[S6-6] A Phase III, Open-Label, Randomized, Multicenter Study of Eribulin Mesylate Versus Capecitabine in Patients with Locally Advanced or Metastatic Breast Cancer Previously Treated with Anthracyclines and Taxanes

Kaufman PA, Awada A, Twelves C, Yelle L, Perez EA, Wanders J, Olivo MS, He Y, Dutcus CE, Cortes. Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Lebanon, NH; Jules Bordet Institute, Brussels, Belgium; Leeds Institute of Molecular Medicine and St James's Institute of Oncology, Leeds, United Kingdom; University of Montreal, Montreal, Canada; Mayo Medical Clinic, Jacksonville, FL; Eisai Ltd., Hatfield, United Kingdom; Eisai Inc., Woodcliff Lake, NJ; Vall D'Hebron University Hospital, Barcelona, Spain

Background: Eribulin is a non-taxane microtubule dynamics inhibitor. In a previous Phase III trial, eribulin demonstrated a statistically significant improvement in overall survival (OS) versus current treatments and a manageable toxicity profile, in heavily pre-treated patients (pts) with metastatic breast cancer (MBC). Here we report results from a Phase III trial of eribulin compared with capecitabine in earlier-line pts with MBC (NCT00337103).

Patients and methods: Pts were randomized 1:1 to eribulin mesylate 1.4 mg/m^2 given on Days 1 and 8 of a 21 day cycle or capecitabine 2.5 g/m^2/day administered orally BID on Days 1 to 14 of a 21 day cycle. Eligible pts had received prior therapy including an anthracycline and taxane, and were receiving study drug as 1st, 2nd, or 3rd line therapy for advanced disease. The co-primary endpoints of this study were OS and progression free survival (PFS): pre-specified statistical significance at final analysis for eribulin versus capecitabine were $p \leq 0.0372$ for OS and $p < 0.01$ for PFS. Secondary endpoints included objective response rate (ORR), quality of life (QoL) measured using the EORTC questionnaire, duration of response, 1-, 2- and 3-year survival, and safety. The study was stratified for geographic region and HER2 status.

Results: Of 1102 pts, 554 were randomized to eribulin and 548 capecitabine (375 and 380 pts were HER2[-], respectively). The median age was 54.0 years (range 24-80). Pts received study treatment as their 1st (27.2%), 2nd (57.4%) or 3rd-line (14.7%) chemotherapeutic regimen in the setting of metastatic disease. The median number of treatment cycles was 6 for eribulin and 5 for capecitabine. Median OS was 15.9 and 14.5 months (hazard ratio [HR] 0.879; 95% confidence intervals [CI] 0.770-1.003; p=0.056), and PFS (independent review) was 4.1 and 4.2 months (HR 1.079; 95% CI 0.932-1.250; p=0.305) for eribulin and capecitabine, respectively. ORR (independent review) were 11.0% (95% CI 8.5-13.9) and 11.5% (95% CI 8.9-14.5; p=0.849), respectively. OS for HER2(-) pts was 15.9 months for eribulin and 13.5 months for capecitabine (HR 0.838; 95% CI 0.715-0.983; p=0.030). AEs were consistent with the known side-effect profiles of both drugs. The most common AEs for eribulin and capecitabine (>20% all grades) were neutropenia (54.2% vs 15.9%), hand-foot syndrome (0.2% vs 45.1%) alopecia (34.6% vs 4.0%), leukopenia (31.4% vs 10.4%), diarrhea (14.3% vs 28.8%), and nausea (22.2% vs 24.4%), respectively.

Conclusion: In this Phase III trial, eribulin demonstrated a trend favoring improved OS, compared with capecitabine, although this improvement does not meet the pre-defined criteria for statistical significance. This study confirms eribulin as an active drug in pts with MBC, and exploratory analyses suggest possible benefits of eribulin in specific subsets of pts, sufficient to warrant further study.