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LETTER

Treatment challenges for community oncologists treating postmenopausal women with endocrine-resistant, hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer

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Dear editor

I read with great interest the review written elegantly by Gradishar addressing the challenges that community oncologists face in treating postmenopausal women with endocrine-resistant, hormone receptor-positive, human epidermal growth factor receptor-2 (HER2)-negative advanced breast cancer in your journal.[1]

As the author correctly stated, resistance to endocrine therapy in women with hormone receptor-positive disease is very frequent and almost inevitable.

Understanding the multiple known mechanisms for endocrine resistance has helped physicians and researchers target these pathways.[2] Many of the recently introduced drugs, such as the mTOR inhibitor everolimus[3] and the cyclin-dependent kinase (CDK 4/6) inhibitor palbociclib,[4] are in clinical practice and have been already incorporated in international guidelines.[5]

While the author had successfully addressed the above issue, the review lacked a discussion about the role of chemotherapy in treating hormone-refractory, HER2-negative metastatic breast cancer. Discussing such challenges can never be complete without addressing the clinical use of chemotherapy in this setting, especially so when such discussion is targeting community-based oncology practice.

Chemotherapy is the mainstay of treatment of metastatic breast cancer in many clinical settings. In addition to its utilization in hormone-negative and rapidly progressing hormone-positive disease, its use in the treatment of hormone-refractory metastatic breast cancer is well established.

In addition to anthracyclines and taxanes, which are used quite often in the adjuvant and early phases of metastatic disease,[6] several new chemotherapeutic drugs have been introduced in an attempt to overcome drug resistance. Such agents include ixabepilone,[7] an epothilone B analog, and eribulin,[8] a nontaxane microtubule inhibitor. The 5-fluorouracil analog capecitibine, the nucleotide analog gemcitabine, and the vinca alkaloid vinorelbine are also widely used agents. Platinum compounds, cisplatin and carboplatin, are effective agents in triple-negative disease, especially in BRCA-mutant patients.[9]

The decision to use hormone-resistance modulators, discussed in detail in the review, versus chemotherapy depends upon the need to obtain a rapid disease response

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and the potential toxicities associated with each approach. Chemotherapy is perceived by many to be associated with increased toxicity, but such an assumption might not always be true. Everolimus[10] and palbociclib[11] are both associated with many specific toxicities which have been nicely discussed in Gradishar's review. Also, the cost involved in using such agents is not necessarily lower than that of chemotherapy.

We all agree that combination chemotherapy generally provides higher rates of objective response and longer time to progression. However, its associated higher toxicity rates limit its use in this setting. Sequential administration of single agents is better tolerated and associated with better quality of life.[12]

We also need to point out that many of these new hormone-resistance modulators are used more often in the frontline treatment of metastatic breast cancer.[13] The National Comprehensive Cancer Network has included the combination of palbociclib and letrozole as a first-line endocrine therapeutic option for postmenopausal patients with hormone receptor-positive, HER2-negative metastatic disease.[5] Obviously, the utilization of such new drugs in upfront therapy will obviously limit their value in disease progression.

In conclusion, the extent of metastatic disease, the pace of disease progression, and the effect of disease and the chosen treatment approach on the quality of life should all be considered when choosing a treatment for breast cancer in the setting under discussion, and as such, chemotherapy is still a very valid option.

Disclosure

The author reports no conflicts of interest in this communication.

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