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Randomised study of anastrozole versus tamoxifen as first-line therapy for advanced breast cancer in postmenopausal women

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Abstract

A total of 668 patients (340 anastrozole and 328 tamoxifen) were randomised in a double-blind, double-dummy multicentre study. Anastrozole was given in a dose of 1 mg once daily and compared with tamoxifen 20 mg daily in postmenopausal patients with tumours that were hormone-receptor positive or of unknown receptor status. The efficacy and tolerability of anastrozole was compared with that of tamoxifen as first-line therapy for advanced breast cancer. The median time to progression was similar for both treatments (8.2 months in anastrozole patients and 8.3 months in tamoxifen patients). Anastrozole was also as effective as tamoxifen in terms of objective response-rate with 33% in the anastrozole group and 32.6% in the tamoxifen group achieving a complete or partial response. Both treatments were well tolerated. However, incidences of thromboembolic events and vaginal bleeding were reported in fewer patients treated with anastrozole than with tamoxifen. In conclusion, these findings indicate that anastrozole can be considered as first-line therapy for postmenopausal women with advanced breast cancer.

Keywords: Breast neoplasms; Aromatase-inhibitors; Anastrozole; Tamoxifen

Since the late 1970's tamoxifen has been accepted as the 'gold' standard first-line treatment for advanced breast cancer in postmenopausal patients. Tamoxifen acts by blocking the binding of the oestrogen receptor (ER) and has an overall response rate of 30–35% when used as first-line therapy for advanced breast cancer [1]. Adverse effects that have been associated with tamoxifen can be classified as either due to its anti-oestrogenic actions (e.g. hot flushes, vaginal bleeding, discharge or dryness), or more general effects (e.g. nausea, vomiting,

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tumour flare and skin rash). In adjuvant studies involving patients who took either placebo or tamoxifen, thromboembolic events were rare overall, but were more common with tamoxifen than with placebo [2]. A 2–3-fold increase in the risk of developing endometrial cancer has been documented in association with long-term tamoxifen use [3,4]. The new generation non-steroidal aromatase inhibitor anastrazole is both potent and selective and can be given orally. A combined analysis of two large randomised trials in postmenopausal women with advanced breast cancer who had failed on tamoxifen therapy has shown that 1 mg anastrozole significantly increases survival time compared with megoestrol acetate at a mean follow-up of 31 months [5]. Here we present the results of a trial comparing the efficacy and tolerability of anastrozole and tamoxifen in postmenopausal women with advanced breast cancer.

1. Results

A randomised, double blind, double-dummy was designed to demonstrate equivalent efficacy of anastrozole 1 mg once daily relative to tamoxifen 20 mg once daily in patients with tumours that were hormone receptor-positive or of unknown receptor status, and who were eligible for endocrine therapy. The primary endpoints of the study were time to progression (TTP) and objective response (OR) and tolerability. A total of 668 patients (340 anastrozole and 328 tamoxifen) were randomised to treatment and followed for a median of 19 months. The median TTP was similar for both treatments (8.2 months in anastrozole and 8.3 months in tamoxifen patients). The tamoxifen–anastrozole hazard ratio was 0.99 demonstrating that the anastrozole was at least equivalent to tamoxifen. Anastrozole was also as effective as tamoxifen in terms of OR, with 33% of the anastrozole-group and 32.6% of the tamoxifen-group achieving a complete or partial response. Clinical benefit (CR + PR + stabilisation of $\geqslant$24 weeks) rates of 56.2% and 55.5% were observed for anastrozole and tamoxifen respectively. No statistical analysis of subgroups according to receptor known- or unknown disease was performed for this trial since the larger combined dataset from this trial and the North American trial provides the most appropriate setting for statistical exploration of subgroups. However, in the receptor positive subgroup there was a separation of the curves, suggesting a benefit in favour of anastrozole. Both treatments were well tolerated. The incidence-rates of depression, tumour flare, gastrointestinal disorders, hot flushes, vaginal dryness and weight gain were similar in both treatment arms. However, incidences of thromboembolic events and vaginal bleeding were reported in fewer patients treated with anastrazole than with tamoxifen (4.8 versus 7.3% thromboembolic events and 1.2 versus 2.4% vaginal bleeding), respectively.

In conclusion, anastrozole satisfied the pre-defined criteria for equivalence to tamoxifen. Together with the lower observed incidence of thromboembolic events and vaginal bleeding, these findings indicate that anastrozole can be considered as first-line therapy for postmenopausal women with advanced breast cancer.

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