gastrointestinal tumours, colorectal

INTERIM SAFETY RESULTS FROM STEAM: A RANDOMIZED PHASE 2 TRIAL OF SEQUENTIAL AND CONCURRENT FOLFOXIRI–BEVACIZUMAB (BEV) VS FOLFOX–BEV FOR THE FIRST-LINE (1L) TREATMENT (TX) OF PATIENTS (PTS) WITH METASTATIC COLORECTAL CANCER (MCRC)

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Aim: Recent randomized trials of FOLFOXIRI–BEV in mCRC showed improved progression-free survival (PFS) and overall response rates (ORR) vs either FOLFIRI–BEV or FOLFOX–BEV. The efficacy and safety of FOLFOXIRI–BEV have yet to be investigated in the US.

Methods: STEAM (NCT01765582) is a randomized, open-label, US-based, phase 2 trial. Pts are randomized 1:1:1 to FOLFOXIRI–BEV (arm A), sequential FOLFOXIRI–BEV (FOLFOX or FOLIRI every 2 weeks [q2w] alternating every 2 cycles; arm B), and FOLFOX–BEV (arm C) q2w in previously untreated mCRC (BEV 5 mg/kg in each arm). After a 4- to 6-mo induction phase, pts receive 5-fluorouracil (5-FU)/leucovorin + BEV (5 mg/kg) q2w or capecitabine + BEV (7.5 mg/kg) q3w as maintenance tx until disease progression (PD). Pts receive second-line (2L) 5-FU-based chemotherapy (physician’s choice) + BEV (2.5 mg/kg/qw) until 2L PD. Primary objectives are to evaluate 1L ORR (arm A vs arm C), 1L PFS (arms A + B vs arm C), and safety. Adverse events (AEs) were analyzed per a preplanned interim analysis.

Results: At data cutoff (12/3/13), 94/280 pts were randomized, and 93 pts had received ≥1 dose of study tx. Pt characteristics were generally balanced across tx arms; more grade (gr) ≥3 AEs occurred in arm A than in arms B or C (Table). Five (15%) gr 4 neutropenia AEs occurred in arm A; all pts recovered within a week after temporary dose reduction and/or receiving growth factors, and they continued study tx per protocol. One pt in arm A died from unknown reasons; 2 pts died in arm B from PD.

Table: 521P

<table>
<thead>
<tr>
<th>Adverse Event Category</th>
<th>n (%)</th>
<th>Arm A (FOLFOXIRI–BEV) n = 33</th>
<th>Arm B (Sequential FOLFOXIRI–BEV) n = 30</th>
<th>Arm C (FOLFOX–BEV) n = 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAE</td>
<td>32 (97)</td>
<td>30 (100)</td>
<td>29 (97)</td>
<td></td>
</tr>
<tr>
<td>Any gr ≥3 TEAE</td>
<td>26 (79)</td>
<td>15 (50.0)</td>
<td>16 (53)</td>
<td></td>
</tr>
<tr>
<td>Any gr 4 TEAE Neutropenia Diarrhea CO₂ embolism during surgical procedure</td>
<td>6 (18) 5 (15) 1 (3)</td>
<td>6 (20.0)</td>
<td>8 (27)</td>
<td></td>
</tr>
<tr>
<td>Deaths</td>
<td>1 (3)</td>
<td>2 (7)</td>
<td>1 (3) 1 (3)</td>
<td></td>
</tr>
<tr>
<td>Any serious TEAE</td>
<td>10 (30)</td>
<td>6 (20.0)</td>
<td>8 (27)</td>
<td></td>
</tr>
<tr>
<td>Any TEAE of special interest to BEV Bleeding/hemorrhage Hypertension Venous thromboembolic events Proteinuria Wound-healing complications Arterial thromboembolic events Gastrointestinal perforation Congestive heart failure Fistula/abscess Posterior reversible encephalopathy syndrome</td>
<td>15 (45) 8 (24) 6 (18)</td>
<td>1 (3) 2 (6)</td>
<td>3 (10) 3 (10)</td>
<td></td>
</tr>
<tr>
<td>Any gr ≥3 AESI to BEV</td>
<td>1 (3)</td>
<td>4 (13)</td>
<td>6 (20)</td>
<td></td>
</tr>
<tr>
<td>Any TEAE to dose reduction, tx interruption, or tx discontinuation</td>
<td>26 (79)</td>
<td>12 (40)</td>
<td>18 (60)</td>
<td></td>
</tr>
<tr>
<td>Any TEAE leading to withdrawal from study tx</td>
<td>8 (24)</td>
<td>1 (3)</td>
<td>4 (13)</td>
<td></td>
</tr>
<tr>
<td>Any TEAE leading to premature study discontinuation</td>
<td>2 (6)</td>
<td>–</td>
<td>1 (3)</td>
<td></td>
</tr>
</tbody>
</table>

BEV, bevacizumab; CO₂, carbon dioxide; gr, grade; TEAE, treatment-emergent adverse event; tx, treatment

Conclusions: The overall AE profile of FOLFOXIRI–BEV in the STEAM trial is similar to previous trials of FOLFOXIRI–BEV. Rates of tx-emergent AEs in the sequential FOLFOXIRI–BEV arm appear similar to the FOLFOX–BEV arm. The trial is continuing with no changes in dosing or design.

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