Interim analysis (n=150) of the multi-national, prospective, non-interventional ELEANOR study observing real-life extended adjuvant treatment with neratinib in patients with HER2+ / HR+ early breast cancer (E)

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Background

- Therapies targeting the Human Epidermal Growth Factor Receptor 2 (HER2) in the neoadjuvant or (post-)adjuvant setting demonstrated a substantial benefit in patients with HER2-positive (HER2+) eBC. However, with longer follow-up, a considerable risk of local and distant disease recurrence still exists.

- Neratinib is an irreversible pan-HER tyrosine kinase inhibitor registered in Europe as extended adjuvant treatment for adult patients with HER2+ eBC. Rationale: ELEANOR (ES).

Methods

- ELEANOR is a prospective, longitudinal, multi-national, prospective, non-interventional study, ELEANOR (ES).

Population

- Table 1 summarizes the main demographic characteristics in the included patients (ES).

Results

- Patient population

- Table 1 shows the main demographic characteristics in the included patients (ES).

- At primary diagnosis, 87.2% of patients presented with an invasive carcinoma of no special type and were mainly reported with a clinical stage cT1 (50.7%) and/or cN0 (61.5%).

- 63.5% of patients were at increased risk of disease recurrence (Figure 1).

- 18.9% of patients had upfront surgery followed by adjuvant treatment while 80.4% received neoadjuvant therapy in the adjuvant setting, anti-HER2 treatment mostly consisted of trastuzumab only (71.4%), where-as in the neoadjuvant setting most patients received trastuzumab and pertuzumab (57.8%).

- 58.8% of patients with pCR received trastuzumab only and 32.8% received trastuzumab plus pertuzumab in the post-neoadjuvant setting. For patients with non-UCR, TDM-1 was the most commonly used post-neoadjuvant treatment (34.9%), followed by trastuzumab plus pertuzumab (30.4%) (Figure 2).

- Neoadjuvant treatment

- Median time from completion of previous trastuzumab-based therapy to start of neratinib treatment was 3.7 months (inter-quartile range [IQR]: 1.9 – 8.7 months, MAS).

- 92.0% of patients received endocrine treatment following neoadjuvant therapy.

- At time of data cutoff, 78 patients (56.9%) were still under neratinib treatment.

- Median treatment duration with neratinib was 10.3 months (IQR: 9.0 – 12.0 months).

- 11.7% of patients had completed treatment as per SmPC while treatment was prematurely discontinued due to adverse events in 16% or following treatment with neratinib.7

- Safety

- 88.3% of patients received trastuzumab prophylaxis at least once and 71.5% of patients had any kind of corrective diarrhoea.

- Non-serious and serious AE were reported for 87.5% and 4.4% of patients, respectively. For 24.3% of patients, AE grade ≥3 were reported. No fatal AE occurred (Safety Set, SAE).

- The most common AEs of any grade were diarrhoea (77.9%), nausea (22.1%), and fatigue (19.1%). The most common grade 3 AEs were reported for 25.8% of patients and grade 4 AEs for 3.1% of patients.

- 50.3% of patients started neratinib treatment at a daily dose lower than 240 mg with planned dose escalation (25.7%), due to patient’s request (2.9%), or for other reasons (9.5%). The incidence of grade ≥3 AE was 18.0% for patients who started at a lower daily dose as compared to 27.9% for patients starting at 240 mg day and grade 3 diarrhoea was observed less frequently (Figure 3).

- No relevant difference in the incidence of severe diarrhoea was observed between patients with different pretreatments.

Conclusion

- The pattern of anti-HER2 pretreatment reported by the patients in ELEANOR reflects the current treatment landscape for HER2+ eBC in Germany, Austria, and Switzerland.

- The proportion of patients with grade 3 diarrhoea was lower than reported previously and is in line with the ELEANOR study (18.4% vs. 35%).

- This might be a result of growing awareness towards the risk of diarrhoea and increasing use of the dose escalation approach. A positive signal is the slight decrease of grade 3 diarrhoea, as compared to the previous ELEANOR interim analysis.

- These preliminary safety results emphasize the contribution of diarrhoea management strategies, such as diarrhoea prophylaxis or dose escalation, additionally decreasing the incidence of grade 3 diarrhoea.

Limitations

When interpreting these results, the relatively short observation period in this early interim analysis, with a limited number of patients and the majority of patients still on treatment, should be taken into account.

Updated results with additional endpoints will be reported after the 200th patient has been observed. Updated results with additional endpoints will be reported after the 200th patient has been observed for 3 months.

References


3. Chan, A. et al. Final Efficacy Results of Neratinib in HER2-positive Metastatic Breast Cancer (HER2+ MBC) for HER2+ breast cancer patients (Provisional). Poster D19. ASCO 2023; 2023.06.01.


