S4. THE TAMARISK-STUDY, A COHORT STUDY OF THE CLINICO-PATHOLOGICAL AND MOLECULAR CHARACTERISTICS, AND THE PROGNOSIS OF UTERINE MALIGNANCIES AFTER TAMOXIFEN

Hoogendoorn WE[a], Hollema H[b], Nederlof PM[a], van Boven HH[a], Mourits MJ[b], van Leeuwen FE[a]. *[a] Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands; [b] Academic Hospital Groningen, PO Box 30.001, 9700 RB Groningen, The Netherlands*

Introduction: Many studies have consistently shown that long-term use of tamoxifen is associated with an increased risk of corpus uteri cancer [1]. Furthermore, in a recent study of our own group among women with corpus uteri cancer following breast cancer diagnosed in the Netherlands up to 1996, it was found that the corpus uteri tumours of long-term tamoxifen users had less favourable histology and higher International Federation of Gynecology and Obstetrics (FIGO) stage and were more often P53-positive and oestrogen-receptor-negative than corpus uteri tumours in women not treated with tamoxifen [2].

The purpose of the TAMARISK (Tamoxifen Associated Malignancies: Aspects of RISK)-study is to examine whether selective clinico-pathological characteristics and ultimate prognosis of uterine malignancies subsequent to tamoxifen treatment are indeed different from those of uterine malignancies in patients not treated with tamoxifen. In addition, we want to identify differences in protein expression, gene expression and specific genomic aberrations in uterine tumour samples of women with and without tamoxifen use. This may give more insight into the mechanism of tamoxifen-induced carcinogenesis.

Patients and Methods: For this study, a cohort of patients with a uterine malignancy following breast cancer is being formed. The study has a retrospective and a prospective part. For the retrospective part, patients diagnosed 1996–2001 ($n = 300$) were identified through the population-based Netherlands Cancer Registry. Detailed information about breast cancer treatment, gynaecological surveillance in the interval between the two malignancies, symptoms of the uterine malignancy, results of diagnostic tests and follow-up is abstracted from the medical records of all cases by registration clerks of the 9 Comprehensive Cancer Centres in The Netherlands. To review the histological diagnosis, tissue blocks of corpus uteri cancer will be obtained. These tissue blocks will also be used to examine genomic aberrations by array-comparative genomic hybridisation (CGH) and to examine hormone receptor status and gene-expression profiles at the protein level using appropriate antibodies.

For the prospective part of the study, patients ($n = 90$) are identified by gynaecologists in participating hospitals. Identification of incident cases is necessary in order to obtain fresh tumour samples that will be used for gene expression analysis using the micro-array (cDNA) technique. Since cases with a uterine malignancy after breast cancer are relatively rare, it is crucial not to miss any patients.

In cooperation with the Dutch Network and National Database for Pathology (PALGA), a novel signalling system has been developed (see Fig. 1). The study coordinator receives information on patients with a newly diagnosed uterine malignancy and breast cancer in the medical history from PALGA on a weekly basis. This gives us the opportunity to contact the pathology laboratory where the diagnosis was made and subsequently the treating gynaecologist.

Results and conclusions: The current status of the project is as follows. For the retrospectively selected patients diagnosed from 1996 to 2001, medical record data are now being collected. Fifty-five out of 57 pathology laboratories have given permission for the signalling system. Ninety-seven out of 104 Departments of Gynaecology have agreed to participate in the prospective part of the study. Up to March 2004, we have collected fresh frozen tissue from 52 patients.

The results so far indicate that we will be able to reach the planned number of 90 patients for the prospective part of the study. With the signalling system, we have found a very effective method for the population-based collection of fresh tumour tissue. This system can also be of use in other studies of relatively rare patient groups.

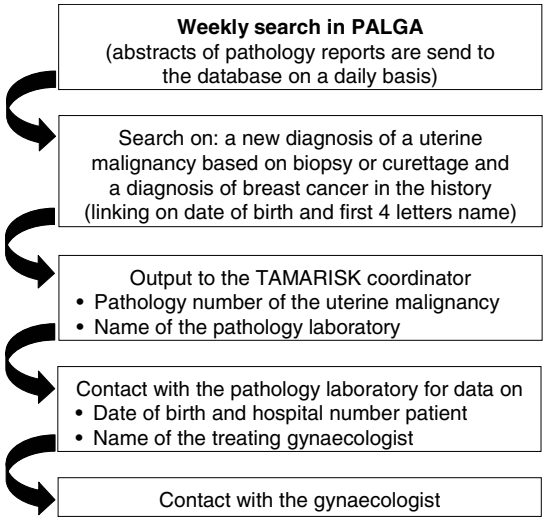

Fig. 1. Schematic presentation of the signalling system through PALGA (Dutch Network and National Database of Pathology).

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