Medical Oncology (2024) 41:154
https://doi.org/10.1007/s12032-024-02383-9

LETTER TO THE EDITOR

Hormone/HER2 receptor crosstalk in breast cancer needs further investigation

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Received: 18 February 2024 / Accepted: 8 April 2024

To The Editor,

I'd like to congratulate Horpratraporn and colleagues on their article [1] exploring the combination of lapatinib and palbociclib to inhibit cell proliferation and invasion via the AKT signaling pathway in endocrine-resistant breast cancer cells. According to their findings, combining lapatinib and palbociclib inhibits cell proliferation and invasion via AKT signaling pathway in endocrine-resistant breast cancer cells. This information demonstrated better antiproliferative, anti-invasive effects, and suppression of EMT protein and pAKT than a single drug. The findings of this study suggest that biopsy from metastatic sites is required in metastatic hormone receptor-positive-HER2-negative breast cancer patients who develop endocrine treatment with CDK4/6 inhibitors. If a biopsy shows HER2 overexpression, a combination of lapatinib and palbociclib may be the best treatment option. Furthermore, HER2-positive breast cancer patients with the germline TSC2 nonsynonymous variant c.4349 C > G (p.Pro1450Arg) are resistant to anti-HER2 therapy. TSC2 c.4349 C > G reverses the inhibitory effect on mTOR and downstream signaling by increasing TSC2 phosphorylation at Thr1462, providing significant lapatinib resistance in vitro and in vivo. The combination of lapatinib and the CDK4/6 inhibitor palbociclib inhibits the cyclin D1/CDK4/Rb alternative pathway as well as TSC2 phosphorylation, partially inhibiting mTOR activity and inducing TSC2-mutant cell blockage at G1/G0. In vitro and xenograft models, palbociclib + lapatinib outperforms monotherapy in anti-tumor activity and overcomes the resistance of the TSC2 c.4349 C > G-related variant to anti-HER2 therapy [2]. There have been no studies on the use of this combination treatment in humans with the potential side effects. Other drug combinations with different mechanisms of action in human studies have been described in the literature, with promising results [3]. In conclusion, the relationship between hormone receptor status and HER2 overexpression is extremely complex and warrants further investigation.

Author contributions I myself wrote and reviewed this paper.

Data Availability No datasets were generated or analyzed during the current study.

Declarations

Competing interest The authors declare no competing interests.

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Published online: 14 May 2024