Real-World Use of Neratinib in HER2-Positive Early Breast Cancer in Korea: Updated Follow-up from a Multicenter Observational Study

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Background

Extended adjuvant neratinib improves invasive disease-free survival (iDFS) in patients with HER2-positive, hormone receptor-positive (HR+) early breast cancer (eBC) following adjuvant trastuzumab-based therapy, as shown in the ExteNET trial(1). **However, real-world evidence in the post-pertuzumab/T-DM1 era is limited.** We report updated outcomes from a Korean multicenter cohort.

Method

We retrospectively analyzed **48 HR+/HER2+ eBC patients who received neratinib between May 2022 and June 2025 at four academic hospitals in Korea.** Patients had completed trastuzumab-based neoadjuvant or adjuvant therapy within 12 months prior to initiating neratinib. Data on prior regimens, neratinib administration, adverse events (AEs), and recurrence were collected. **The primary endpoint was treatment pattern and tolerability; the secondary endpoint was iDFS.**

Results

The median age was 50 years (range, 37–66), and all patients were hormone receptor-positive. Most patients (75%) received the TCHP regimen**. Post-neoadjuvant HER2-targeted therapies included: trastuzumab emtansine in 20 patients (41.7%), trastuzumab plus pertuzumab in 16 (33.3%), trastuzumab alone in 11 (22.9%), and trastuzumab deruxtecan in 1 patient (2.1%).** Neratinib was initiated at 240 mg/day in 46 patients (95.8%), and at 120 mg/day with subsequent dose escalation in 2 patients. The median treatment duration was 11.2 months (range, 1.0–12.0). Diarrhea prophylaxis was administered in 85.4% of patients.

The most common treatment-emergent adverse event (TEAE) was **diarrhea (88.6%), followed by fatigue (29.5%) and skin reaction (20.5%),** mostly grade 1 or 2. Grade ≥3 toxicities occurred in 12.5% of patients. Adverse events led to dose modifications in 9 patients (18.8%), including both dose interruptions and reductions.

Permanent discontinuation due to AEs occurred in 4 patients (8.3%); AEs leading to dose modification included: diarrhea (n=6), nausea (n=2), oral mucositis (n=1), and duodenal ulcer (n=1). AEs leading to discontinuation included: vomiting (n=1), COVID-19 (n=1), diarrhea (n=1), nausea (n=1), fever (n=1), and duodenal ulcer (n=1). **At a median follow-up of 11.8 months, no invasive disease recurrence was observed.** Among the 48 patients, 31 completed the full 1-year course of neratinib, 7 remained on treatment, and 7 were lost to follow-up.

Conclusion

In this real-world Korean cohort, neratinib was commonly used after pertuzumab or T-DM1. Treatment was feasible and generally well tolerated with appropriate supportive care. No recurrence was observed during early follow-up.

To our knowledge, this represents the first Asian real-world data on neratinib in the extended adjuvant setting.

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