study arms using the endpoint of TDM may be clearly separated, but that clear separation between study arms may never be reached with the endpoint of overall survival.

IV. USE OF A GENE ARRAY AS A PROGNOSTIC FACTOR FOR BREAST CANCER PATIENTS, USING THE ENDPOINT OF TDM—THE LOI STUDY

In a study of breast cancer, Loi et al. (20) analyzed biopsies from 417 breast cancer patients. Only patients where tumors were ER-positive were included in the study.

All breast cancer biopsies were ER-positive. The patients had received surgery, but no systemic chemotherapy. ER means estrogen receptor.

Gene expression from each tumor biopsy was measured using a microarray sensitive to 97 genes. These 97 genes are identified by Sotiriou et al. (21). As a matter of introduction to the genes included in this set, it was found that the top overexpressed genes included *UBE2C*, *KPNA2*, *TPX2*, *FOXM1*, *STK6*, *CCNA2*, *BIRC5*, and *MYBL2*. The trivial names for all of these genes, as well as the nucleotide sequences of these genes, can easily be found on the world wide web at ncbi.nlm.nih.gov.

Gene expression was used to provide a score, namely, the *Gene expression Grade Index* (GGI). The score was either low or high, that is, high-grade GGI or low-grade GGI. Gene expression from biopsies of all patients provided individual scores from each biopsy. These two groups, high GGI versus low GGI, represented two subgroups of the study population. A Kaplan–Meier plot was used to present the data, where the plot had two different curves. One curve corresponded to high-GGI patients experiencing distant metastasis, while the other curve corresponded to low-GGI patients experiencing distant metastasis. The results demonstrated that a low-GGI score is prognostic for good outcome, while a high-GGI score is prognostic for poor outcome.

An eventual goal of the researchers was to use the 97-gene microarray for guidance in choosing the best treatment for breast cancer patients.

V. USE OF MICRO-RNA EXPRESSION DATA AS A PROGNOSTIC FACTOR FOR BREAST CANCER PATIENTS—THE FOEKENS STUDY

In a study of breast cancer patients, Foekens et al. (22) examined gene expression by tumor biopsies, and attempted to find correlations between gene expression and the endpoint of TDM. All of the genes were in the class micro-RNA (miRNA). All of the biopsies were from tumors that were ER-positive (ER+). A gene array consisting of 249 different miRNA sequences was used, and a comparison of expression versus TDM revealed a specific group of genes, showing a large expression difference in patients with a poor TDM versus in patients with a favorable TDM. This specific group of genes included, *miR-7*, *miR-22*, *miR-34b*, *miR-128a*, *miR-145*, *miR-151*, *miR-193b*, *miR-205*, *miR-210*, *miR-449*, *miR-489*, and *miR-516–3p*.

[20] Loi S, Haibe-Kains B, Desmedt C, et al. Definition of clinically distinct molecular subtypes in estrogen receptor-positive breast carcinomas through genomic grade. J. Clin. Oncol. 2007;25:1239–46.

[21] Sotiriou C, Wirapati P, Loi S, et al. Gene expression profiling in breast cancer: understanding the molecular basis of histologic grade to improve prognosis. J. Natl Cancer Inst. 2006;98:262–72.

[22] Foekens JA, Sieuwerts AM, Smid M, et al. Four miRNAs associated with aggressiveness of lymph node-negative, estrogen receptor-positive human breast cancer. Proc. Natl Acad. Sci. USA 2008;105:13021–6.