Background
Neratinib (NERLYNX®), a small-molecule irreversible pan-HER tyrosine kinase inhibitor (TKI), significantly improves invasive disease-free survival (DFS) compared with placebo in patients with HER2-positive (HER2+)-positive early-stage breast cancer after castration-based adjuvant treatment.

The benefit with neratinib in the extended adjuvant setting as demonstrated by the APHINITY trial on the HER2+ population was limited to 5 years and for 2 years did not improve outcomes. Neratinib and trastuzumab were thought to be effective for different subpopulations of patients. An extended follow-up (10 years) of the APHINITY trial, which was the first randomized trial to compare placebo with trastuzumab (14) and neratinib for 5 years in the HER2+ early-stage population, was completed.

CNS outcomes
In the metastatic setting, neratinib has shown central nervous system (CNS) activity, defined as time from randomization to death of any cause.

CNS-specific endpoints
- Cumulative incidence of CNS recurrences: defined as time from randomization to first recurrence. Any patient who was alive and for whom CNS recurrence had not been observed by the data cut-off was censored at the date of their last physical examination (prespecified endpoint). Any CNS failure (whether primary or secondary) was considered an event from randomization to CNS death or death from any cause and the last follow-up. Detailed data of CNS outcomes have been previously published.

Conclusions

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Overall survival
In the ITT population, 495 patients (33%) died in the placebo group and 459 patients (32%) in the neratinib group. One patient in the placebo group died due to treatment-related adverse events (TRAEs) in the neratinib group.

Overall survival (%)

CNS outcomes
In the HR+/≤1-year population and subgroups are presented in Table 4 and 5.

In the ITT population:

Events, n

In the HR+/≤1-year population:

Events, n

Follow-up anti-cancer therapy
For the ITT population, uncomfortable medications during follow-up were presented in Table 6.

Conclusions
The main finding of the current analysis was that neratinib was associated with significant differences in OS in the ITT population, and a benefit in the HR+/≤1-year population and subgroups:1

- OS was defined as time from randomization to death of any cause.
- Competing risk of death was assessed by the Kaplan-Meier method, and tested via Gray’s method.
- Cumulative incidence of CNS recurrences were calculated by competing risks analysis, and tested via a diagnostic tool.

Appendix

Key baseline characteristics

Table 3

Table 4

Table 5

Table 6

Follow-up anti-cancer therapy
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