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Abstract

Purpose: Patients with HER2-positive (HER2+) inflammatory breast cancer (IBC) presenting with de novo metastatic disease have markedly improved survival compared with other IBC subtypes, largely due to the efficacy of modern HER2-targeted therapies. Trimodality therapy (TMT), defined as systemic therapy, surgery, and radiation, is associated with improved outcomes in IBC. We evaluated outcomes among patients with de novo metastatic HER2+ IBC according to receipt of TMT.

Methods: A prospective institutional registry of patients diagnosed with IBC between 2004 and 2022 at a tertiary cancer center was queried. Eligible patients had biopsy-confirmed HER2$^+$ de novo stage IV IBC and survived ⩾8 months without progression. The primary endpoint was survival with no evidence of disease (SWNED), defined as being alive and free of clinical or radiographic disease. SWNED was analyzed using death-censored Kaplan–Meier methods and competing-risks cumulative incidence functions (CIFs), treating death as a competing event. Among patients receiving TMT (n=56, 62%), outcomes were further stratified by pathologic complete response (pCR) (n=20, 36%). Group comparisons used the log-rank and Gray's tests, respectively. Multivariable Fine–Gray regression was used to estimate subdistribution hazard ratios (SHRs) for achieving NED, adjusting for age, BMI, race, ethnicity, ER, PR, grade, and clinical nodal stage.

Results: Ninety-one patients met inclusion criteria (median follow-up 7.9 years [IQR 6.2–9.8]; median age 46 years [IQR 37–53]). Baseline demographic and tumor characteristics were similar between groups; 78% of tumors were grade 3, 50% ER-positive, and 37% PR-positive. Among non-TMT patients (n=35, 39%), 20% underwent surgery and 9% received radiation. Patients who received TMT had a significantly higher likelihood of achieving NED (Gray's p=0.003; log-rank p=0.006) and longer median SWNED (108 months, 95% CI 38–NR vs. 19 months, 95% CI 15–26). Among TMT recipients, the cumulative incidence of achieving NED before death was higher in those achieving pCR (Gray's p=0.03). In multivariable Fine–Gray analysis, TMT remained independently associated with a greater likelihood of achieving NED before death (SHR 3.13, 95% CI 1.51–6.50, p=0.002). No other covariates were significant.

Conclusion: Among patients with HER2+ de novo metastatic IBC, TMT was independently associated with a greater likelihood of achieving and maintaining NED, and with significantly longer SWNED. Aggressive locoregional therapy in addition to systemic treatment may allow selected patients to live longer and remain disease-free. Validation in multi-institutional and prospective studies is warranted.