The PENOB-8 trial did not show improvement in invasive disease-free survival (DFS) with the addition of palbociclib to endocrine therapy (ET) in patients with high-risk early breast cancer (BC) after neoadjuvant chemotherapy (NACT). Biomarkers may be able to identify subgroups of patients benefiting from palbociclib and endocrine therapy. The addition of a progesterone receptor (PR)-positive (PR+) regimen to ET and palbociclib (PBflo) may further increase tamoxifen resistance in PR+ breast cancer (BC).

**Background**

- For patients with high Cyclin D1 (Cyclin D1) expression, PBflo is benefitting from independent treatment from ET.
- PBflo is correlated with Ki-67, but in this analysis we studied additional expressions of Cyclin D1 (Cyclin D1) and phosphatidylinositol 3-kinase (PI3K)/Akt signaling.
- High expression of Ki-67 was associated with poor prognosis.

**IHCBiomarkers, Subtypes, & Statistics**

- Data for ER, PgR, and Cyclin D1 and phospho-ER (Ser 816/Thr) immunohistochemistry were available from surgical resections after NACT from 1250 patients enrolled in PENOB-8.
- The percentage of positive ER and PgR cells and Ki-67 assessed in surgical specimens after NACT were utilized to obtain an immunohistochemical score (IHC3) for Ki-67. Low vs high was based on the median IHC3 score.
- Cyclin D1 and phospho-ER Ser 816/Thr immunohistochemistry (phospho-ER) scores were analyzed in residual tumors after NACT (range: 0-12).
- BC subtypes were determined using absolute intrinsic molecular subtyping (AMaS) on tumors for which HER2 analysis had been performed on the biospecimen (n=259) and residuals (n=1250).

**Results**

- Patients with high Cyclin D1 expression were associated with increased independence from ET treatment.
- PBflo is correlated with Ki-67, but in this analysis we studied additional expressions of Cyclin D1 and phosphatidylinositol 3-kinase (PI3K)/Akt signaling.
- High expression of Ki-67 was associated with poor prognosis.

**Future Directions**

- Validation of these findings in an independent cohort will be required to address the clinical benefit of the combination of palbociclib with ET in select patient subgroups.

**References**

