Patients and treatment

- **Neratinib (Herceptin(TM)),** an irreversible pan-HER tyrosine kinase inhibitor, is approved for extended adjuvant therapy in patients with early-stage HER2-positive (HER2+) breast cancer following adjuvant trastuzumab-based therapy and in combination with capecitabine for patients with HER2+ metastatic breast cancer.

- Diarrhea is the most frequently reported on-treatment side effect associated with neratinib and is common in the absence of proactive management.2

- In the ExteNET adjuvant trial, where no mandatory anti-diarrheal prophylaxis was used, 40% of patients reported grade 3 diarrhea and 17% of patients discontinued neratinib due to diarrhea.2,3

- The CONTROL trial showed that pre-emptive anti-diarrheal prophylaxis (loperamide alone or in combination with mesalamine or celecoxib) or neratinib dose escalation (DE) reduced the rate, severity, and duration of grade 3 diarrhea compared with the neratinib arm in ExteNET.4–6

- In the CONTROL trial, cohorts were enrolled sequentially, with no quantitative assessment or statistical comparison to determine the best regimen or to compare CONTROL with ExteNET.1

**Methods**

- To identify the best diarrhea mitigation strategy in the CONTROL trial.

- To compare the best regimen with the neratinib treatment arm in ExteNET, in which diarrhea prophylaxis was not mandated.

- **Patients and treatment**

  - In CONTROL, patients ≥18 years of age with stage I–III HER2+ breast cancer received neratinib 240 mg/day or matching placebo for one year. In ExteNET, patients with stage I–III HER2+ breast cancer received neratinib 120 mg/day on days 1–7, 160 mg/day on days 8–14, then 240 mg/day to day 101, with loperamide used as previously described.7

- **Diary data**

  - For diarrhea frequency and severity, a diary was kept

  - Patients were asked to record if they had nausea, vomiting, constipation, diarrhea, abdominal pain, and any adverse events.

  - Patients were asked to record their daily intake of diarrhea medications (prazosin, loperamide, and budesonide).

**Objectives**

- To identify the best diarrhea mitigation strategy in the CONTROL trial.

- To compare the best regimen with the neratinib treatment arm in ExteNET, in which diarrhea prophylaxis was not mandated.

**Results**

- Diarrhea was the most common TEAE (n=340) followed by nausea (n=197) and vomiting (n=169).

- The CONTROL DE cohort ranked best among the five CONTROL cohorts in terms of tolerability by this method.

**Conclusion**

- These data also reveal greater compliance with neratinib DE in CONTROL (fewer early discontinations, longer treatment duration, higher cumulative dose, as well as reduced impact on quality of life), suggesting improved tolerability versus the ExteNET neratinib arm.

- Neratinib DE may allow patients to stay on neratinib for the recommended time period, providing them the opportunity to receive the full benefit of treatment.