

Expanded View Figures

Figure EV1. Overview of frequently mutated genes in targeted DNA-seq and RNA-seq across 275 ABiM samples.

A, B Waterfall plot of the 20 most mutated genes (rows) across 275 ABiM samples (columns) in (A) targeted DNA-seq and (B) RNA-seq. Genes are ranked by variant frequency. Samples are sorted by histological subtype and alteration occurrence. Mutations are colored by predicted functional impact.

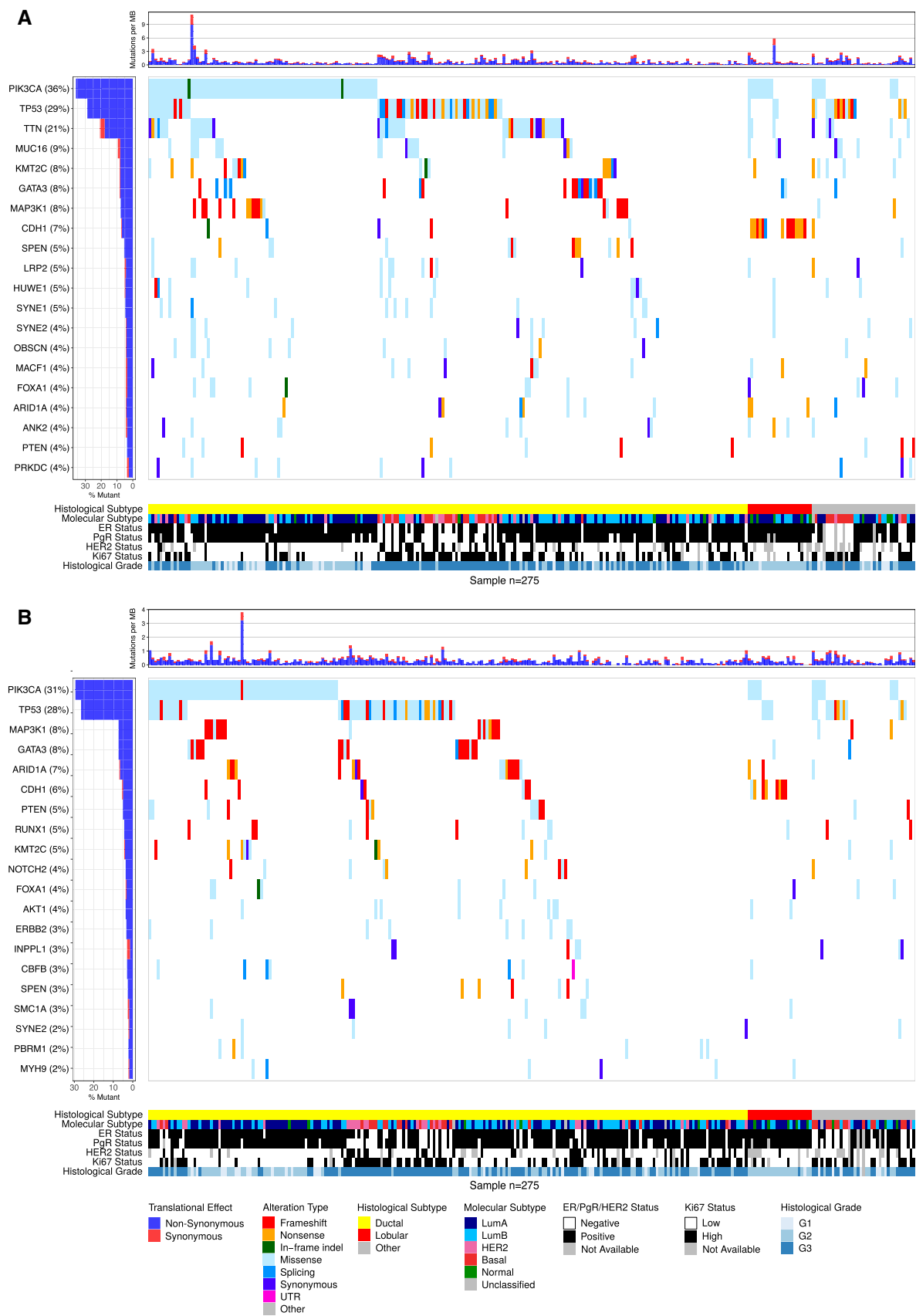


Figure EV1.

Figure EV2. Impact of gene mutations on overall survival across clinical subgroups.

A–E Overall survival (OS) of patients with tumors containing mutations in the genes (A) *TP53*, (B) *PIK3CA*, (C) *ERBB2*, and (D) *PTEN*. (E) OS by *PTEN*-MutExp genotype (“low” defined as *PTEN* mutation or *PTEN* expression in the lower quartile across the cohort, “normal” otherwise) stratified by the clinical patient subgroups HoR⁺/HER2[−] (HoR⁺ when ER⁺ and PgR⁺, HoR[−] otherwise; $n = 2,134$), HoR⁺/HER2⁺ ($n = 230$), HoR[−]/HER2⁺ ($n = 104$), and TNBC ($n = 137$). Specific treatments in these groups are detailed in Table EV4. In each Kaplan–Meier plot, wild-type (wt) and normal cases are plotted in blue, mutated (mut) and low cases are plotted in red, the log-rank P value is given, and the hazard ratio (HR) for mutation/low is given with a 95% CI and after univariable and multivariable (MV) Cox regression adjustment. Covariables included in the MV analysis were age at diagnosis, lymph node status, tumor size, and the variables denoted by the following symbols: α , ER, PgR, and NHG; #, NHG. ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HoR, hormone receptor; NHG, Nottingham histological grade; PgR, progesterone receptor; TNBC, triple-negative breast cancer.

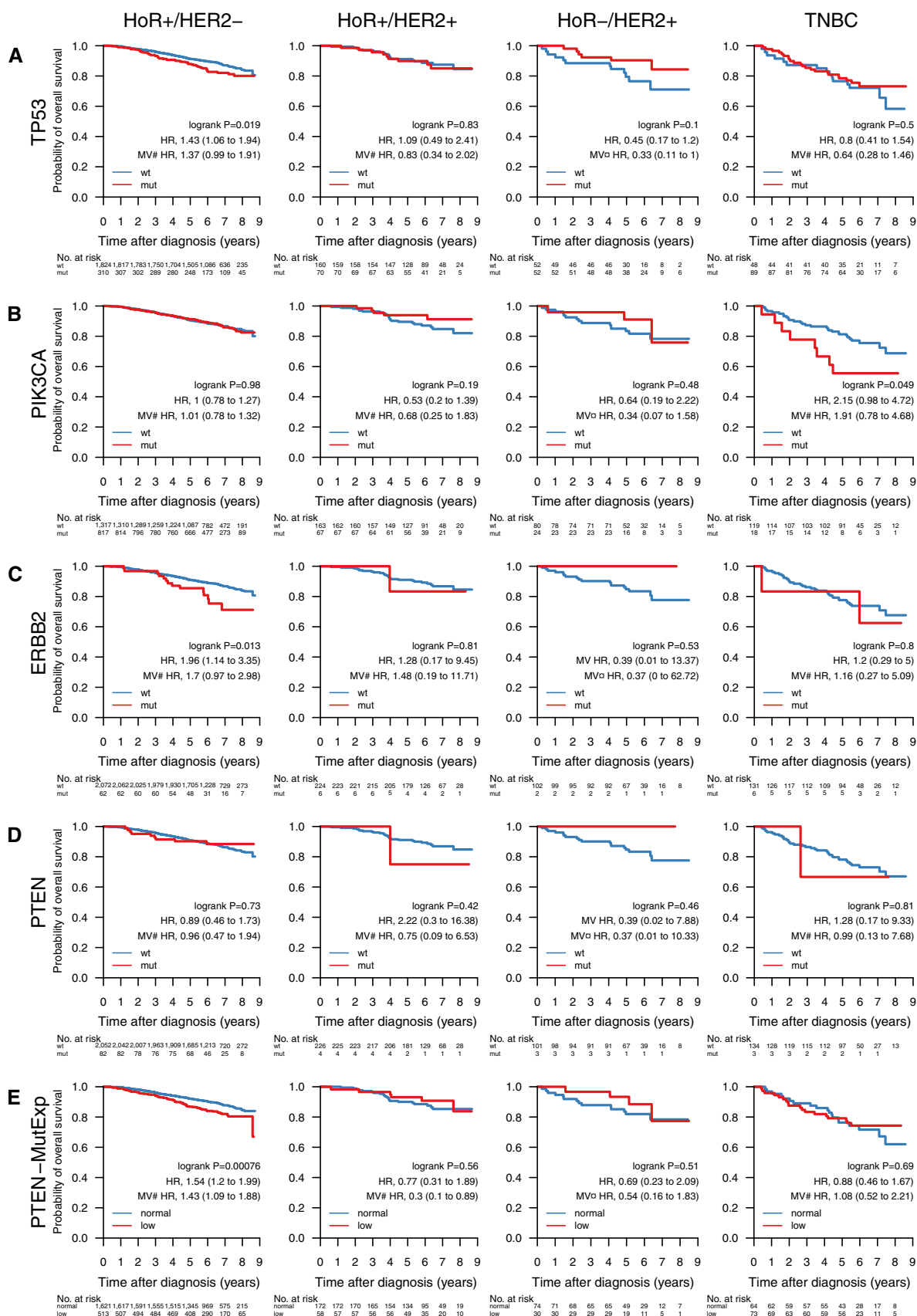


Figure EV2.

Figure EV3. Impact of pathway mutations on overall survival across clinical subgroups.

A–E Overall survival of patients with tumors containing mutations in pathways (A) WNT signaling, (B) Hedgehog signaling, (C) cell cycle, (D) p53 independent DNA damage repair, and (E) TGF β signaling, stratified by the clinical patient subgroups HoR⁺/HER2[−] (HoR⁺ when ER⁺ and PgR⁺, HoR[−] otherwise; $n = 2,134$), HoR⁺/HER2⁺ ($n = 230$), HoR[−]/HER2⁺ ($n = 104$), and TNBC ($n = 137$). Specific treatments in these groups are detailed in Table EV4. In each Kaplan–Meier plot, wild-type (wt) cases are plotted in blue, mutated (mut) cases are plotted in red, the log-rank P value is given, and the hazard ratio (HR) for mutation is given with a 95% CI and after univariable and multivariable (MV) Cox regression adjustment. Covariables included in the MV analysis were age at diagnosis, lymph node status, tumor size, and the variables denoted by the following symbols: α , ER, PgR, and NHG; #, NHG. ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; NHG, Nottingham histological grade; PgR, progesterone receptor.

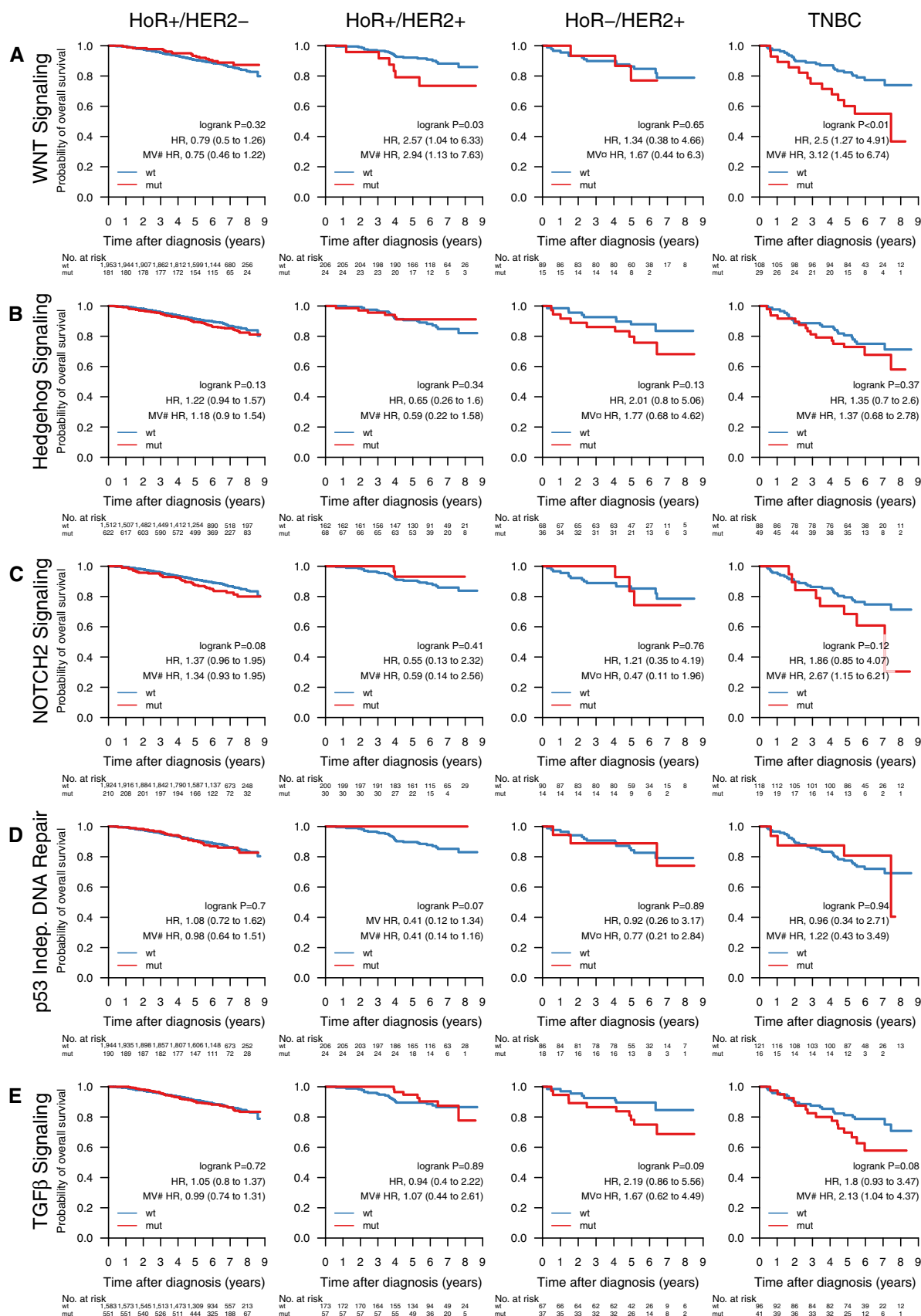


Figure EV3.

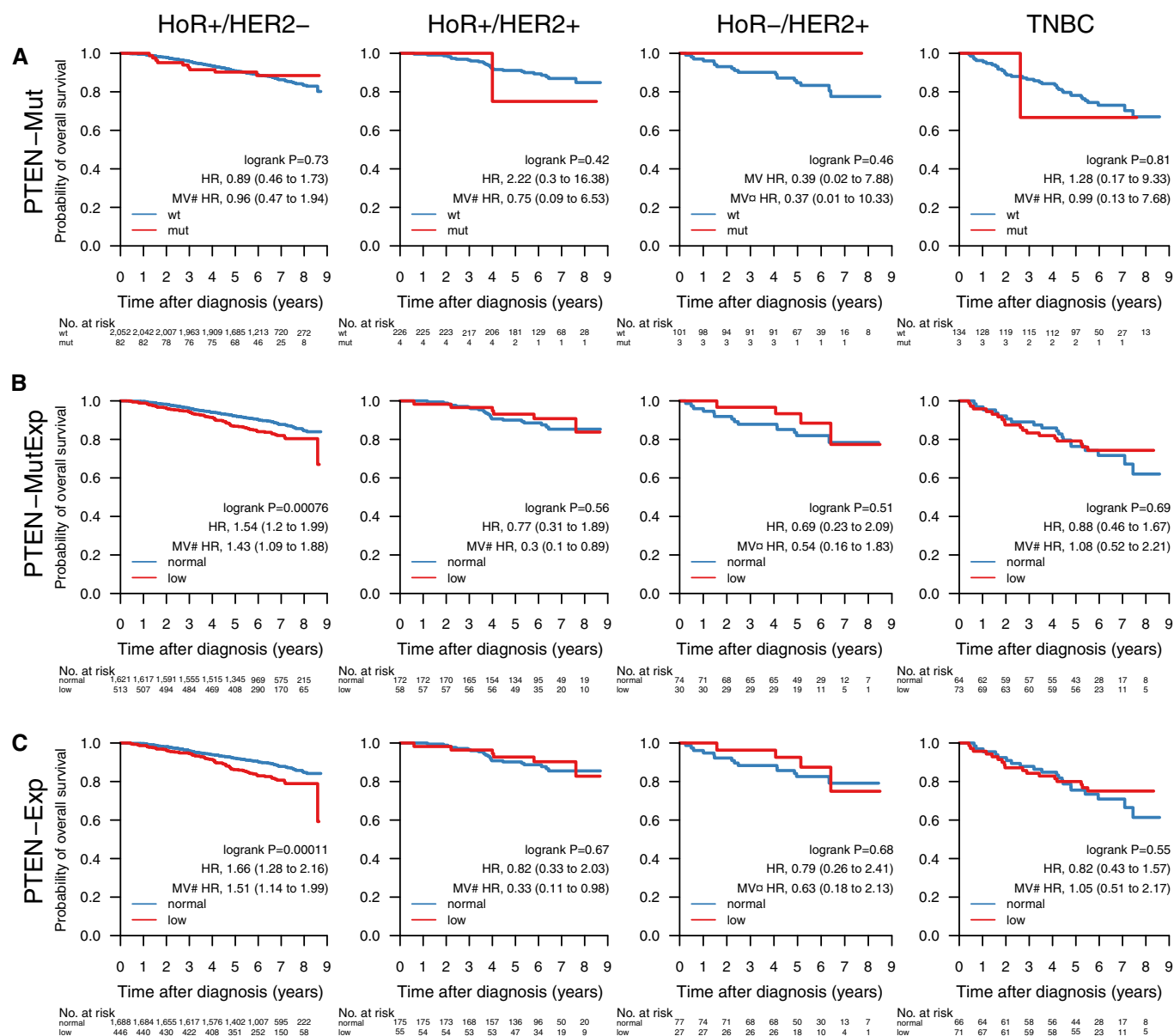


Figure EV4. Impact of *PTEN* mutation and expression on overall survival across treatment groups.

A–C Overall survival of patients with tumors containing a (A) *PTEN* mutation (*PTEN*-Mut), (B) a *PTEN* mutation and/or *PTEN* expression in the lower cohort-quartile (*PTEN*-MutExp), or (C) *PTEN* expression in the lower cohort-quartile (*PTEN*-Exp) in the clinical patient subgroups HoR⁺/HER2[−] (HoR⁺ when ER⁺ and PgR⁺, HoR[−] otherwise; *n* = 2,134), HoR⁺/HER2⁺ (*n* = 230), HoR[−]/HER2⁺ (*n* = 104), and TNBC (*n* = 137). Specific treatments in these groups are detailed in Table EV4. In each Kaplan–Meier plot, wild-type (wt) and normal cases are plotted in blue, mutated (mut) and low cases are plotted in red, the log-rank *P* value is given, and the hazard ratio (HR) for mutation/low is given with a 95% CI and after univariable and multivariable (MV) Cox regression adjustment. Covariables included in the MV analysis were age at diagnosis, lymph node status, tumor size, and the variables denoted by the following symbols: α , ER, PgR, and NHG; #, NHG. ER, estrogen receptor; HoR, hormone receptor; HER2, human epidermal growth factor receptor 2; NHG, Nottingham histological grade; PgR, progesterone receptor; TNBC, triple-negative breast cancer.

Figure EV5. Impact of tumor mutational burden on overall survival across clinical subgroups.

Association of tumor mutational burden (TMB) with overall survival in 3,217 patients, and within the biomarker patient subgroups ER⁺, ER⁻, PgR⁺, PgR⁻, HER2 amplified, HER2 normal, Ki67-high, Ki67-low, NHG Grade 1–3, HoR⁺/HER2⁻, HoR⁺/HER2⁺, HoR⁻/HER2⁺, TNBC, and molecular subtypes Luminal A and B, HER2-enriched, and basal-like according to the PAM50 gene list. In each Kaplan–Meier plot, TMB-low cases are plotted in blue, TMB-high cases are plotted in red, the log-rank *P* value is given, and the hazard ratio (HR) for TMB-high is given with a 95% CI and after univariable and multivariable (MV) Cox regression adjustment. Covariables included in the MV analysis were age at diagnosis, lymph node status, tumor size, and the variables denoted by the following symbols: ¶, ER, PgR, HER2, and NHG; ^, ER, PgR, HER2; □, ER, PgR, and NHG; \$, HER2 and NHG; #, NHG. ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HoR, hormone receptor; NHG, Nottingham histological grade; PgR, progesterone receptor; TMB, tumor mutational burden; TNBC, triple-negative breast cancer.

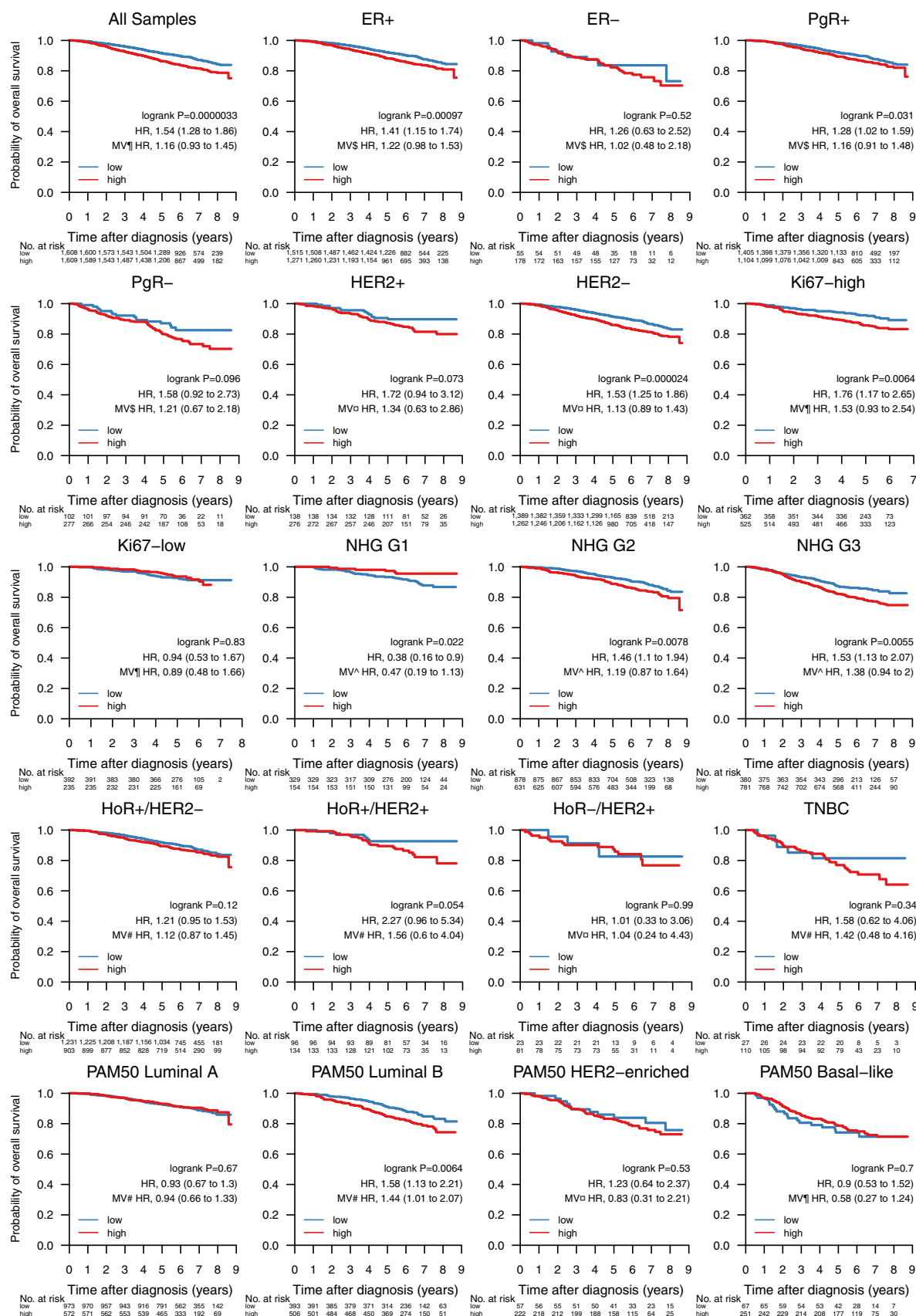


Figure EV5.