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The Challenging Decision to Commence Neoadjuvant Chemotherapy for Hormone-Receptor-Positive Breast Cancer

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Neoadjuvant treatment for non-metastatic breast cancer serves several purposes, such as averting the spread to metastatic sites, boosting overall survival rates, and enabling less extensive surgery that leads to better cosmetic results, organ preservation during dissection, and reduced occurrence of post-surgery lymphedema.

However, the idea that achieving a high pathological complete response (PCR) after neoadjuvant chemotherapy serves as a reliable indicator for increased overall survival is challenged by findings from randomized trials and a meta-analysis. These studies have shown comparable mortality rates whether similar systemic therapy is administered before or after surgery.[1-6] Additionally, in hormone receptor-positive HER2-negative early breast cancer, the reported PCR falls within very low ranges from 6% to 11%.[7]

The attempt to predict the risk levels of hormone receptor-positive HER2-negative early breast cancer has resulted in various criteria. Different definitions for the high-risk group, such as having four or more positive axillary lymph nodes, or one to three positive lymph nodes with at least one of grade III disease, a tumor size of 5cm or higher, or a KI67 proliferation index of at least 20%, have been established.[8] The IRIDE working group[9], focusing on the same type of breast cancer, identified grade 3 histology, pT3-pT4 and/or pN2-pN3 staging, Ki67>30%, expression of estrogen receptors<10% and/or progesterone receptors < 20%, and a high-risk class based on gene profiling assays as indicators of the high-risk group.

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Bozdogan *et al.* set some criteria for neoadjuvant chemotherapy in hormone receptor-positive early breast cancer, considering the involvement of one to three lymph nodes without inflammatory or bilateral disease or HER2 positivity and KI67 more than 20% sticking to ST Gallen 2013 guidelines.[10]

Decision-making for a complete course of combination chemotherapy for 24 weeks as neoadjuvant chemotherapy before surgery for early HR-positive breast cancer by Bozdogan *et al.* is challenging due to the low rate of PCR and high rate of poly-chemotherapy toxicity.

The role of KI67, discovered in 1983 as a nuclear protein expressed in proliferating cells and widely used to predict patient prognosis and to guide treatment decisions, is also under scrutiny. Logistic issues in determining a standard calculation of KI67 in tumor specimens and reproducibility concerns have led to its non-universal adoption in hospitals and medical centers. [11]

The introduction of ER-low breast cancer, as outlined by the 2020 ASCO/CAP guidelines, characterized by low ER expression (positivity in 1–10% of tumor cells), presents challenges in management due to the aggressive nature of these tumors.[12] This contradicts Bozdogan *et al.*'s assertions regarding ER less than 85% as a predictor of the response to neoadjuvant chemotherapy in hormone receptor-positive tumors.[10] The conflicting results underscore the necessity for validation through prospective studies.

To summarize, even for the hormone receptor-low patient group, it is advisable to explore micro-metastasis before and after neoadjuvant therapy using CTC, CT-DNA, and a multigene assay along with clinic-pathologic measures.[13] These considerations should be factored into discussions with patients and the decision-making process.

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REFERENCES

1. Gralow JR, Burstein HJ, Wood W, Hortobagyi GN, Gianni L, von Minckwitz G, Buzdar AU, et al. Preoperative therapy in invasive breast cancer: pathologic assessment and systemic therapy issues in operable disease. *J Clin Oncol*. 2008 Feb 10;26(5):814-9. doi: 10.1200/JCO.2007.15.3510.
2. Schwartz GF, Hortobagyi GN. Proceedings of the consensus conference on neoadjuvant chemotherapy in carcinoma of the breast, April 26-28, 2003, Philadelphia, Pennsylvania. *Cancer* 2004; 100:2512. doi: 10.1002/cncr.20298.
3. Mamtani A, Barrio AV, King TA, Van Zee KJ, Plitas G, Pilewskie M, et al. How Often Does Neoadjuvant Chemotherapy Avoid Axillary Dissection in Patients With Histologically Confirmed Nodal Metastases? Results of a Prospective Study. *Ann Surg Oncol*. 2016 Oct;23(11):3467-3474. doi: 10.1245/s10434-016-5246-8.
4. Scholl SM, Fourquet A, Asselain B, Pierga JY, Vilcoq JR, Durand JC, et al. Neoadjuvant versus adjuvant chemotherapy in premenopausal patients with tumours considered too large for breast conserving surgery: preliminary results of a randomised trial: S6. *Eur J Cancer* 1994; 30A:645. doi: 10.1016/0959-8049(94)90537-1.
5. Mieog JS, van der Hage JA, van de Velde CJ. Preoperative chemotherapy for women with operable breast cancer. *Cochrane Database Syst Rev* 2007;:CD005002.
6. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials. *Lancet Oncol* 2018; 19:27.
7. Kim HS, Yoo TK, Park WC, Chae BJ. Potential benefits of neoadjuvant chemotherapy in clinically node-positive luminal subtype breast cancer. 2019;22(3):412-24. doi:10.4048/jbc.2019.22.e35.
8. Harbeck N, Rastogi P, Martin M, Tolaney SM, Shao ZM, Fasching PA, et al. Adjuvant abemaciclib combined with endocrine therapy for high-risk early breast cancer: Updated efficacy and Ki-67 analysis from the monarchE study. *Ann. Oncol*. 2021, 32, 1571–1581.
9. Garutti M, Griguolo G, Botticelli A, Buzzatti G, De Angelis C, Gerratana, L, et al. Definition of High-Risk Early Hormone-Positive HER2-Negative Breast Cancer: A Consensus Review. *Cancers* 2022, 14, 1898.
10. Bozdogan A, Emiroglu S, Abuaisha A, Basar OD. Risk factors of response to neoadjuvant chemotherapy in patients with luminal (HER2 negative) breast cancer: ROC curve and logistic regression model results. *Archives breast cancer*. 2024;11(1):67-75. doi: 10.32768/abc.202411167.74
11. Höller A, Nguyen-Sträuli BN, Frauchiger-Heuer H, Ring A. Diagnostic and Prognostic Biomarkers of Luminal Breast Cancer: Where are We Now? *Breast Cancer: Targets and Therapy*. doi: 10.2147/BCTT.S340741
12. Ignatiadis M, Sledge GW, Jeffrey SS. Liquid biopsy enters the clinic - implementation issues and future challenges. *Nat Rev Clin Oncol*. 2021;18:297–312. doi:10.1038/s41571-020-00457-x
13. Carlo Pescia C , Guerini-Rocco E, Viale G, Fusco N. Advances in Early Breast Cancer Risk Profiling: From Histopathology to Molecular Technologies. *Cancers* 2023, 15, 5430. doi: 10.3390/cancers15225430.

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