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Answer to the comments of the reviewer

1. The reviewer indicated that we did not present the four major molecular categories of breast cancer.

We thank the reviewer for this comment. In this review, only the tumor biology of ER-positive, HER2-negative breast cancer is discussed. Other molecular categories, such as triple-negative, hormone receptor-negative and HER2-positive, and hormone receptor-positive and HER2-positive, were not included in this review.

2. The reviewer mentioned that Ki67 and multigene assays are not the only methods of differentiating these molecular subtypes from one another.

We appreciate the reviewer's input. However, Coates, *et al.*, in their special article (St Gallen International Expert Consensus on the primary Therapy of Early Breast Cancer 2015, Ann Oncol) that PgR and Ki67 are the two key factors used to classify luminal A-like, intermediate and luminal B-like tumors in hormone receptor (ER)-positive, HER2-negative breast cancer as shown below. For this reason we focused on PgR and Ki67 in this manuscript.

Table 2. Treatment-oriented classification of subgroups of breast cancer

Clinical grouping	Notes
Triple-negative	Negative ER, PgR, and HER2
Hormone receptor-negative and HER2-positive	ASCO/CAP guidelines
Hormone receptor-positive and HER2-positive	ASCO/CAP guidelines
Hormone receptor-positive and HER2-negative luminal disease as a spectrum:	ER and/or PgR positive $\geq 1\%$ ^a
High receptor, low proliferation, low tumor burden (luminal A-like)	Multiparameter molecular marker 'favorable prognosis' if available. High ER/PgR and clearly low Ki-67 ^b . Low or absent nodal involvement (N 0–3), smaller T size (T1–T2).
Intermediate	Multiparameter molecular marker 'intermediate' if available ^c . Uncertainty persists about degree of risk and responsiveness to endocrine and cytotoxic therapies.
Low receptor, high proliferation, high tumor burden (luminal B-like)	Multiparameter molecular marker 'unfavorable prognosis' if available. Lower ER/PgR with clearly high Ki-67 ^b . More extensive nodal involvement, histological grade 3, extensive lymphovascular invasion, larger T size (T3).

^aER values between 1% and 9% were considered equivocal. Thus, endocrine therapy alone cannot be relied upon for patients with these values.

^bKi-67 scores should be interpreted in the light of local laboratory values: as an example, if a laboratory has a median Ki-67 score in receptor-positive disease of 20%, values of 30% or above could be considered clearly high; those of 10% or less clearly low.

^cNot all multiparameter molecular marker tests report an intermediate score.

3. The reviewer indicated that the title does not mention that the article focuses on HER2 negative disease.

We appreciate the valuable comment.

“HER2-negative” has now been incorporated into the title, so that the title has been changed to ‘Tumor biology in estrogen receptor-positive, HER2-negative breast cancer: Mind the menopausal status’ in the revised manuscript.

The change has been highlighted in the revised manuscript.