

Exemestane

A Viewpoint by Per E. Lønning

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The importance of endocrine therapy in the treatment of advanced breast cancer cannot be overrated. A median survival time of about 2 years, with a few patients becoming long term survivors, underlines the palliative goals of therapy for this disease.

Lack of cross-resistance to different endocrine treatment options has been known for decades. Whereas a limitation with previous therapeutic options was their significant adverse effects, new non-toxic endocrine drugs now offer the possibility of disease control for durable periods through the application of sequential endocrine therapies to patients with a hormone-sensitive tumour.

Exemestane, a novel steroidal aromatase inactivator, is an interesting new drug in this setting. Exemestane, like nonsteroidal aromatase inhibitors such as letrozole and anastrozole, has a low toxicity profile and seems to improve the clinical benefits compared with conventional therapy. Interestingly, exemestane, like formestane, may

achieve clinical benefits in patients previously exposed to the first-generation aromatase inhibitor aminoglutethimide. In addition, recent data show that a significant proportion of patients may also obtain durable stable disease (some also an objective response) when exposed to exemestane following therapeutic failure on novel nonsteroidal aromatase inhibitors. This provides further therapeutic benefits to patients and may also provide an important insight into the mechanism of drug resistance.

While treatment of metastatic breast cancer is palliative, it is well documented that the anti-estrogen tamoxifen may cure patients in an adjuvant setting. This suggests that even modest benefits in advanced disease may be translated into survival benefits in the adjuvant setting, supporting evaluation of novel aromatase inhibitors and inactivators in the adjuvant setting. Exemestane is currently being explored as a sequential treatment option, along with tamoxifen, in this setting. The hope for the future is that this may be translated into a survival benefit in patients with early breast cancer. ▲