Fulvestrant for advanced male breast cancer patients: a case series

Male breast cancer is rare and treatment recommendations are mainly extrapolated from the results of trials on women. Most breast cancers in men are estrogen receptor (ER)/progesterone receptor (PgR) positive; as a consequence, tamoxifen remains the standard adjuvant treatment and is also the mainstay first-line treatment of advanced disease, with reported response rates varying from 25% to 80% [1].

However, few data are available on treatments (e.g. aromatase inhibitors) for tamoxifen-resistant disease, and the novel ER antagonist fulvestrant has been very little studied. In postmenopausal women, fulvestrant has been shown to be effective in patients in whom tamoxifen or aromatase inhibitors failed and has also demonstrated activity in patients with visceral and human epidermal growth factor receptor (HER-2)-overexpressing disease [2]. Since men almost always develop ER-/PgR-positive breast cancer, fulvestrant is likely to be useful in male metastatic disease. By analogy with data in women, it may also show activity in HER2-overexpressing disease.

We evaluated fulvestrant in five men with progressive visceral metastatic breast cancer (the largest series reported so far). The drug was injected i.m. at a loading dose of 500 mg on day 1 followed by 250 mg injected i.m. monthly thereafter, until disease progression. Response was assessed according to RECIST criteria. Partial response (PR) lasting 12 months was obtained in one heavily pretreated patient; while another patient, with HER-2-positive cancer metastatic to lung, had stable disease (SD) lasting 22 months. Another patient with HER-2-positive disease had SD lasting 6 months, after early PD on first- and second-line treatments with aromatase inhibitors; the patient died of causes unrelated to breast cancer a month after reevaluation. Of our two cases progressing on fulvestrant, one had low hormone receptor positivity (ER 20% and PgR 30%), which might explain the lack of response. No side-effects to fulvestrant were reported by all patients.

A reason for trying fulvestrant is that aromatase inhibitors do not have a clear role in metastatic male breast cancer; in our limited experience, anastrozole and exemestane were not effective. These drugs inhibit aromatase, the enzyme that produces estrogens by peripheral aromatization of circulating androgens. In men, however, testicular production of estrogens is independent of aromatase and accounts for ~20% of circulating estrogens. It has also been found that testosterone levels increase markedly after anastrozole treatment in men [5]. It is possible that the hypothalamic–pituitary feedback loop is responsible for this increased testosterone (substrate for peripheral aromatization), thereby rendering complete estrogen suppression impossible and explaining why treatment with aromatase inhibitors is less effective in males than females.

To conclude, our data indicate that fulvestrant may be an effective and safe treatment of hormone receptor-positive pretreated metastatic male breast cancer, including cases that overexpress HER2.

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disclosure

The authors declare no conflict of interest.

references


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