Supplementary Materials: Use of Germline Genetic Variability for Prediction of Chemoresistance and Prognosis of Breast Cancer Patients

Viktor Hlavac, Maria Kovacova, Katerina Elsnerova, Veronika Brynychova, Renata Kozevnikovova, Karel Raus, Katerina Kopeckova, Sona Mestakova, David Vrana, Jiri Gatek, Pavel Ostasov, Radka Vaclavikova and Pavel Soucek

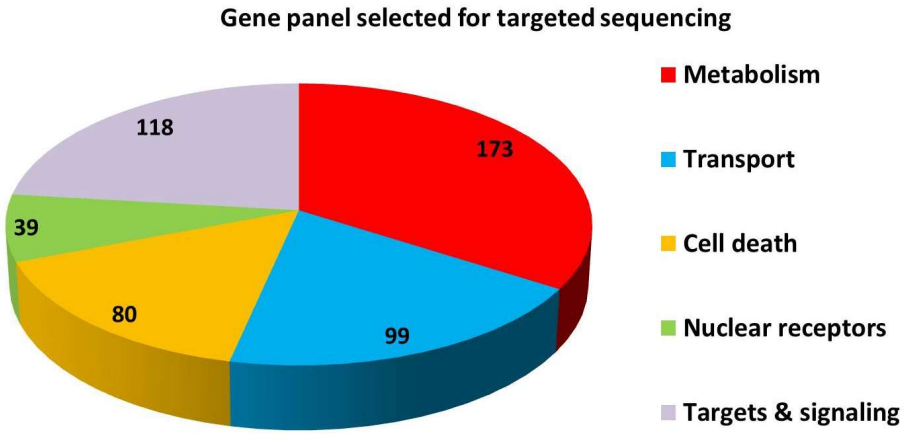
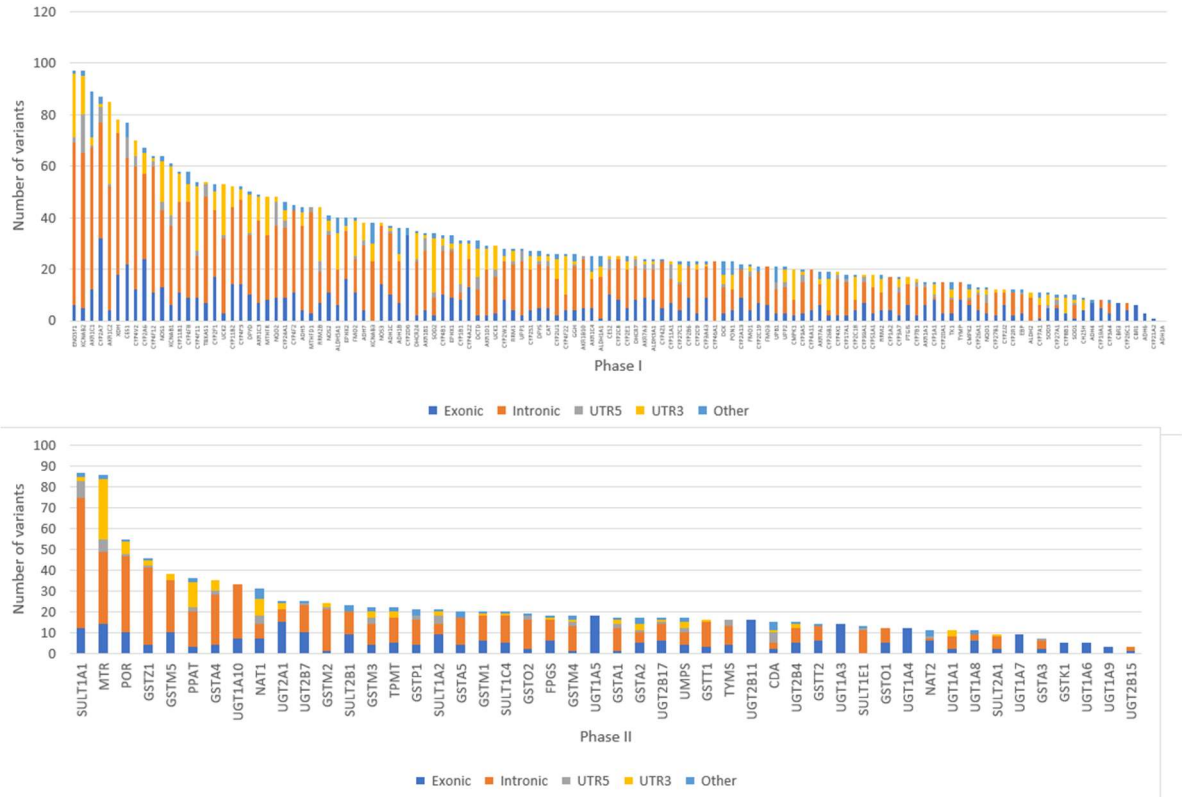
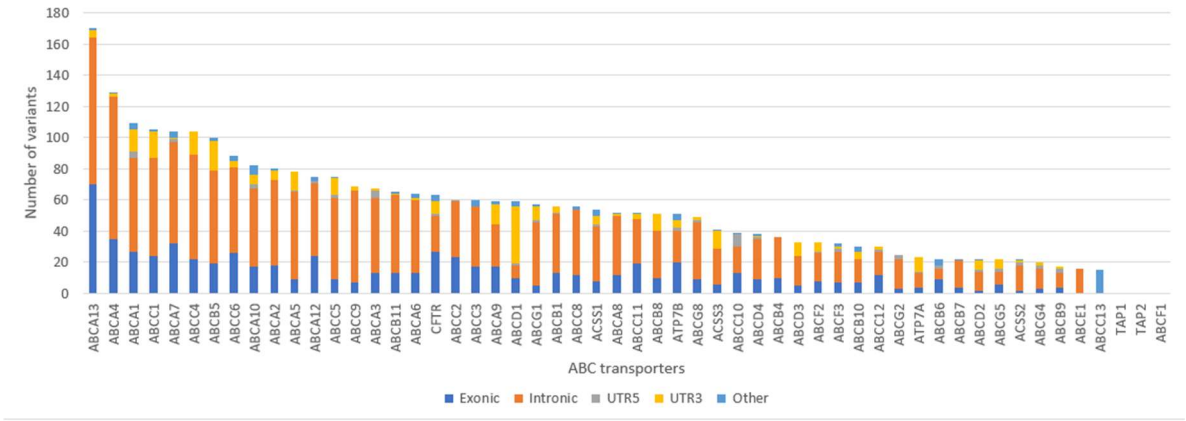
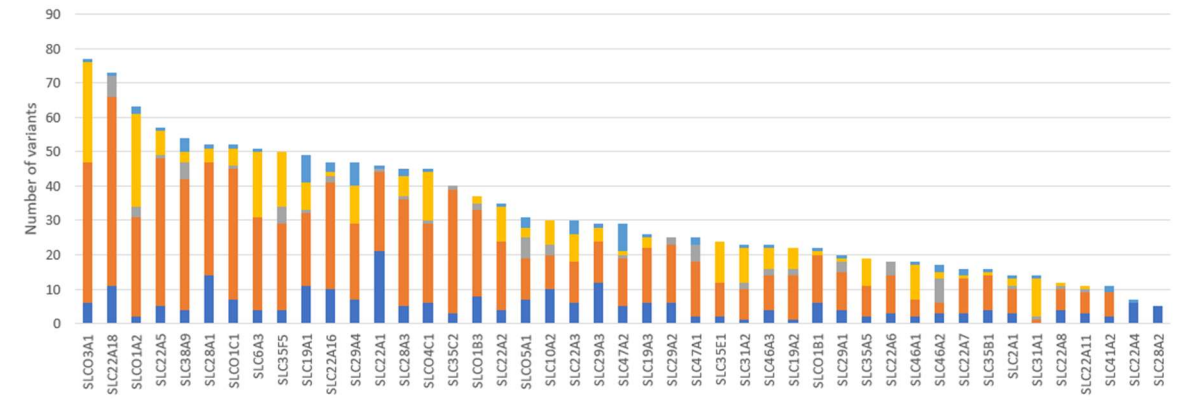
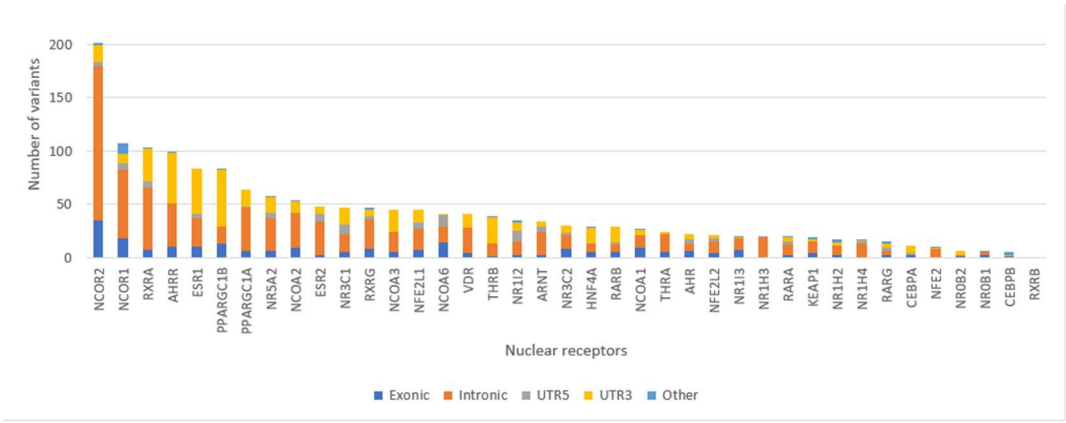


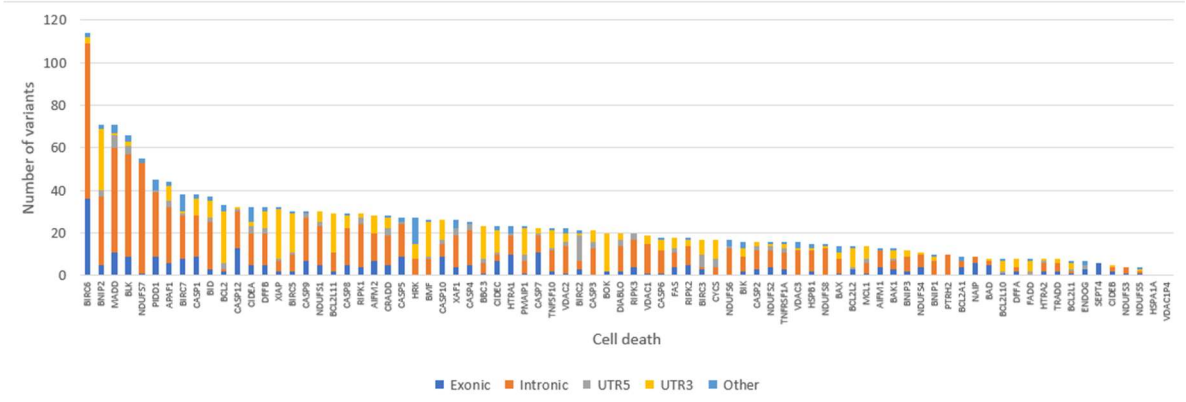
Figure S1. Groups of genes selected for the study.




Number of variants
ABC transporters
Exonic
Intronic
UTR5
UTR3
Other


Number of variants


Number of variants
Nuclear receptors
Exonic
Intronic
UTR5
UTR3
Other


Number of variants
Cell death
Exonic
Intronic
UTR5
UTR3
Other

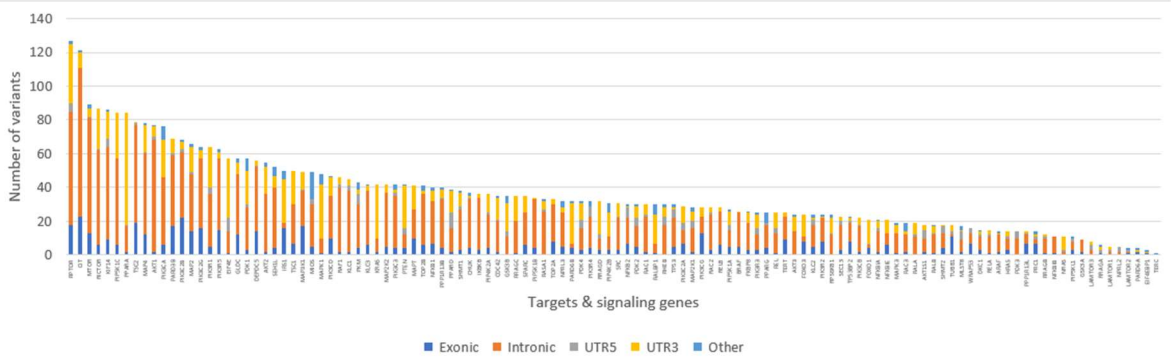


Figure S2. Detailed distribution of alterations in the studied groups of genes.

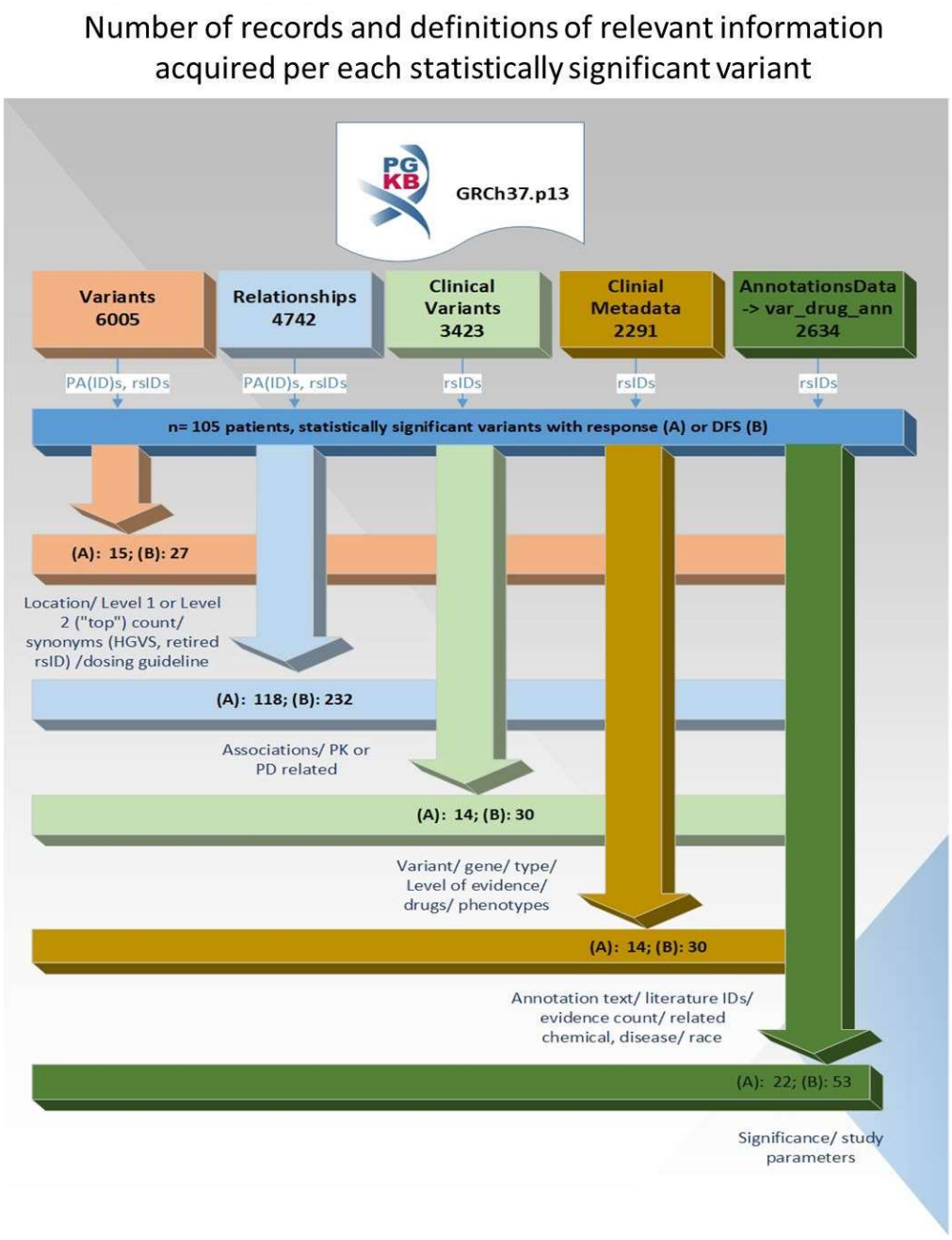


Figure S3. Data curation from PharmGKB data files.

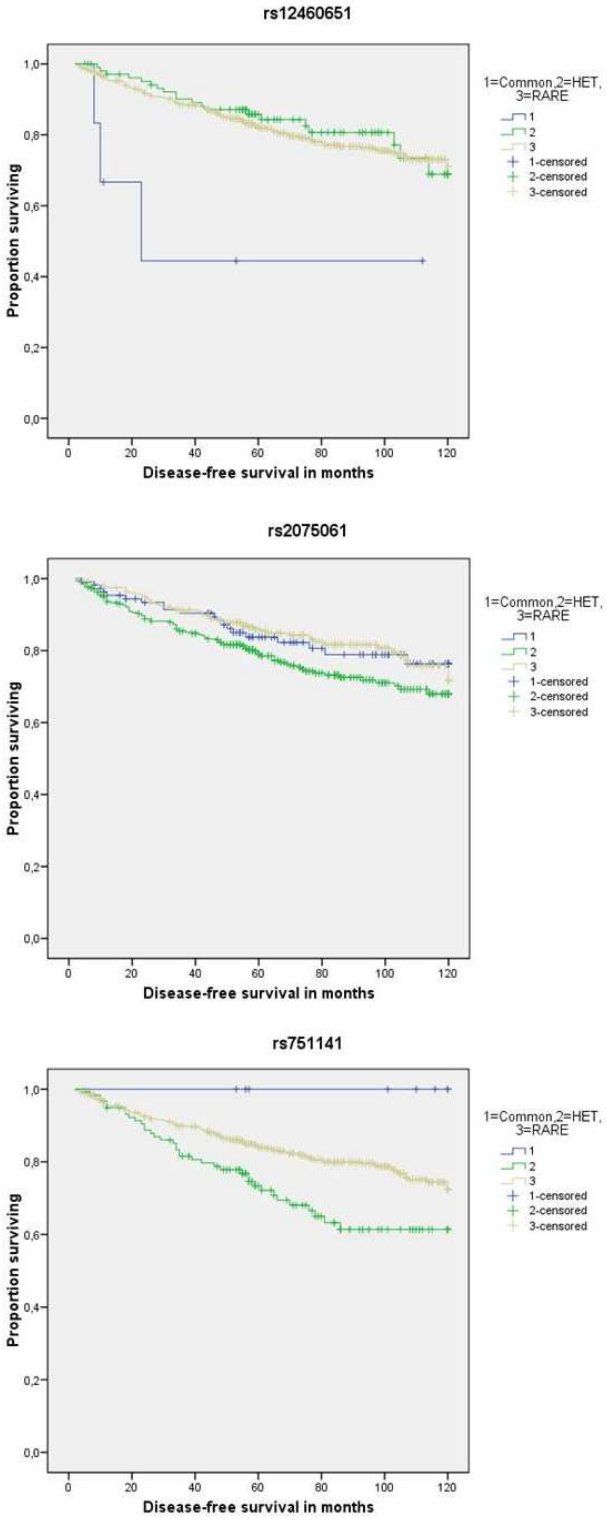


Figure S4. Kaplan-Meier plots representing associations of variants with DFS of whole set of patients (rs12460651 and rs751141) or patients treated with hormonal without cytotoxic therapy (rs2075061)

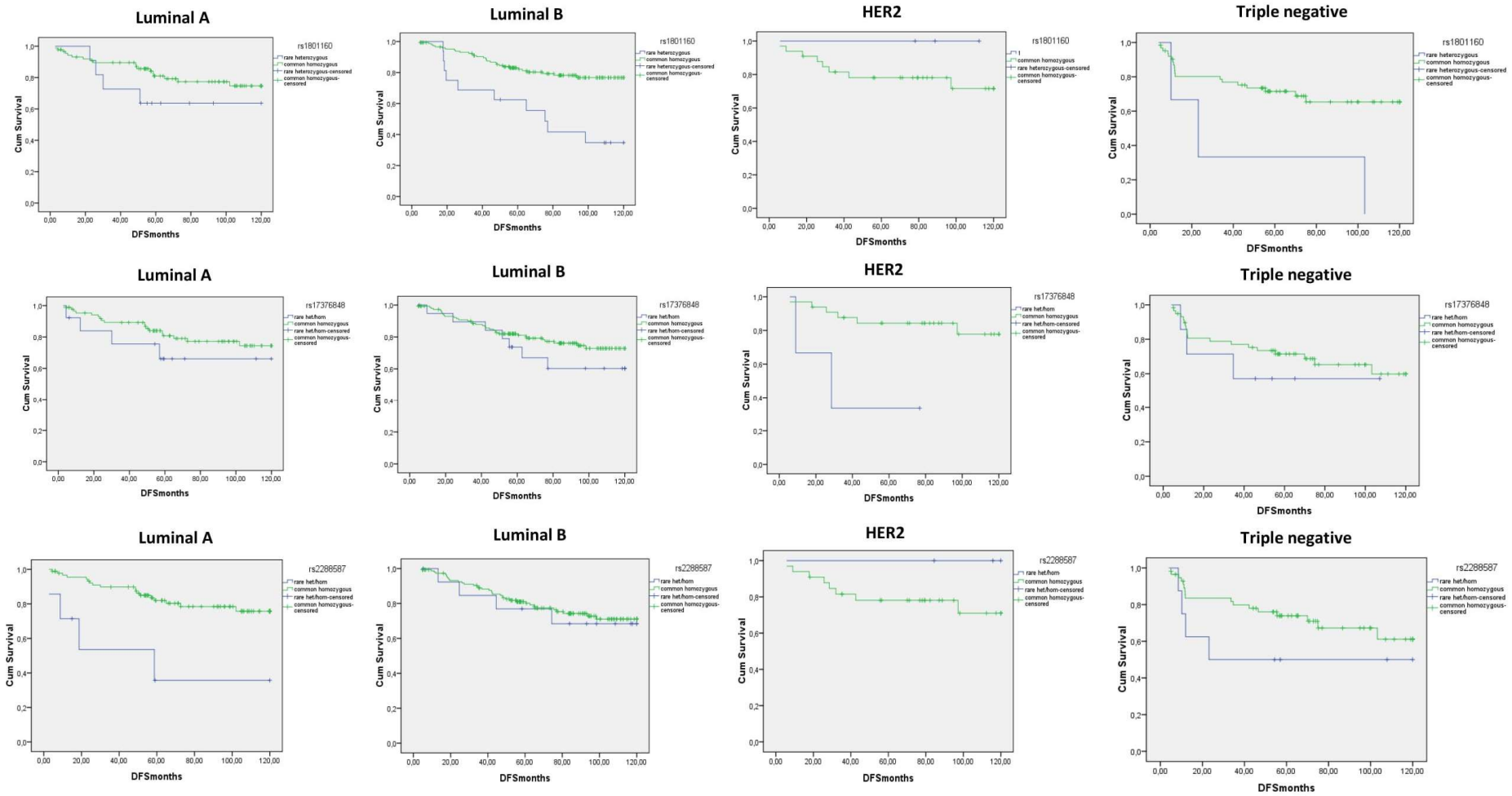


Figure S5. Kaplan-Meier plots representing associations of variants with DFS of patients stratified according to their molecular subtype.

Table S1. Treatment regimens in the testing set of patients.

A. Neoadjuvant cytotoxic therapy (*n* = 68).

Drugs (regimen)	*N*
anthracycline with cyclophosphamide (and 5-fluorouracil)	22
anthracycline with taxane	6
anthracycline with cyclophosphamide (and 5-fluorouracil) followed with taxane	39
other (1× taxane with vinorelbine)	1

B. Adjuvant cytotoxic therapy (*n* = 32) [1].

Drugs (regimen)	*N*
anthracycline with cyclophosphamide (and 5-fluorouracil)	15
anthracycline with cyclophosphamide followed with taxane	15
taxane monotherapy	1
other (1× capecitabine with vinorelbine)	1

Footonote: [1] In five patients no cytotoxic therapy was used.

Tables S2–S4 are in other separated files.

Table S5. Treatment regimens in the validation set of patients.

A. Neoadjuvant therapy (*n* = 180) [1].

Drugs (regimen)	*N*
anthracycline with cyclophosphamide (and 5-fluorouracil)	55
anthracycline with taxane	12
anthracycline with cyclophosphamide (and 5-fluorouracil) followed with taxane	95
taxane monotherapy	2
other (1× taxane with vinorelbine, 15× hormonal therapy)	16

B. Adjuvant cytotoxic therapy (*n* = 300).

Drugs (regimen)	N
anthracycline with cyclophosphamide (and 5-fluorouracil)	143
anthracycline with taxane	3
anthracycline with cyclophosphamide (and 5-fluorouracil) followed with taxane	63
taxane monotherapy	75
Other [2] (10× CMF, 2× CMF followed with taxane, 1× GEMOX followed with taxane, 1× monotherapy with vinorelbine, 1× monotherapy with anthracycline, 1× monotherapy with capecitabine)	16

C. Adjuvant hormonal therapy (*n* = 585) [3].

Drugs (regimen)	N
tamoxifen monotherapy	299
aromatase inhibitors monotherapy	181
tamoxifen and aromatase inhibitors switch	101
other (3x monotherapy with Zoladex)	3

In 54 patients targeted therapy with herceptin was used in monotherapy (*n* = 22) or in combination with cytotoxic or hormonal therapy (*n* = 32). In 83 patients no hormonal or cytotoxic therapy was used in neoadjuvant or adjuvant setting. For 84 patients information about therapy was not available.

Footnotes: [1] adjuvant cytotoxic therapy was used in 88 patients pretreated with neoadjuvant therapy (all patients included in part B); [2] CMF = cyclophosphamide, methotrexate and 5-fluorouracil;

GEMOX = gemcitabine with oxaliplatin; [3]adjuvant hormonal therapy without cytotoxic agents was used in 312 patients (the distribution of treatment regimens was comparable to C).