Anastrozole: a review of its use in the management of postmenopausal women with advanced breast cancer
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Authors' objectives
To examine the use of anastrozole in the management of postmenopausal women with advanced breast cancer.

Searching
Medical literature published since 1966 on anastrozole was identified using AdisBase, MEDLINE and EMBASE. References also identified from reference lists of published articles. Bibliographic information, including contributory data was also requested from the company developing the drug.

Search terms: anastrozole, armidex, ic-d-1033, zd-1033 (all databases), breast cancer, aromatase inhibitor (AdisBase only), 120511-73-1 (MEDLINE and EMBASE only). Searches last updated 1 September 1988.

Study selection
Study designs of evaluations included in the review
Multicentre, randomised, parallel-group double-blind for anastrozole and non-blind for megastrol clinical trials.

Specific interventions included in the review
Anastrozole 1 mg once daily compared with anastrozole 10 mg once daily and oral megastrol 40 mg 4 times daily.

Participants included in the review
Women with breast cancer which had progressed during anti-oestrogen therapy for advanced disease, or had relapsed during or after adjuvant tamoxifen therapy for early disease. All women were postmenopausal, had measurable lesions or evaluable but non-measurable lesions, had a WHO performance status score >=2 and had tumours with an oestrogen receptor-positive or unknown-status. Patients exposed to more than one previous course of cytotoxic therapy (except adjuvant chemotherapy) or hormonal therapy for advanced breast cancer were not included.

Outcomes assessed in the review
Primary end points - overall response rate, time to disease progression, objective responses according to the UICC definition (complete and partial response).

Secondary end points - survival (duration of response, time to treatment failure or subjective symptom scores), quality of life (assessed using the Rotterdam Symptom Checklist).

Adverse effects - weight gain, oedema, thromboembolic disorder, gastrointestinal disturbance, hot flushes, vaginal dryness.

How were decisions on the relevance of primary studies made?
Inclusion of studies based mainly on methods section of trials.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.
Methods of synthesis
How were the studies combined?
Intention-to-treat analysis was performed using logistic regression, and on time to progression, time to treatment failure and survival using the cox proportional hazards model.

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

Results of the review
Two primary studies (n=764) and one study in which two studies were combined.

Primary end points.
No significant difference between treatment groups at a median follow-up of 6 months in respect to overall response rate and time to disease progression. The higher dosage of anastrozole did not result in additional clinical benefit. No significant difference in objective response rate between sub-groups of patients according to presence of measurable lesions, disease status, oestrogen receptor status or prior response to hormonal therapy.

Secondary end points.
No significant differences between treatment groups in terms of duration of response, time to treatment failure or subjective symptom scores. In combined analysis statistically significant survival advantage in the anastrozole 1mg/day treatment group - median time to death in anastrozole patients was 26.7 months versus 22.5 months in patients treated with megastrol (p<0.025). Improvement in quality of life parameters were similar in all treatment groups.

Side effects.
Incidence of hot flushes, vaginal dryness and thrombo-embolic disease were similar among all treatment groups. Gastro-intestinal disturbances were more common in anastrozole recipients, especially those receiving 10mg/day, oedema and weight gain were more common with megastrol. Combined analysis showed similar incidence of serious adverse effects in all 3 treatment groups. Withdrawal due to adverse events was 1.9, 2.8 and 4.0 % in the anastrozole 1mg, 10mg and megastrol treatment groups. There were no deaths due to adverse drug reactions in the anastrozole treatment groups, mortality was 0.8% among megastrol recipients (one patients died from a pulmonary embolism and another from stroke).

Authors' conclusions
Anastrozole is indicated for the second-line treatment of postmenopausal women with advanced breast cancer whose disease progressed after tamoxifen or other anti-estrogen therapy. The recommended dosage of anastrozole is 1mg taken orally once daily. Treatment should be continued until there is evidence of disease progression.

CRD commentary
From the results presented there appears to be very little difference in the effectiveness of anastrozole compared to megastrol, although there is some suggestion of fewer side effects with anastrozole, especially in the lower dose treatment group. This review only identified two relevant studies, although a thorough literature search was undertaken. The two studies were not assessed for validity. This paper also discusses the pharmacodynamic and pharmokinetic properties of anastrozole and so the conclusions drawn by the authors may be influenced by this information.

Implications of the review for practice and research
Practice: Data from the limited number of studies reviewed suggest that anastrozole may be indicated for the second-line treatment of postmenopausal women with advanced breast cancer. Anastrozole is similar in its effectiveness
compared to megestrol, although it may cause fewer side effects and lead to a slight increase in survival time.

Research: Further studies are necessary to investigate more fully the effectiveness of anastrozole in the treatment of postmenopausal women with advanced breast cancer.

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