

Supplementary Online Content

Schroth W, Goetz M, Hamann U, et al. Association between CYP2D6 polymorphisms and outcomes among women with early stage breast cancer treated with tamoxifen. *JAMA*. 2009;302(13):1429-1436.

eAppendix. Participating Centers/Genotyping Methods/Statistical Calculations

eTable. Investigated *CYP2D6* Variants

eFigure. Kaplan-Meier Estimates of Time-To-Recurrence Stratified by *CYP2D6* Copy Numbers

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Participating Centers/Genotyping Methods/Statistical Calculations

Participating Centers

Breast Center, Robert Bosch Krankenhaus Stuttgart, Germany; Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Stuttgart, Germany; Frauenklinik Städtisches Klinikum Karlsruhe, Germany; University Breast Center Franconia, University Hospital Erlangen, Germany; Department of Gynecology and Obstetrics, University of Mainz, Germany; Department of Oncology, Mayo Clinic, Rochester, Minnesota (patients from NCCTG 89-30-52 randomized phase 3 clinical trial in postmenopausal women comparing tamoxifen alone versus tamoxifen in combination with the androgen fluoxymesterone).

Genotyping Methods

Genotyping at Dr. Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Stuttgart, was with matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS) using Sequenom platform. Genotyping at Mayo Clinic was done with Taqman Real Time quantification. For *CYP2D6* gene duplication and *5 deletion allele a Taqman Real Time quantification assay was applied to blood and fresh-frozen tumor-derived DNA, but not for paraffin-derived samples for technical reasons.

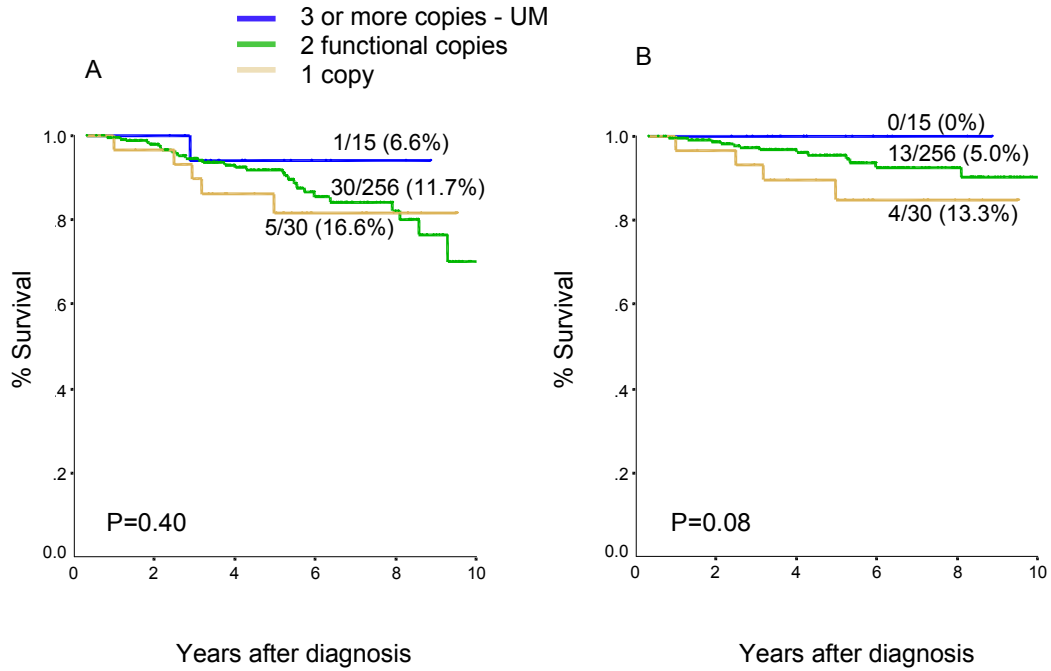
Statistical Analysis: Calculation of the Hypothetical Survival Curve for Anastrozole

Supposing the Cox proportionality hazard assumption, a hypothetical anastrozole survival curve was calculated via an assumed hazard ratio of $HR_{AI/TAM} = 0.76$ for anastrozole relative to tamoxifen²⁹ and the Kaplan-Meier \hat{S}_{TAM} estimate of the unstratified tamoxifen cohort of the present study. Precisely, our estimate \hat{S}_{AI} of the anastrozole survival curve is computed by $\ln(\hat{S}_{AI}(t)) = HR_{AI/TAM} \cdot \ln(\hat{S}_{TAM}(t))$ for every time point t .⁴⁰

eTable. Investigated *CYP2D6* Variants

Variant	Position / Change	Predicted phenotype
No variant		EM
*3	2549A>del	PM
*4	1846G>A	PM
*5	Gene deletion	PM
*1, *2 X 2	Gene duplication	UM
*10	100C>T	IM
*41	2988G>A	IM

eFigure. Kaplan-Meier Estimates of Time-to-Recurrence Stratified by *CYP2D6* Copy Numbers



Kaplan-Meier recurrence-free-time distributions truncated after 10 years for UM (3 or more functional copies), 2 functional copies, and one single copy of the *CYP2D6* gene with number of events/number of patients (percent of patients with event). A. All recurrences used as endpoint. B. Local breast events including contralateral breast cancer used as endpoint.