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VIKTORIA-1: Updated results of a randomized, open-label, phase 3 study of gedatolisib (geda) + fulvestrant (fulv) ± palbociclib (palbo) vs standard of care in patients (pts) with HR+/HER2- advanced breast cancer (ABC) (Study 2)

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Background

Geda is a PI3K/mTOR inhibitor that blocks the PAM pathway. VIKTORIA-1 enrolled pts with HR+/HER2- ABC in two studies by *PIK3CA* mutation status (wild-type [wt] and mutant [MT]). Both met their primary mPFS endpoint (Hurvitz et al, JCO 2026; ASCO 2026), leading to FDA approval in *PIK3CA* wt ABC. Here we report an update for Study 2 (*PIK3CA* MT), including subgroup efficacy and deeper safety analyses.

Methods

Pts in Study 2 were randomized 3:3:1 to: geda + palbo + fulv (Arm D, n=155); alpelisib (alp) + fulv (Arm E, n=155); or geda + fulv (Arm F, n=52); all given in 28-day cycles.

Results

The primary endpoint of Study 2 was met, with geda + palbo + fulv significantly improving mPFS vs alp + fulv. This improvement was also observed in pts with visceral metastasis (mets) (9.8 mo vs 5.6 mo, HR 0.52, 95% CI 0.37–0.74) and without visceral mets (21.5 mo vs 9.2 mo, HR 0.38, 95% CI 0.19–0.82); with liver mets (9.1 mo vs 4.6 mo, HR 0.47, 95% CI 0.31–0.70) and without liver mets (21.5 mo vs 9.1 mo, HR 0.46, 95% CI 0.28–0.78). Geda + fulv also improved mPFS vs alp + fulv in pts with visceral mets (mPFS 11.3 mo vs 5.6 mo, HR 0.53, 95% CI 0.33–0.85) and without visceral mets (not reached vs 9.2 mo, HR 0.40, 95% CI 0.13–1.31), as well as in pts with liver mets (11.1 mo vs 4.6 mo, HR 0.38, 95% CI 0.20–0.69), with a numerical improvement observed in pts without liver mets (11.5 mo vs 9.1 mo, HR 0.71, 95% CI 0.37–1.39). Median duration of response including unconfirmed PR per RECIST v1.1 was longer in the geda-containing arms: Arm D, 19.4 (95% CI 11.1–25.1); Arm F, 27.8 (95% CI 9.2–NE); Arm E, 7.5 (95% CI 5.6–16.6) months. TEAEs (≥1%) led to geda withdrawal in 8 pts (Arm D, 5.2%) and 2 pts (Arm F, 3.8%) and included stomatitis (1.3%, 0%), infusion-related reaction (0%, 1.9%), and pneumonitis (0%, 1.9%) (Arms D, F, respectively). Most stomatitis events occurred within the first 1-2 weeks of treatment, with <3% grade 3 stomatitis beyond cycle 2. Geda regimens had no clinically meaningful impact on fasting or non-fasting glucose levels.

Conclusions

These results continue to support geda-combination regimens for the treatment of pts with HR+/HER2- *PIK3CA* MT ABC.

Clinical trial identification

NCT05501886.

Legal entity responsible for the study

Celcuity.

Funding

Celcuity.

Disclosure

B. Pistilli: Financial Interests, Institutional, Advisory Board: AstraZeneca, Seagen, Lilly, Daiichi Sankyo, MSD; Financial Interests, Institutional, Invited Speaker: Gilead, Novartis; Financial Interests, Personal, Advisory Board: Pierre Fabre, Daiichi Sankyo; Financial Interests, Personal, Other, travel support: AstraZeneca, Pierre Fabre, MSD, Daiichi Sankyo, Gilead; Financial Interests, Personal, Other, Travel support: Pfizer; Financial Interests, Institutional, Advisory Board, Advisory Board and member of Steering Committee: Olema; Financial Interests, Institutional, Steering Committee Member: AstraZeneca, Novartis; Financial Interests, Institutional, Research Grant: AstraZeneca; Financial Interests, Institutional, Local PI: AstraZeneca, Gilead, Seagen, MSD, Novartis; Financial Interests, Institutional, Funding: Daiichi Sankyo; Non-Financial Interests, Project Lead: UNICANCER. G. 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Interests, Personal, Other, DSMB: Alliance Foundation, Atossa, Quantum Leap; Financial Interests, Institutional, Other, DSMB: Roche; Financial Interests, Personal, Stocks/Shares, spouse owns: ROM Tech; Financial Interests, Personal, Royalties, author medical book: McGraw; Financial Interests, Personal, Royalties: Elsevier, Springer, Sage, Wolters Kluwer, Wiley; Financial Interests, Institutional, Local PI: AstraZeneca, Novartis, Stemline; Financial Interests, Institutional, Coordinating PI: Boehringer Ingelheim, Briacell, Daiichi Sankyo; Financial Interests, Coordinating PI: Celcuity; Financial Interests, Trial Chair: Genentech/Roche; Financial Interests, Institutional, Steering Committee Member: Jazz/Zymeworks; Financial Interests, Steering Committee Member: Novartis, Stemline, Genentech/Roche, Seagen/Pfizer, Eli Lilly, Gilead Sciences; Non-Financial Interests, Advisory Role: Novartis; Non-Financial Interests, Member: ASCO, AACR; Non-Financial Interests, Other, speaker: National Breast Cancer Coalition. All other authors have declared no conflicts of interest.

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