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# High dose raloxifene in patients with advanced breast carcinoma

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## Keywords

Anti-oestrogen, breast cancer, postmenopausal women, selective oestrogen receptor modulator (SERM)

# Introduction

Tamoxifen, a selective ER modulator (SERM) with both oestrogen antagonistic and agonistic properties is the standard first line endocrine therapy in all stages of breast cancer. Nevertheless, its partial-agonistic properties result in side effects such as endometrial proliferation and uterine cancer. Thus, the development of SERMs with an improved toxicity profile has been under way for some time. Raloxifene is one such agent, demonstrating a lack of effect upon the postmenopausal uterus, while retaining beneficial impact upon bone mineral density and lipid profile. In preclinical models, raloxifene also has antiproliferative effects upon breast carcinomas. An early clinical trial of raloxifene, carried out in women with progressive metastatic breast carcinoma who had initially responded to tamoxifen, suggested no antitumour activity for raloxifene in tamoxifen-refractory disease. However, considering the preclinical data and preliminary clinical data indicating a reduction in breast cancer risk in females taking raloxifene for osteoporosis, it remained unclear whether or not raloxifene had direct anti-tumour efficacy.

# Aims

To evaluate the safety and activity of raloxifene in patients with advanced breast cancer.

# Comments

The development of raloxifene has generated a great deal of excitement in view of its lack of proliferative effect upon uterine endometrium or myometrium. The observation that women receiving raloxifene for osteoporosis appeared to have a decreased incidence of breast cancer led to claims that raloxifene was an appropriate therapy for the prevention of breast cancer. Nevertheless, the anti-tumour efficacy of raloxifene remained unproven. This trial has demonstrated that whilst raloxifene exerts some

antitumour efficacy, its activity is modest given the highly selected nature of the patient population. These were all patients with initial oestrogen receptor (ER)-positive disease, many of whom had not been exposed to previous endocrine therapy. Thus, a response rate of greater than the reported 19% would have been reasonably expected. The good tolerability of raloxifene was confirmed, although about a quarter of the patients reported hot flushes (a previously recognised side effect). In view of the development of pure oestrogen antagonists and the further development of the aromatase inhibitors, it remains unclear if and where raloxifene will fit in our treatment options for advanced breast cancer.

# Methods

Twenty-two postmenopausal women with recurrent locoregional or metastatic breast carcinoma were given raloxifene HCl, 150 mg twice daily, until tumour progression occurred. Patients with early breast cancer and who were ER-positive were chosen and prior systemic treatment of metastatic disease was not allowed. Prior adjuvant chemotherapy or hormonal therapy was required to have been completed at least 1 year before entry into the study. Tumour response was evaluated every other month. Functional assessment of cancer therapy (FACT-B) quality of life data were also collected.

# Results

Twenty-one patients were eligible for efficacy analysis; of these, six had been treated previously with tamoxifen for a median duration of 34 months. There were no complete tumour responses, but four patients (19%; 95% CI: 2.2-36%) had a partial response. These responses lasted 6.3, 17.5, 24 and 28 months, respectively. Prolonged stable disease (>6 months) was seen in three patients, lasting 8, 12, and 25 months, respectively, and so there was an overall clinical benefit rate (partial responses plus prolonged stable disease) of 33% (95% CI: 13-53%). Of the remaining 14 patients, 10 had stable disease for less than 6 months and four had early disease progression. There were no serious adverse events or laboratory changes that appeared to be therapy-related. The most reported adverse events were hot flushes, pain, depression and insomnia. There appeared to be no impact upon quality of life.

# Discussion

Raloxifene HCl, 150 mg, administered twice daily was safe, well tolerated, but only modestly effective in highly selected postmenopausal women with advanced breast carcinoma.

# References

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