Impact of neratinib on development and progression of central nervous system metastases in patients with HER2-positive metastatic breast cancer: Findings from the NALA, NEfERT-T, and TBCRC 022 trials

Ahmed Awada,1 Adam Budzisz,2 Cristina Saura,3 Rachel A. Freedman,4 Nancy U. Lin,5 Judith Bobok,6 Ping Xu,7 and Sara A. Hurvitz8


Background

Although HER2-directed therapies have improved the control of systemic disease and survival of patients with HER2-positive breast cancer, central nervous system (CNS) metastases present a clear unmet medical need: – Approximately one half of patients with advanced breast cancer eventually develop brain metastases.1,2 – Even though outcomes for patients with brain metastases from HER2-positive breast cancer have improved over time, recurrent CNS events remain a major cause of morbidity and adversely impact overall survival for many patients.3,4 – Treatment options, particularly systemic approaches, remain limited.5

Methods

ClinicalTrials.gov.6–16

Abbreviations:

CBR, clinical benefit rate; CNS, central nervous system; DoR, duration of response; ORR, objective response rate; OS, overall survival

Table 1. Study endpoints: NALA, NEfERT-T and TBCRC 022

Table 3. Landmark analysis: PFS and OS by CNS objective response (NALA, NEfERT-T and TBCRC 022)

Figure 1. Study design: NALA, NEfERT-T and TBCRC 022

Figure 2. CNS outcomes: NALA, NEfERT-T and TBCRC 022

Figure 3. Landmark analysis: PFS and OS by CNS objective response (NALA, NEfERT-T and TBCRC 022)

References

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Conclusions

Neratinib demonstrated notable and consistent activity against CNS metastases in patients with HER2-positive breast cancer in two independent phase II studies and one phase III study,1–5 with significant benefits for predefined CNS prevention endpoints first reported in NEfERT-T and replicated in NALA.6

An analysis of patients with baseline CNS lesions demonstrated shrinkage of CNS lesions and promising CNS objective response rates with neratinib-based therapy in all 3 studies in different settings (i.e. progressive CNS metastases, asymptomatic and stable CNS metastases).

Patients with CNS objective responses experienced longer PFS and OS than those without CNS objective responses.