progression-free survival (PFS) and objective response rate (ORR) vs 5-FU/LV in patients (pts) with metastatic pancreatic ductal adenocarcinoma (mPAC) previously treated with gemcitabine-based therapy. Herein, we present a post hoc subgroup analysis of the Asia cohort in the NAPOLI-1 study.

Methods: Pts were randomly assigned (1:1:1) to receive nal-IRI (80 mg/m², equivalent to 70 mg/m² of irinotecan base) + 5-FU/LV (2400/400 mg/m² q2w, nal-IRI (120 mg/m², equivalent to 100 mg/m² of irinotecan base) q3w, or 5-FU/LV (2000/200 mg/m² q3w) for weeks 1-4 q4w). The primary endpoint was OS.

Results: Of 132 pts randomized in Asian centers, 34 were assigned to treatment with nal-IRI + 5-FU/LV, 50 with nal-IRI, and 48 with 5-FU/LV. In the Asia cohort, nal-IRI + 5-FU/LV significantly improved median OS versus 5-FU/LV (8.9 vs 3.7 months, P-value < 0.0001) (Table). Improvements in PFS and ORR were also observed. There were no significant differences in outcomes between 5-FU/LV and nal-IRI monotherapy. Grade ≥3 treatment-emergent adverse events in ≥15% of pts in either nal-IRI arm were neutropenia (55%, 34%, and 2% in the nal-IRI + 5-FU/LV, nal-IRI, and 5-FU/LV arms, respectively), white blood cell count decreased (21%, 8%, 0%), diarrhea (3%, 16%, 5%), and anemia (18%, 24%, 14%). There were no cases of Grade ≥3 peripheral neuropathy.

Conclusions: This subgroup analysis confirmed that nal-IRI + 5-FU/LV is an efficacious treatment option with a manageable safety profile in patients with mPAC treated in Asia. Nal-IRI + 5-FU/LV may represent a new standard of care for patients with mPAC previously treated with gemcitabine-based therapy.

Clinical trial identification: NCT01849506

Legal entity responsible for the study: Merrimack

Funding: Merrimack

Disclosure: L.-T. Chen: Received data monitoring board, statistician, and support of medical writer from Merrimack, and honorarium from Pharmadigm, Inc. F. de Jong: Employee of and hold stock in Shire, M. Pipas: Employee of and hold stock in Merrimack. B. Belanger: Employee of, hold stock in, and have received reimbursement for travel/accommodations/expenses from Merrimack. E. Wang: Employee of
## Table: 221PD

### Summary of Treatment Efficacy

<table>
<thead>
<tr>
<th>End Point</th>
<th>Nal-IRI + 5-FU/LV Combo (N = 34)</th>
<th>5-FU/LV Control (N = 35)</th>
<th>HR (95% CI)*</th>
<th>P value†</th>
<th>Nal-IRI Mono Control (N = 50)</th>
<th>5-FU/LV Control (N = 48)</th>
<th>HR (95% CI)*</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS, months, median (95% CI)</td>
<td>8.9 (4.4, 10.4)</td>
<td>3.7 (2.7, 6.4)</td>
<td>0.5087 (0.28, 0.93)</td>
<td>0.0281</td>
<td>5.7 (4.8, 7.4)</td>
<td>3.1 (1.7, 5.7)</td>
<td>0.8339 (0.53, 1.3)</td>
<td>0.4263</td>
</tr>
<tr>
<td>PFS, months, median (95% CI)</td>
<td>4.0 (1.5, 5.7)</td>
<td>1.4 (1.2, 2.0)</td>
<td>0.4818 (0.27, 0.85)</td>
<td>0.0116</td>
<td>2.8 (1.5, 4.1)</td>
<td>1.4 (1.3, 1.9)</td>
<td>0.6874 (0.44, 1.1)</td>
<td>0.0950</td>
</tr>
<tr>
<td>ORR, %</td>
<td>8.8%</td>
<td>0%</td>
<td>8.8 (-0.1, 18.4)</td>
<td>0.1142</td>
<td>10.0%</td>
<td>0%</td>
<td>10.0 (1.7, 18.3)</td>
<td>0.0564</td>
</tr>
</tbody>
</table>

*Values reported for ORR represent a difference in proportions rather than a HR, and the CI limits for the difference in ORR are based on normal approximation.

P value is based on Fisher exact test. P values are 2-sided.

---

PharmaEngine, Inc. The company has the licensing partnership with Merrimack Pharmaceuticals for the product. Y-J. Bang. Consultant for Merrimack. All other authors have declared no conflicts of interest.