Capecitabine (Cap) with bevacizumab (Bev) with or without vinorelbine (Vin) in first-line metastatic breast cancer (MBC): First safety results from the randomized CARIN trial


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Updated Abstract:

Background

In RIBBON-1 1, the combination of Bev with Cap as 1st-line therapy for MBC significantly improved progression-free survival (PFS) compared with Cap alone, with limited impact on tolerability. Vin and Cap are active agents with few overlapping toxicities. The CARIN trial aims to further improve efficacy by adding Vin to Cap/Bev, giving a non-taxane alopecia-sparing regimen.

Methods

Patients (pts) are randomized (1:1) to receive Cap 1000 mg/m² BID days 1–14 + Bev 15 mg/kg q3w (Arm A) or the same Cap/Bev regimen combined with iv Vin 25 mg/m² days 1+8 (Arm B). Treatment is continued until progression or unacceptable toxicity (Figure 1). Key eligibility criteria include measurable or non-measurable HER2-negative MBC or locally recurrent disease, no prior chemotherapy for MBC, ECOG ≤2, and no evidence of CNS metastases. Endpoints include PFS (primary), objective response rate, overall survival, and safety. As of February 2011, all 400 pts planned had been enrolled. This interim safety analysis includes the first 50 pts from each study arm, who were to receive 6 cycles of study therapy.

Results

The patient demographics and clinical characteristics represent available data from all pts enrolled (Tables 1+2). Median age of all pts was 61 years. A total of 518 cycles were analysed. On average, the pts included in the safety analysis received 10.4 cycles of study medication in Arm A and 9.9 cycles in Arm B. 16 pts in Arm A and 12 in Arm B discontinued before completing 6 cycles due to progression or other reasons. Adverse events (AEs) led to discontinuation in 3 vs 5 pts, respectively. AEs were less frequent in Arm A (658 events vs 962 in Arm B); grade 3/4 AEs were rare (65 vs 112, respectively). The most common grade 3/4 AEs were neutropenia (2 events in Arm A, 33 in Arm B; 2 vs 17 pts, respectively) and hand-foot syndrome (15 events in Arm A vs 8 in Arm B; 15 vs 7 pts). Typical Bev-associated grade 3/4 AEs were hypertension (3 vs 1 pt, thromboembolic events 1 in Arm A, 3 in Arm B). Safety analysis overview and data on selected adverse events are summarized in Tables 3+4.

Dose intensity and dose delay data are available for the first 4 cycles only, average Cap dose intensity was 93.3% in Arm A and 84.6% in Arm B. Vin average dose intensity was 92.5%. Dose delays were less common in Arm A (19 cycles vs 58 in Arm B).

Conclusions

The Vin/Cap/Bev regimen is tolerable. Additional AEs in Arm B were consistent with the known safety profile of Vin. Importantly, although the dose intensities were reasonably high in both arms, the slightly increased incidence of AEs in Arm B did not lead to a higher discontinuation rate.

![Figure 1: Study Design](image1.png)

![Table 1: Patient Demographics and Clinical Characteristics](image2.png)

![Table 2: Prior Treatments](image3.png)

![Table 3: Overview of Safety Analysis](image4.png)

![Table 4: Selected Adverse Events](image5.png)