therapy: 5 cases have been published. Existing evidence associating tamoxifen treatment with uterine leiomyosarcoma may be regarded as unsubstantiated and anecdotal.

In women thought to have uterine fibroids, tamoxifen is, nevertheless, given with cautious clinical and ultrasonographic follow-up. Because the enlargement of fibromyomas occurs sporadically, expectant management is allowed. Surgical exploration is carried out when symptoms are emerging and/or when the size of each individual fibroid equals or exceeds 5 cm, in order to rule out malignancy. The patient is eventually restarted on long-term use of tamoxifen until planned duration administration.

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II.4 Is Ovarian Cyst Formation Related to Tamoxifen Use?

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The non-steroidal anti-oestrogen tamoxifen has a number of gynaecological side-effects. Apart from an increased risk of endometrial carcinoma, recently ovarian cyst formation during tamoxifen has been observed. This induces the problem of whether or not intervention for these cysts is required. In a cross-sectional study of breast cancer patients receiving tamoxifen, patients only developed ovarian cysts if ovaries responded to tamoxifen, as shown by oestradiol production. Ovarian cysts were not likely to develop in women with amenorrhoea > 1 year or following high-dose chemotherapy. © **1998 Elsevier Science Ltd. All rights reserved.**

TAMOXIFEN IS a non-steroidal anti-oestrogen with gynaecological side-effects. Tamoxifen is extensively used as adjuvant treatment in breast cancer patients and in case of metastatic breast cancer. Over the last decade the concern about the side-effects of tamoxifen has focused on the occurrence of endometrial carcinoma with a 2.3–6.4-fold increased risk compared to non-users [1–3]. Only recently ovarian cyst formation during tamoxifen has been reported [4–6]. There are several situations known in gynaecological practice that can induce a higher incidence of cysts in the ovary such as treatment with certain oral contraceptives [7] and ovulation induction therapy. The major concern in case of cysts in the ovary is the fact that these cysts may be indicative for malignancy. This dilemma is even more pronounced in case of breast cancer patients as BRCA1- and BRCA2-carriers are at increased risk to develop ovarian cancer.

We reported earlier on a cross-sectional study that was performed in 75 breast cancer patients who used tamoxifen [8]. According to previous chemotherapy four groups were defined: 5 cycles standard-dose fluorouracil/epirubicin/cyclophosphamide (FEC) (group A, $n=25$), 4 cycles FEC plus one cycle high-dose cyclophosphamide, thiotepa and carboplatin chemotherapy (group B, $n=22$), miscellaneous chemotherapy (group C) and no chemotherapy (group D). The first two groups participated in a randomised adjuvant study in patients below 56 years of age with more than 3 tumour positive lymph nodes. The programme comprised transvaginal ultrasonography (TVU) and endocrine analysis (LH, FSH, oestradiol (E_2) and inhibin in serum). No patient had abdominal symptoms. Uni- or bilateral adnexal cysts were observed by TVU in 12 patients. Multiple regression analysis showed that cyst development was related to high E_2, younger age, and absence of high-dose chemotherapy. These parameters were, however, related to each other. No cysts occurred in patients with amenorrhoea > 1 year. All patients after high-dose chemotherapy had amenorrhoea, $E_2 <$ 0.10 nmol/l and did not develop ovarian cysts. In this study breast cancer patients receiving tamoxifen only developed ovarian cysts if ovaries responded to tamoxifen as indicated by E_2 production. Ovarian cysts were not likely to develop in women with amenorrhoea > 1 year or following high-dose chemotherapy.

There is increasing evidence that ovarian cysts occur at a higher rate during tamoxifen treatment. Further research is required to define whether medical or surgical intervention is indicated in patients with this type of cysts.

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II.5 Tamoxifen and other Genital Tissues: Vagina, Cervix and Ovaries

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It has been demonstrated that postmenopausal tamoxifen (TAM) treatment induces an oestrogen-like effect on the vaginal epithelium, including gradual increase in cellular maturity with a consequent increase of intermediate and superficial cells. No association between postmenopausal TAM treatment and vaginal malignancy was reported. Several investigators could not find significant differences in the incidence of new primary cervical cancers in postmenopausal breast cancer patients with TAM treatment as compared to controls and the relative risk for the development of new cervical cancer was low. The incidence of benign ovarian pathologies among postmenopausal breast cancer patients with TAM treatment was found to be higher than that reported for similar pathologies in controls, or among non-selected, asymptomatic and untreated postmenopausal women. © **1998 Elsevier Science Ltd. All rights reserved.**

IT HAS been demonstrated that postmenopausal tamoxifen (TAM) treatment induces oestrogen-like effects on the vaginal epithelium. Maturation index (MI) and Karyopicnotic index (KPI) assessment revealed a significant gradual increase in cellular maturity with a consequent increase of intermediate and superficial cells in the vaginal epithelium of such patients, following TAM treatment for up to 8 weeks [1–4].

No association between postmenopausal TAM treatment and vaginal malignancy was reported. Several investigators could not find significant differences in the incidence of new primary cervical cancers in postmenopausal breast cancer patients with TAM treatment as compared to controls [5–7] and the relative risk for the development of new cervical cancer was low [5–7]. The effect of TAM therapy on the postmenopausal ovary, if any, is not clear. However, since TAM has been found to be a causative agent for various endometrial pathologies and bearing in mind the common ancestry of ovarian and endometrial epithelium and their stroma, it may be speculated that TAM's oestrogen-like action on the ovary may potentially stimulate either ovarian enlargement or the development of ovarian pathological conditions [8].

Several studies showed no significant differences in the incidence of new primary ovarian cancers in postmenopausal breast cancer patients with TAM treatment as compared to controls [5–7]. The relative risk for the development of new ovarian malignancy was also low [5–7]. The incidence of benign ovarian pathologies among postmenopausal breast cancer patients with TAM treatment was found to be higher than that reported for similar pathologies in controls [9] or among non-selected, asymptomatic and untreated postmenopausal women [8].