Cost Effectiveness of Letrozole in the Treatment of Advanced Breast Cancer in Postmenopausal Women in the UK

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Abstract

Objective: To simulate the treatment of postmenopausal women with advanced breast cancer from second-line hormone therapy to death, and to generate estimates of the cost and effectiveness of letrozole and megestrol in order to determine the incremental cost effectiveness of letrozole, expressed as cost per life-years gained.

Design: A decision-analytic model, using Markov process techniques, was designed to evaluate the lifetime clinical and economic consequences of treatment with letrozole compared with standard care with megestrol. The model was based on clinical trial results showing a clear advantage of letrozole in terms of time to progression and duration of response.

Setting: The setting of the study was that of the UK healthcare system in 1996.

Patients and participants: A hypothetical cohort of patients, identical to the patients recruited for the AR/BC2 clinical trial, who were postmenopausal women with advanced breast cancer who had previously failed to respond to first-line or adjuvant anti-estrogen therapy.

Interventions: The dosages of medications were 2.5 and 160 mg/day for letrozole and megestrol, respectively. The analysis covered the period from treatment initiation until death (lifetime model). Effectiveness was expressed as survival and time without progression, and the model also included all relevant economic measures.

Main outcome measures and results: Based on the model, the average survival time of the letrozole group was 2.1 years (25.3 months) versus 1.9 years (21.5 months) for the megestrol group, a gain in survival of 2.4 months (10.5%). The average time without progression, cumulatively calculated over the different treatment options, amounted to 20.2 months for letrozole and 17.8 months for megestrol, an increase of 13.7% for the former patients. The total average cost per patient for the treatment of advanced breast cancer starting from second-line hormone therapy until death was higher in the letrozole group at £7547 versus £6820 for the megestrol group (discounted at an annual rate of 5%), leading to
Breast cancer is the second leading cause of death from cancer in the female population after lung cancer. In the UK, breast cancer is the most common type of cancer in women; 1 in 11 women develop the disease at some time in their life. This represents approximately 26,000 women in the UK who are newly diagnosed with breast cancer each year.[1] Although some women with small localised tumours and favourable prognostic features may be cured by surgery and radiotherapy, there are still approximately 16,000 deaths each year from breast cancer,[2,3] caused mainly by metastatic disease. Although about 90% of women with breast cancer present with a tumour clinically limited to the breast and axillary lymph nodes, nearly 50% of these women with early (operable) disease will later develop metastases.

The high prevalence of breast cancer and the morbidity and mortality associated with the disease result in a significant economic burden. The treatment of advanced breast cancer poses a particular economic burden. An Australian study showed a clear relationship between the stage of disease and the costs of treatment, more advanced stages of disease incurring higher treatment costs.[4] Many studies have tried to evaluate the cost of treating the disease, but they are difficult to interpret because of the large variation in existing treatment practices.[2,5-7] A study by Richards et al.[8] showed that the costs of patients with advanced breast cancer in the UK varied between £317 and £27,860, with an average of £7,620. More than half the costs (56%) were accounted for by hospitalisation followed by laboratory and radiological investigations (13%).[8] Only a relatively small proportion (between 7 and 10%) of the total treatment costs were accounted for by chemotherapy. This finding was supported by the results of other studies.[9,10]

For patients with advanced breast cancer, the main objective of systemic therapy is palliation, either through chemotherapy or hormone therapy. Chemotherapy will usually be used as first-line treatment in estrogen receptor (ER)-negative patients with rapidly growing tumours, in whom response rates to hormone manipulation may be as low as 5 to 10%. Chemotherapy is usually delivered using a multidrug regimen. Combination therapy produces a response rate of 50 to 60% with a median response duration of 10 to 18 months,[11] whereas cytotoxic drugs used as single agents show response rates of approximately 20 to 40% with a response duration of 3 to 9 months.

Patients most likely to respond to hormone therapy are those with an estrogen and/or progesterone receptor-positive tumour, a long disease-free interval, disease limited to soft tissues and prior documented response to hormone therapy.[12] Approximately one-third of human breast cancers are hormone-dependent. In medical practice, anti-estrogens, aromatase inhibitors and progestins seem most relevant for the treatment of advanced breast cancer in postmenopausal patients with ER-positive tumours.[12,13] Response rates to hormone treatment range from 30 to 35% among unselected patients and from 60 to 70% in patients with high positive tumour ER levels. The median duration of response is usually 9 to 12 months.[13] Tamoxifen is generally considered the preferred first-line treatment, with progestins and aromatase inhibitors used as second-line hormone therapy. Following relapse after response to a first-line hormone therapy, patients may be switched to treatment with another hormone or chemotherapy. Around 40% of patients relapsing after tamoxifen may achieve further clinically useful tumour control with second-line therapy,[14,15] but several choices for second-line treatment exist. Progestins and aromatase inhibitors are both commonly used: progestins (megestrol and medroxyprogesterone) can cause oedema, bodyweight gain, vaginal bleeding, hy-