Aim: In CLEOPATRA, 808 pts with HER2-positive MBC were randomized to receive 1L placebo (Pla) + T + D or Ptz + T + D. At primary analysis, pertuzumab was shown to increase progression-free survival significantly, with a strong trend to OS benefit. At a second interim analysis (May 2012), OS was improved to a degree which was both statistically significant and clinically meaningful (HR = 0.66, 95% CI 0.52–0.84; P = 0.0008) but the median OS in pts who received Ptz was not reached. Here we report results of a subsequent prespecified OS analysis.

Methods: This OS analysis was planned when ≥385 deaths were reported. The log-rank test, stratified by prior treatment status and geographic region, was used to compare OS between arms, applying the Lan–DeMets α-spending function with an O'Brien–Fleming threshold of p ≤ 0.0456. The Kaplan–Meier approach was used to estimate HR and 95% CIs. Subgroup analyses of OS were performed for stratification factors and other key baseline characteristics.

Results: Median follow-up time was 50 months (mos) and the statistically significant improvement in OS in favor of Ptz + T + D was maintained (HR = 0.68, 95% CI 0.56–0.84; p = 0.0002). Median OS was 40.8 mos in the Pla arm and 56.5 mos in the Ptz arm, the difference at the medians being 15.7 mos. The OS benefit in predefined subgroups was consistent with previous observations. It is to be noted that following the previous report of OS benefit, cross-over therapy was allowed and 48 pts in the Pla arm crossed over to the Ptz arm. The safety profile of Ptz + T + D in the overall population and in pts who crossed over to the Ptz arm was consistent with the known safety profile of Ptz and the long-term cardiac safety profile was maintained.

Conclusions: 1L treatment with Ptz + T + D significantly improved OS for pts with HER2-positive MBC compared with Pla + T + D, providing a 15.7 mo increase in the median values. The 56.5 mo median OS is unprecedented in 1L MBC and this substantial improvement confirms the Ptz regimen as 1L standard of care for pts with HER2-positive MBC.

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