UPDATED EFFICACY, BIOMARKER, AND EXPOSURE-RESPONSE DATA FROM A PHASE 2 STUDY OF RILOTUMUMAB (R) PLUS EPIRUBICIN, CISPLATIN, AND CAPECITABINE (ECX) IN GASTRIC (G) OR ESOPHAGO GaSTRIC JUNCTION (EGJ) CANCER

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Background

R (AMG 102) is an investigational, fully human monoclonal antibody to hepatocyte growth factor/scatter factor, the MET receptor ligand. Safety and efficacy of a placebo-controlled, double-blind, randomized phase 2 study of R + ECX in G/EGJ cancer from a 12.5-month (mo) follow up were previously reported (Iveson et al, Eur J Cancer. 2011; 47(suppl 1):S443. abstract 6.504). Updated data from a 21.7-mo follow up are presented.

Methods

Eligibility included unresectable, locally advanced or metastatic G/EGJ adenocarcinoma; ECOG PS ≤1; and no prior systemic therapy for this disease. Patients (pts) were randomized 1:1:1 to ECX (50 mg/m² IV day 1, 60 mg/m² IV day 1, 625 mg/m² BID orally days 1–21, respectively) + R 15 mg/kg (Arm A); R 7.5 mg/kg (Arm B); or placebo (Arm C) IV day 1 every 3 weeks. Overall survival (OS) and progression-free survival (PFS) were evaluated. MET protein was measured in archival tumor samples by IHC. R serum concentrations for all pts were measured. Individual R steady-state Cminss were estimated with a population PK model.

Results

121 pts (Arms A/B/C: 40/42/39) were randomized Oct 2009 to June 2010. See table for data (Jan 16, 2012 cutoff).

Conclusions

Within the context of a small, randomized phase 2 study, R + ECX improved outcomes in G/EGJ cancer pts. The treatment effect was strongest in pts with high MET tumors and high R exposure. Consistent with previously reported data, these results show continued separation of Arm A + B vs C beyond 16 mo. A planned phase 3 study will test the safety and efficacy of R + ECX in MET-positive G/EGJ cancer.

Table: 687P

<table>
<thead>
<tr>
<th>Median OS (80% CI), mo</th>
<th>OS HR (95% CI)</th>
<th>Median PFS (80% CI), mo</th>
<th>PFS HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm A + B n = 82</td>
<td>10.6 (9.5–12.0)</td>
<td>5.7 (5.1–6.9)</td>
<td></td>
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<tr>
<td>All pts</td>
<td>8.9 (5.7–10.6)</td>
<td>4.2 (3.7–4.6)</td>
<td>0.60 (0.39–0.91)</td>
</tr>
<tr>
<td>Arm A + B vs C</td>
<td>0.70 (0.45–1.09)</td>
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</tr>
<tr>
<td></td>
<td>Arm A + B n = 27</td>
<td>Arm C n = 11</td>
<td>Arm A + B vs C</td>
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<tr>
<td>METH*</td>
<td>11.5 (9.2–12.1)</td>
<td>5.7 (4.5–10.4)</td>
<td>0.34 (0.15–0.78)</td>
</tr>
<tr>
<td>METH*, RH†</td>
<td>6.9 (5.5–7.5)</td>
<td>4.6 (3.7–5.2)</td>
<td>0.44 (0.20–0.96)</td>
</tr>
</tbody>
</table>

*Pts with >50% tumor cells MET positive, †Pts with R median Cminss ≥ 94 µg/mL.

**Disclosure**

T. Iveson: Dr. Iveson received research funding and travel payment from Amgen Inc.

Y. Jiang: Dr. Jiang is an employee of and owns stock in Amgen Inc.

M. Zhu: Dr. Zhu is an employee of and owns stock in Amgen Inc.

K.S. Oliner: Dr. Oliner is an employee of and owns stock in Amgen Inc.

S. Dubey: Dr. Dubey is an employee of and owns stock in Amgen Inc.

E. Loh: Dr. Loh is an employee of and owns stock in Amgen Inc.

All other authors have declared no conflicts of interest.

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