Outcomes and Toxicity of Combination Chemotherapy and HER2-Targeted Therapy Versus HER2-Targeted Therapy Alone in Elderly Patients with HER2-Positive Breast Cancer

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Background

- The optimal approach for treating elderly patients (age ≥70) with HER2-positive breast cancer is uncertain, especially when balancing the benefits of combination chemotherapy with HER2-targeted agents versus targeted therapy alone.
- Given the increased risk of treatment-related toxicities in older adults, it is crucial to understand real-world outcomes and risks associated with these regimens in this population

Objectives

- To evaluate real-world survival outcomes and treatment-related toxicities of combination chemotherapy plus HER2-targeted therapy compared with HER2-targeted therapy alone in elderly patients (≥70 years) with HER2-positive breast cancer.

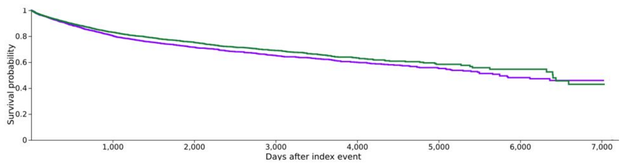
Methods

- We conducted a retrospective, real-world cohort study using the TriNetX platform. We identified two cohorts of patients aged ≥70 years withHER2-positive breast cancer.
- Cohort A (n=4,178) included patients who received HER2-targeted therapy (trastuzumab or trastuzumab deruxtecan) without concurrent chemotherapy (excluding docetaxel/paclitaxel).
- Cohort B (n=7,607) included those treated with HER2-targeted therapy in combination with chemotherapy (docetaxel or paclitaxel).
- Propensity score matching was performed, yielding 3,595 patients per cohort for comparative analyses.
- Outcomes were assessed with Kaplan-Meier survival curves and hazard ratios (HR) for mortality and major toxicities

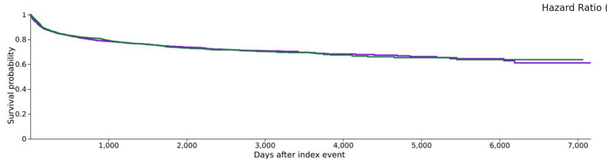
Results

- After 1:1 propensity score matching, 3,595 patients were included in each cohort.
- Mortality was slightly higher in the HER2-only group (25.96%)compared to the combination group (23.91%) (HR 1.136, 95% CI: 1.036-1.247, p=0.007).
- Hospitalization occurred more frequently in the combination group(36.2%) compared to the HER2-only group (30.3%; HR 0.830, 95% CI: 0.749-0.919, p=0.001).
- Outpatient visits were more frequent in the HER2-only group(56.1% vs. 32.6%; HR 1.649, 95% CI: 1.072-2.537, p=0.016).
- Rates of cancer progression were similar between groups (24.6% combination vs. 23.8% HER2-only; HR 1.004, p=0.951).

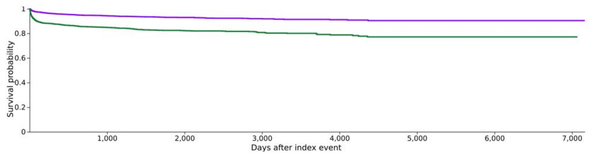




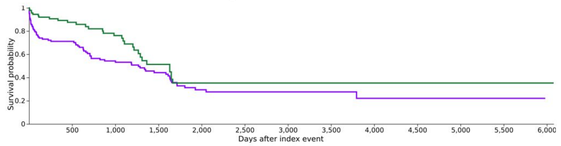
All-cause Mortality



Progression of Cancer



Neutropenia



Outpatient visits



Results (continued)

- Cardiomyopathy was more frequent in the combination group (12.7% vs. 10.4%; HR 0.834, p=0.012), while heart failure showed anon-significant trend towards higher frequency in the combination group (15.5% vs. 13.6%; HR 0.886, p=0.060).
- Treatment-related toxicities were consistently higher in the combination group, including neutropenia (16.3% vs. 6.0%; HR 0.359, p<0.001), anemia (35.1% vs. 24.9%; HR 0.661, p<0.001),thrombocytopenia (12.3% vs. 10.0%; HR 0.829, p=0.010), peripheral neuropathy (32.3% vs. 16.2%; HR 0.461, p<0.001), nausea/vomiting (33.0% vs. 21.7%;HR 0.608, p<0.001), mucositis (8.2% vs. 3.9%; HR 0.485, p<0.001), and diarrhea (32.1% vs. 20.9%; HR 0.598, p<0.001).
- Infections such as pneumonia, as well as heart failure with reduced ejection fraction (HFrEF) and severe sepsis, were also more frequent in the combination group, although not all differences reached statistical significance.

Conclusions

- Among elderly patients with HER2-positive breast cancer, combination chemotherapy plus HER2-targeted therapy provided a modest but statistically significant improvement in survival compared to HER2-targeted therapy alone.
- However, this benefit was accompanied by substantially higher rates of hematologic, cardiac, neurologic, and gastrointestinal toxicities.
- Importantly, the risk of cancer progression was not significantly different between regimens.
- These results suggest that HER2-targeted therapy alone may be a reasonable and safer alternative in select elderly patients who are frail and have significant comorbidities, offering similar cancer control with significantly less toxicity.

Limitations

- This was a retrospective database study and may be subject to selection bias and residual confounding despite propensity matching.
- Treatment sequencing and dosing details were not uniformly available.
- Toxicities and outcomes relied on diagnostic coding, which may underreport certain events.
- Functional status, frailty, and performance scores were not captured.
- Causality cannot be firmly established due to the observational design.

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