Neoadjuvant Immunotherapy for Early-stage High-risk, ER+/HER2– Breast Cancer: Physician Practices, Therapy Choice, and Barriers Among U.S. Oncologists

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Background

- Despite improved prognosis among patients with early-stage estrogen receptor positive (ER+) human epidermal growth factor receptor 2 negative (HER2–) breast cancer, those with higher-risk disease (e.g., larger and higher-grade tumors, lymph node-positive disease) continue to experience a substantial risk of recurrence.[1]
- Neoadjuvant treatment in this setting can limit tumor growth and enhance surgical outcomes.
  - Current therapy options include anthracycline and taxane regimens with ongoing research exploring the use of immunotherapy with pembrolizumab or nivolumab.[2]
- The phase III KEYNOTE-756 trial revealed that addition of neoadjuvant pembrolizumab (versus placebo) to chemotherapy prior to surgery, followed by adjuvant pembrolizumab (versus placebo) and endocrine therapy, resulted in a significant increased pathological complete response among patients with early-stage, high-risk, ER+, HER2– breast cancer.[3-5]

Objective

- This survey-based study aimed to examine US oncologists' utilization and perceptions of neoadjuvant treatment options in early-stage, high-risk, ER+/HER2- breast cancer.

Methods

- US-based oncologists/hematologists attended two live meetings in February and March 2024 to discuss clinical updates from scientific meetings, including the 2023 San Antonio Breast Cancer Symposium.
- A survey to assess clinical practices regarding neoadjuvant therapy for early-stage high-risk, ER+/HER2– breast cancer and perceptions of KEYNOTE-756 was administered to the physicians.
- Participant demographics and practice details were collected via an online premeeting survey.
- Aggregate responses were summarized using descriptive statistics.

Results

- Among respondents (N=98), 76% were community-based with an average of 20.6 years of clinical experience.

Before reviewing KEYNOTE-756

- Over one-quarter of respondents reported use of neoadjuvant therapy in ≥40% of patients with early-stage, high-risk, ER+/HER2– breast cancer in the past 6 months.
- Nearly two-thirds of respondents reported a preference for neoadjuvant chemotherapy for early-stage high-risk, ER+/HER2– breast cancer.
- Respondents reported nodal involvement (54%) and stage of disease (45%) as top influential factors in neoadjuvant treatment selection.

After reviewing KEYNOTE-756

- Nearly 96% of respondents anticipated they would incorporate neoadjuvant pembrolizumab plus chemotherapy for early-stage, high-risk, ER+/HER2– breast cancer patient subgroups including positive lymph nodes, those with programmed death-ligand 1 (PD-L1) combined positive score (CPS) ≥1, and PD-L1 CPS ≥1 and ER-positivity <10%.
- Respondents reported that top barriers to prescribing neoadjuvant immunotherapy included limited long-term survival data (54%), cumbersome payer approval process (29%), and toxicity concerns (27%).

Table 1: Physician demographics and characteristics

	Count (%) (N=98)
Region of practice (n, %)*	
Midwest	21 (21)
Northeast	20 (20)
South	23 (24)
West	34 (35)
Practice setting (n, %)	
Community	74 (76)
Academic	22 (22)
Other	2 (2)
Primary medical specialty (n, %)	
Medical oncology	45 (46)
Hematology oncology	51 (52)
Other	2 (2)

Before reviewing KEYNOTE-756 data

Figure 1: Preference for Neoadjuvant Therapy

Question: Within the past 6 months, what proportion of your patients with early-stage, high-risk, ER+/HER2– breast cancer received neoadjuvant therapy?

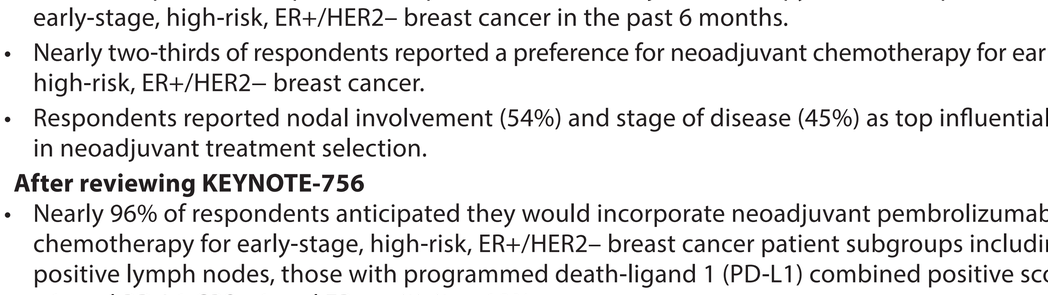
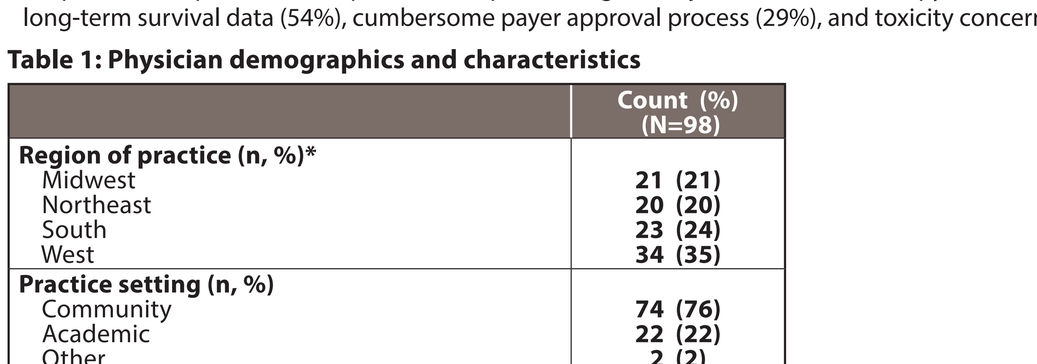


Figure 2: Preferred Neoadjuvant Regimen

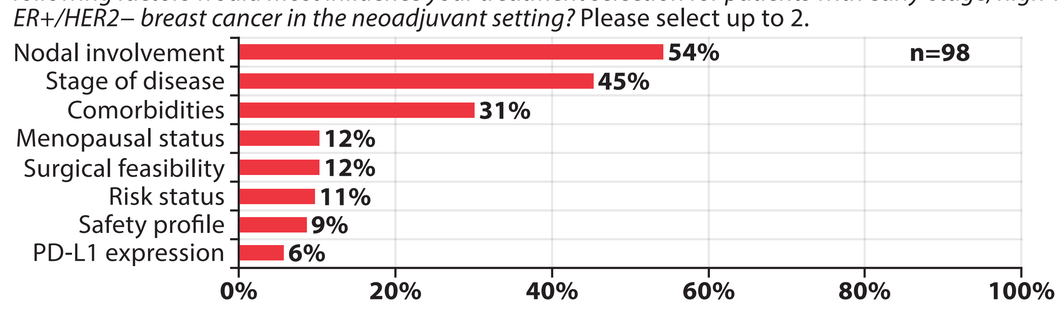
Question: What is your preferred neoadjuvant treatment regimen for patients with early-stage, high-risk (i.e., T2N1), ER+/HER2– breast cancer?



Results, continued

Figure 3: Top Factors in Neoadjuvant Treatment Selection

Question: Assuming that all treatment options are safe, affordable, and covered by insurance, which of the following factors would most influence your treatment selection for patients with early-stage, high-risk, ER+/HER2– breast cancer in the neoadjuvant setting? Please select up to 2.



After reviewing KEYNOTE-756 data

Figure 4: Potential Use of Neoadjuvant Pembrolizumab + Chemotherapy

Question: Based on the KEYNOTE-756 data and assuming FDA approval and/or guideline recommendation, which of the following best describes your anticipated utilization of neoadjuvant pembrolizumab + chemotherapy for patients with early-stage, high-risk, ER+/HER2– breast cancer?

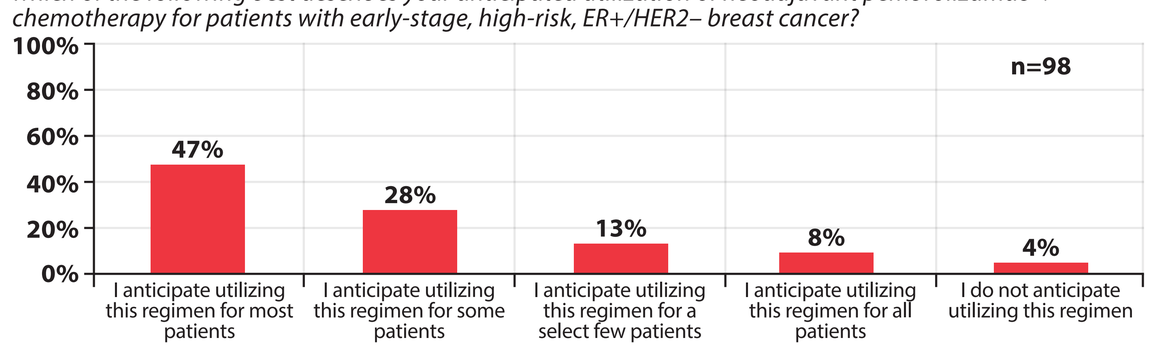


Figure 5: Physician Perceptions of Subgroups which benefit most with addition of Pembrolizumab to Neoadjuvant Chemotherapy

Question: After reviewing the KEYNOTE-756 data for patients with early-stage, high-risk, ER+/HER2– breast cancer, which of the following subgroups would most benefit from the addition of pembrolizumab to chemotherapy in the neoadjuvant setting? Please select up to 2.

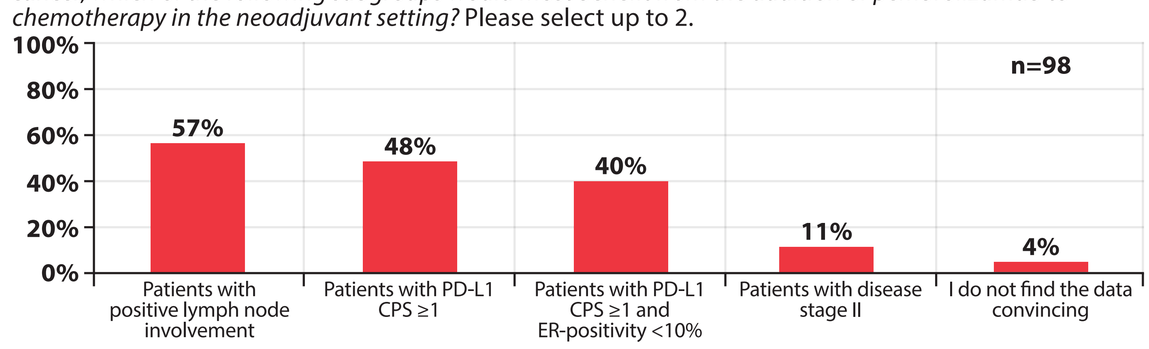
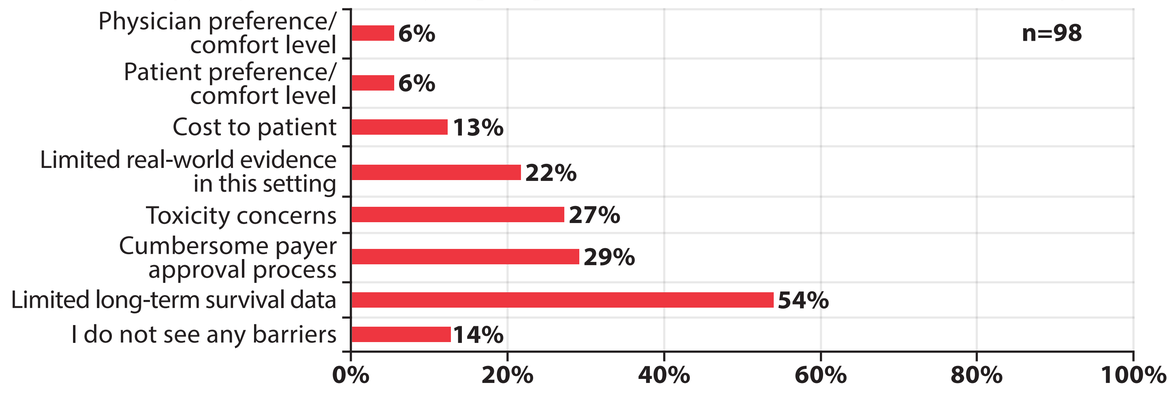


Figure 6: Perceived Barriers for Use of Neoadjuvant Immunotherapy

Question: After reviewing the KEYNOTE-756 data and assuming FDA approval and/or guideline recommendation, which of the following do you perceive as the greatest barriers to using neoadjuvant immunotherapy for patients with early-stage, high-risk, ER+/HER2– breast cancer? Please select up to 2.



Conclusions

- Overall, oncologists were receptive to adding pembrolizumab to neoadjuvant chemotherapy for high risk, ER+/HER2- breast cancer after reviewing data from the KEYNOTE-756 trial.
- Other ongoing investigations into survival data from KEYNOTE-756 holds promise for informing neoadjuvant treatment decisions and optimizing therapy selection in ER+/HER2– breast cancer.
- If approved by the FDA, the KEYNOTE-756 regimen may provide a new standard of care for this patient population.
- It remains to be seen how these data will impact clinical practice, and these data can be enhanced through future real-world evidence studies designed to identify the optimal neoadjuvant therapy for patients with ER+/HER2- breast cancer.

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