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ASO Author Reflections: Biological Diversity of Histologic Subtypes

Audree B. Tadros and Monica Morrow, MD

Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Past

Surgical treatment of breast cancer has evolved tremendously over the last half century. Breast-conservation therapy was proven to be a safe alternative to mastectomy, with equivalent survival outcomes in multiple prospective, randomized, clinical trials.^{1,2} These clinical trials were not only largely comprised of patients with the most common histologic subtypes (invasive ductal and invasive lobular carcinoma) but also included patients with special histologic subtypes.³ Patients with special histologic subtypes of breast cancer, including tubular, mucinous, papillary, and cribriform, have traditionally been thought to have superior outcomes compared with the more common histologic subtypes. For that reason, the majority of patients with special histologic subtypes of breast cancer do not receive adjuvant chemotherapy. As the use of molecular assays such as the 21-gene Oncotype DX Breast Recurrence Score assay have been incorporated into the adjuvant systemic therapy decision-making process, a more personalized treatment approach is now taken.

Present

The 21-gene Oncotype DX Breast Recurrence Score assay is now routinely ordered by many clinicians to determine the risk of recurrence as well as the benefit of chemotherapy for patients with early-stage, hormone receptor-positive, HER2-negative breast cancer.⁴ The use of this test has demonstrated significant biologic heterogeneity among the most common histologic subtypes of breast cancer. However, the biologic heterogeneity of special histologic subtypes of breast cancer was not known. Our study of 610,350 breast cancer specimens demonstrated that there is indeed biologic diversity in the special histologic subtypes,⁵ among which 8.8% had a high recurrence score (RS) result when using the cutoff of >25 as defined in the TAILORx trial, 36.2% had a low RS result, and 55% had an intermediate RS result.⁶ Patients with papillary and mucinous carcinoma were more likely to have a high RS result than those with tubular or cribriform carcinoma. These results suggest that there is a high-risk group of patients among those with special histologic subtypes who would derive a benefit from chemotherapy.

CORRESPONDING AUTHOR Monica Morrow, MD, morrowm@mskcc.org.

DISCLOSURES

Conflicts of Interest Monica Morrow is a consultant for Genomic Health.

Future

Genomic profiling of breast tumors has become increasingly available and affordable through the use of next-generation sequencing,⁷ which has led to the development of novel therapeutics targeting specific genomic alterations.⁸ As the discovery of actionable genomic alterations increases, additional targeted therapy is likely to become available and the role for chemotherapy will change. While our study showed that there is a small group of patients with special histologic subtypes of breast cancer who will derive a benefit from chemotherapy, it is likely, as our knowledge increases, a combination of molecular assays and genomic profiling will be used to determine a more personalized treatment for these patients.

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