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Fulvestrant and male breast cancer: a case series

Male breast cancer is an uncommon malignancy, accounting for ~1% of all diagnosed breast cancers [1]. The rarity of these neoplasms has resulted in a relatively limited amount of literature. Unfortunately, clinical-trial reports in men are lacking and conclusions have been drawn from female trials. Consequently, men with breast cancer are treated similarly to women, except for the hormonal treatment [1]. More specifically, tamoxifen is the gold standard in the adjuvant endocrine treatment of male breast cancer and plays a key role in the metastatic setting [1]. However, the role of aromatase inhibitors (AIs) and fulvestrant remains controversial.

Fulvestrant is a synthetic estrogen receptor (ER) antagonist or a selective ER down-regulator. Unlike tamoxifen and the AI, fulvestrant binds competitively to ERs in breast cancer cells, resulting in ER deformation and decreased estrogen binding. In postmenopausal women, fulvestrant has confirmed efficacy in women previously treated with tamoxifen or AIs [2]. However, there have only been limited data regarding the use of fulvestrant in male breast cancer [3, 4]. Its mechanism of action, along with the available in vitro data [5], indicates that this agent may represent a useful treatment option for male breast cancer patients.

In this retrospective chart review, cases with male breast cancer treated with fulvestrant were evaluated. Eligible patients derived from the Department of Medicine I/ Division of Oncology, Vienna, Austria and from the 1st Propaedeutic Surgical Department of Hippocrateio Hospital, University of Athens, Athens, Greece. In all cases, fulvestrant was administered at a loading dose of 500 mg on day 1 followed by 250 mg on day 14 and monthly thereafter, until disease progression. The response was assessed according to the RECIST criteria. Overall survival (OS) was defined as the interval between initial diagnosis and time of death, whereas time to treatment progression (TTP) was defined as the interval between initiation of fulvestrant and time of progression.

Fourteen men aged 53–76 years (63.5 ± 6.8, mean ± SD) were included in this case series. Patients' characteristics are depicted in Table 1. None of the patients had received chemotherapy treatment for metastatic disease. In the majority of cases, fulvestrant was given as a second-line hormonal treatment in six (42.9%) patients, as a third-line agent in seven (50%) patients and as fourth line in one (7.1%) patient. In all cases, fulvestrant was tolerated well, without grade 3 and 4 adverse events being reported. Regarding the best response, partial response (PR) was noted in three (21.4%) patients, stable disease (SD) in seven (50%) patients, whereas progressive disease (PD) was observed in four (28.6%) patients. The median time to treatment progression (TTP) was equal to 5 months, ranging between 2 and 7 months. The median overall survival (OS) was 61.5 months. The study was approved by local ethics committees. According to our knowledge, this is the largest case series reported in the literature with fulvestrant administration in male breast cancer.

Table 1. Patients' characteristics

Number	Age (years)	Type	Grade	Initial stage at diagnosis	ER-Allred Score	HER2 status	PR status	Ki-67 (%)	Adjuvant hormonal treatment	Adjuvant chemotherapy	Fulvestrant (line)	Best response with fulvestrant	Overall survival (OS) (months)	TTP (months)
1.	68	IDC	3	IIIC	8	Neg	Pos	60	Yes	A + T	Second	SD	55	6
2.	65	IDC	3	IIA	5	Neg	Pos	45	Yes	A + T	Third	SD	79	5
3.	71	ILC	3	IIIC	8	Neg	Pos	30	Yes	A + T	Second	PR	45	4
4.	59	IDC	3	IIB	8	Neg	Pos	15	Yes	A + T	Third	SD	61	6
5.	69	IDC	3	IIA	8	Neg	Neg	10	Yes	A + T	Second	PR	>32	5
6.	58	IDC	2	IIB	7	Neg	Pos	55	Yes	A	Third	SD	73	6
7.	59	IDC	2	IIIC	8	Pos	Pos	45	Yes	A + T + H	Fourth	PD	53	2
8.	54	IDC	3	IIA	7	Neg	Pos	20	Yes	A + T	Third	PR	>93	4
9.	76	ILC	1	IIIA	7	Neg	Pos	15	Yes	T	Third	SD	74	5
10.	53	IDC	2	IIIA	6	Neg	Pos	40	Yes	A + T	Second	PD	62	2
11.	64	IDC	3	IIIC	7	Neg	Pos	40	No	A + T	Third	PD	83	2
12.	59	IDC	3	I	8	Neg	Pos	30	Yes	A	Third	SD	64	7
13.	64	IDC	3	I	6	Neg	Pos	20	Yes	None	Second	PD	18	3
14.	70	IDC	2	IIIA	6	Neg	Pos	N/A	Yes	A	Second	SD	39	7

A, Anthracycline-based chemotherapy; T, Taxane-based chemotherapy; H, trastuzumab; PR, partial response; SD, stable disease; PD, progressive disease; TTP, time to treatment progression.

In conclusion, it seems that fulvestrant is an effective and safe treatment of hormone receptor-positive pretreated metastatic male breast cancer. Further trials and large case series focused on male breast cancer and fulvestrant are more than warranted.

disclosure

The authors have declared no conflicts of interest.

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Meat consumption and risk of lung cancer: evidence from observational studies

I read with great interest the recent paper by Yang et al. [1]. They carried out a meta-analysis of 34 studies to investigate the relationship between meat consumption and lung cancer risk. It is an interesting study. However, I would like to raise several concerns related to this paper.

First, the definition of total meat and white meat is not clear in the meta-analysis. The total meat includes red meat, processed meat, poultry and fish. But the total meat definition in the meta-analysis included meat defined in the individual studies as 'all meat' without specifying the type or 'total meat'. Thus, all 34 studies should be eligible for the meta-analysis of total meat intake. In the meta-analysis, the white meat definition included the meat defined in the individual studies as 'white meat', or poultry and fish. However, the authors did not conduct the meta-analysis of white meat intake according to their definition. The meta-analysis of white meat intake only included six studies, but not all the studies on poultry and fish intake. Given this point, their results of total meat and white meat intake were not accurate.

Second, there are some issues in the methods. A meta-analysis should include as much information as possible. But the authors only searched articles published in English, which may lead to language bias. It seems unreasonable for the authors to select eligible study from duplicated reports. In the meta-analysis, when several studies derived from the same study population, the most recent publication was included. In fact, the largest study should be included. Moreover, the authors did not carry out the meta-analysis according to their rule. For example, two studies by De Stefani et al. [2, 3] were derived from the same population, and two studies by Kubik et al. [4, 5] also derived from the same population. However, these studies were all included in the meta-analysis. Generally, in a meta-analysis, when a study reported the results on different ethnicities or countries, we treated them independently. But, in the meta-analysis, when a study reported the results on different gender, the authors also treated them independently, which will result in an increased contribution of the study in the pooled results, and may distort the meta-analysis. Additionally, there was a statistically significant heterogeneity in the meta-analysis. Although some subgroup analyses were carried out, heterogeneity still remained, indicating that the other unknown factors may also contribute to the heterogeneity. Therefore, it is meaningful for the authors to do subgroup analysis by different ethnicities.

Third, in the discussion, the authors stated that 'Another explanation is that high poultry eaters often have a healthier overall eating pattern and lifestyle.' Indeed, the reference cited by the authors did not support the view. Additionally, 20 studies did not report the relative risk with its 95% confidence interval or standard error, and were excluded from the meta-analysis, which may distort the results of meta-analysis.

Collectively, it is an interesting study. Although there were several limitations, the meta-analysis of large sample size still provides new information on the relationship between meat intake and lung cancer risk.

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