

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

Hikmat Abdel-Razeq

Department of Internal Medicine,
King Hussein Cancer Center,
Amman, Jordan

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 everolimus³ 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 capecitabine, 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

Correspondence: Hikmat Abdel-Razeq
Department of Internal Medicine, King
Hussein Cancer Center, 202 Queen
Rania Al Abdullah Street, Amman,
11941 Jordan
Tel +962 6 530 0460 ext 1000
Email habdelrazeq@khcc.jo

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. Everolimus¹⁰ and palbociclib¹¹ 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.

References

1. Gradishar W. Treatment challenges for community oncologists treating postmenopausal women with en-resistant, hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer. *Cancer Manag Res*. 2016;8:85–94.
2. Chang J, Fan W. Endocrine therapy resistance: current status, possible mechanisms and overcoming strategies. *Anticancer Agents Med Chem*. 2013;13(3):464–475.
3. Piccart M, Hortobagyi GN, Campone M, et al. Everolimus plus exemestane for hormone-receptor-positive, human epidermal growth factor receptor-2-negative advanced breast cancer: overall survival results from BOLERO-2. *Ann Oncol*. 2014;25(12):2357–2362.
4. Turner NC, Ro J, Andre F, et al. Palbociclib in hormone-receptor-positive advanced breast cancer. *N Engl J Med*. 2015;373(3):209–219.
5. National Comprehensive Cancer Network [database on the Internet] Fort Washington, PA: NCCN Guidelines for Breast Cancer: Endocrine Therapy for Stage IV or Recurrent Metastatic Disease. Page MS-54-57. Available from: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 13, 2016.
6. King KM, Lupichuk S, Baig L, Webster M, Basi S, Whyte D, Rix S. Optimal use of taxanes in metastatic breast cancer. *Curr Oncol*. 2009;16(3):8–20.
7. Sachdev JC, Jahanzeb M. Use of cytotoxic chemotherapy in metastatic breast cancer: putting taxanes in perspective. *Clin Breast Cancer*. 2016;16(21):73–81.
8. Cortes J, O'Shaughnessy J, Loesch D, et al. Eribulin monotherapy versus treatment of physicians choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomized study. *Lancet*. 2011;377(9769):914–923.
9. Sharma P. Biology and management of patients with triple-negative breast cancer. *Oncologist*. 2016;21(9):1050–1062.
10. Rugo HS, Pritchard KI, Gnant M, et al. Incidence and time course of everolimus-related adverse events in postmenopausal women with hormone receptor-positive advanced breast cancer: insights from BOLERO-2. *Ann Oncol*. 2014;25(4):808–815.
11. Turner NC, Huang Bartlett C, Cristofanilli M. Palbociclib in hormone receptor-positive advanced breast cancer. *N Engl J Med*. 2015;373(17):1672–1673.
12. Cardoso F, Bedard PL, Winer EP, et al. International guidelines for management of metastatic breast cancer: combination vs sequential single-agent chemotherapy. *J Natl cancer Inst*. 2009;101(17):1174–1181.
13. Finn RS, Crown JP, Lang I, et al. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. *Lancet Oncol*. 2015;16(1):25–35.

Dove Medical Press encourages responsible, free and frank academic debate. The content of the Cancer Management and Research 'letters to the editor' section does not necessarily represent the views of Dove Medical Press, its officers, agents, employees, related entities or the Cancer Management and Research editors. While all reasonable steps have been taken to confirm the content of each letter, Dove Medical Press accepts no liability in respect of the content of any letter, nor is it responsible for the content and accuracy of any letter to the editor.

Cancer Management and Research

Publish your work in this journal

Cancer Management and Research is an international, peer-reviewed open access journal focusing on cancer research and the optimal use of preventative and integrated treatment interventions to achieve improved outcomes, enhanced survival and quality of life for the cancer patient. The manuscript management system is completely online and includes

Submit your manuscript here: <https://www.dovepress.com/cancer-management-and-research-journal>

a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Dovepress