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Endometrial evaluation is a very important tool in the management of breast cancer patients

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We previously published the results of a prospective study with evaluation of the endometrium prior to tamoxifen therapy [1]. This evaluation consisted of vaginal echography. In cases of abnormal echography, defined as an endometrial thickness of 5 mm or more, outpatient hysteroscopy was performed. Patients were divided into two groups according to this endometrial screening and were followed-up annually using the same modalities. So far, 510 patients have been evaluated (425 patients in the group with an endometrial thickness of <5 mm and 85 patients in the group with endometrial pathology) [2].

This study has allowed us to identify risk factors for the subsequent development of atypical endometrial lesions while on tamoxifen. These factors are obesity, prior exposure to unopposed oestrogens and endometrial polyps diagnosed at the basal screening [2,3].

80 patients were excluded from the study because of local recurrence or pernicious metastatic evolution of their breast disease. In this group of 80 patients, 31 are still alive and had received aromatase inhibitors (anastrozole 1 mg/day or letrozole 2.5 mg/day) for a minimum of 2 years and are currently evaluable with an endometrial follow-up of two years of treatment. They are being followed up according to the same modalities as previously described for the prospective study with tamoxifen treatment [1].

It is important to note that of these 31 patients, 27 had never been treated for endometrial pathology before or during tamoxifen treatment; however, 4 patients had been treated for endometrial polyps before starting tamoxifen therapy.

The results of this study are shown in Table 1. In this table, the characteristics of these two groups of patients can be observed. The endometrial thickness prior to aromatase inhibitor treatment was 7.5 mm in the group of 27 patients (range 3.0–12.0 mm) 9.2 mm (4.1 to 14.0 mm) in the group of 4 patients, and prior hysteroscopy was performed in 20 of the 27 cases and 3 of the 4 cases. No intracavitary pathology was discovered in the 20 hysteroscopies performed in the first group and no lesions were observed in the three hysteroscopies performed in the second group.

After 2 years of treatment with aromatase inhibitors, the endometrial thickness was 7.2 mm in the group of 27 patients (2.6–12.0 mm) and 8.5 mm (3.8–13.0 mm) in the group of 4 patients. Hysteroscopy was performed in 15 of the 27 patients in the first group and in 3 of the 4 in the second group during follow-up. Intracavitary pathology was noted in both groups: one polyp among the 15 hysteroscopies performed in the first group and one polyp among the three hysteroscopies performed in the second group.

For endometrial histology, 15 endometrial biopsies were performed in the first group which revealed 14 cases of endometrial atrophy (14 endometrial atrophy with no lesions observed and one polyp with proliferative endometrium).

In the second group, three endometrial biopsies were performed and histology of specimens showed 2 cases of atrophic endometrium and one polyp with small foci of atypical hyperplasia.

The number of patients in this study is small and the duration of follow-up is still very short, but we are able to note that we did not observe any significant reduction in endometrial thickness after 2 years of treatment with aromatase inhibitors in patients who were previously treated with tamoxifen.

Histology revealed atrophic endometrium in most of the endometrial specimens, proliferative endometrium in 1 case and small foci of atypical hyperplasia in another. The patient with the atypical lesions had previously undergone 3 years of tamoxifen therapy, was obese and had been treated for an endometrial polyp

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Table 1

	Group of 27 patients	Group of 4 patients
Endometrial thickness prior to aromatase inhibitors	7.5 mm (3.0–12.0)	9.2 mm (4.1–14.0)
Hysteroscopy prior to aromatase inhibitors	20/27	3/4
Intracavitary pathology	None	None
Histology	Atrophic endometrium	Atrophic endometrium
Endometrial thickness after 2 years of treatment with aromatase inhibitors	7.2 (2.6–12.0)	8.5 mm (3.8–13.0)
Bleeding	1/27	1/4
Hysteroscopy	15/27	3/4
Intracavitary pathology	1 polyp	1 polyp
Histology	15 atrophic endometrium (14 without lesions, 1 polyp) 1 polyp: also atrophic endometrium + small foci of proliferative endometrium	2 atrophic endometrium 1 polyp: atrophic endometrium + small foci of atyoical lesions (atypical hyperplasia)

prior to tamoxifen therapy. The incidence of bleeding was not very high in patients receiving aromatase inhibitors and appeared to be equivalent to that described in the literature.

Concomitant or sequential administration of different hormonal modalities is currently being investigated.

Tamoxifen and aromatase inhibitors look very promising in the treatment of breast cancer patients. These modalities are now being tested in adjuvant settings: for example, the ATAC trial uses anastrozole (Arimidex) alone, tamoxifen alone, or the two in combination. To our knowledge, it is the only trial that includes a subendometrial protocol with an endometrial evaluation prior to and during hormonal therapy. This study is very important for the future management of breast cancer patients. It is crucial for us to know exactly where we are going with the latest modalities of hormonal therapy which offer exciting new perspectives in the treatment and curability of breast cancer. In order to obtain the maximum trust and compliance from our cancer patients, it is necessary to study very carefully the side-effects of these treatments, especially the uterine side-effects, and evaluate the oncogenic potential of tamoxifen [4]. The twenty-first century must be able to provide answers to all of the questions regarding the safety of the cancer treatments proposed.

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