ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

CORRESPONDENCE

Letter re: The prognostic and predictive value of the luminal-like subtype in hormone receptor-positive breast cancer: an analysis of the DATA trial

We read with great interest the recently published article by Tjan-Heijnen et al., titled 'The prognostic and predictive value of the luminal-like subtype in hormone receptor-positive breast cancer: an analysis of the DATA trial', in ESMO Open.[1] The study provides valuable insights into the prognostic and predictive implications of luminal A-like and luminal B-like subtypes in the context of extended endocrine therapy. However, we propose an alternative interpretation of these findings, suggesting that the lack of benefit observed with extended anastrozole therapy in luminal B-like tumors may stem from a suboptimal initial endocrine therapy sequence rather than a true limitation of aromatase inhibitor (AI) therapy itself.

A critical factor in this analysis is that all patients in the DATA trial had received 2-3 years of tamoxifen before switching to an AI. Although a common approach historically, this sequence may be suboptimal for luminal B-like tumors, which are characterized by high proliferative activity (Ki-67 $\geq$14%) and lower progesterone receptor expression, both indicative of reduced endocrine sensitivity.[2] Given that the highest risk of recurrence in luminal B occurs within the first 5 years of diagnosis, this period represents a crucial therapeutic window.[3]

Retrospective analyses have suggested that initiating AI therapy upfront, rather than following tamoxifen, is associated with superior long-term outcomes in postmenopausal patients.[4] Furthermore, the well-documented carry-over effect of tamoxifen suggests that its benefits extend beyond the treatment period, potentially altering its utility in long-term endocrine sequencing.[5]

Prolonged AI therapy, although highly effective in early suppression, may contribute to the selection of ESR1-mutant subclones, reducing its efficacy over time. By contrast, a carefully timed transition from AI to tamoxifen might provide sustained tumor suppression while also mitigating AI-associated adverse effects, particularly osteoporosis and cardiovascular risks.

The findings of the DATA trial, therefore, may not signify a failure of extended AI therapy in luminal B-like disease but rather highlight the need to refine endocrine sequencing strategies to maximize benefit in this high-risk group. Future trials should directly compare AI-first versus tamoxifen-first approaches to determine the optimal treatment pathway for luminal B-like breast cancer.

We appreciate the opportunity to engage in this discussion and commend the authors for their significant contributions to the ongoing refinement of endocrine therapy in breast cancer.

Arif Hakan Önder*

Antalya Training and Research Hospital, Antalya, Türkiye
(E-mail: dr_hakanonder@hotmail.com).

Available online xxx

© 2025 The Author. Published by Elsevier Ltd on behalf of European Society for Medical Oncology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

https://doi.org/10.1016/j.esmoop.2025.105066
DOI of original articles: https://doi.org/10.1016/j.esmoop.2025.104154
https://doi.org/10.1016/j.esmoop.2025.105068

FUNDING

None declared.

DISCLOSURE

The author has declared no conflicts of interest.

REFERENCES

1. Lammers SWM, Geurts SME, Hermans KEPE, et al. The prognostic and predictive value of the luminal-like subtype in hormone receptor-positive breast cancer: an analysis of the DATA trial. *ESMO Open*. 2025;10(2):104154.
2. Prat A, Cheang MCU, Martín M, et al. Prognostic significance of progesterone receptor-positive tumor cells within immunohistochemically defined luminal A breast cancer. *J Clin Oncol*. 2013;31(2):203-209.
3. Pan H, Gray R, Braybrooke J, et al. 20-year risks of breast-cancer recurrence after stopping endocrine therapy at 5 years. *N Engl J Med*. 2017;377(19):1836-1846.
4. Burstein HJ, Temin S, Anderson H, et al. Adjuvant endocrine therapy for women with hormone receptor—positive breast cancer: ASCO clinical practice guideline focused update. *J Clin Oncol*. 2014;32(21):2255-2269.
5. Selli C, Dixon JM, Sims AH. Accurate prediction of response to endocrine therapy in breast cancer patients: current and future biomarkers. *Breast Cancer Res*. 2016;18(1):118.