

Supplementary Online Content

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

eMethods

Overview of the analyzed genes on the TruRisk®V2 gene panel:

The TruRisk® gene panel covers the entire coding regions and exon-flanking sequences (± 15 nt) of the following 20 genes: *ATM*, NM_000051; *BARD1*, NM_000465; *BRCA1*, NM_007294; *BRCA2*, NM_000059; *BRIP1*, NM_032043; *CDH1*, NM_004360; *CHEK2*, NM_007194; *FANCM*, NM_020937; *MAP3K1*, NM_005921; *MRE11A*, NM_005591; *NBN*, NM_002485; *PALB2*, NM_024675; *PIK3CA*, NM_006218; *PTEN*, NM_000314; *RAD50*, NM_005732; *RAD51C*, NM_058216; *RAD51D*, NM_002878; *STK11*, NM_000455; *TP53*, NM_000546; *XRCC2*, NM_005431.

Bioinformatic analyses and variant classification:

Bioinformatic analyses were carried out with a minimum cut-off value of 5% for variant fraction (VF) and at least five reads/variant through the VARBANK and VARBANK 2.0 pipeline of the Cologne Center for Genomics. All genetic variants were classified using a 5-tier variant classification system as proposed by the International Agency for Research on Cancer (IARC) Unclassified Genetic Variants Working Group¹, namely, deleterious = class 5, likely deleterious = class 4, variant of uncertain significance (VUS) = class 3, likely benign = class 2, and benign = class 1. Class 4/5 variants were subsequently defined as ‘pathogenic variants’ (PVs).

Variant classification was performed in accordance with the regulations of the international ENIGMA consortium (<https://enigmaconsortium.org>)², as previously described in detail³. My Cancer Genome (<http://www.mycancergenome.org>), IARC TP53 (<https://p53.iarc.fr>), and ClinVar (<https://www.ncbi.nlm.nih.gov/clinvar/>) databases were also considered for variant classification. Variants reported with a minor allele frequency $\geq 1\%$ in the control groups were generally considered benign (class 1).

Clinical model for multivariable analysis

For multivariable analysis, a clinical model was built using backward elimination and stepwise selection with a p-value of .157 as elimination criterion, which is a useful margin for explanatory models^{4,5}. Candidate factors were age ($<$ vs. ≥ 50 years), clinical tumor size (cT; 1 vs. >1), clinical nodal status (cN; 0 vs. >0), central grade (<3 vs. 3), Ki67 ($<$ vs. \geq median value of 75%), and treatment arm for all patients without preselection based on univariable p-values. Factors selected by both backward elimination and stepwise selection methods were considered relevant. Wald odds ratios (OR) or hazard ratios (HR), along with 95% confidence intervals (CI), were calculated for the effect of each tPV, controlling for the relevant clinical factors by incorporating tPV into the resulting clinical model for each endpoint/treatment group combination.

Tumor variants in rarely mutated cancer predisposition (RCP) genes (*BARD1*, *CHEK2*, *CDH1*, *FANCM*, *PALB2*, *RAD50*, *RAD51C*, *RAD51D*, *STK11*, *XRCC2*) are combined as “rare cancer predisposition genes” (RCP) to enable explorative analyses due to small numbers.

eResults

Impact of other molecular genetic subgroups on pathologic complete response (pCR) rate:

An overview of the pCR rate according to tumor pathogenic variants (tPVs) in non-*BRCA1/2* genes is given in eTable 3. *TP53*-tPVs did not have a substantial effect on pCR in our cohort with the largest odds ratio (OR) in the nab-paclitaxel/gemcitabine arm (all: OR, 1.25; 95% confidence interval (CI); 0.47-3.30; $P = .66$; gemcitabine: OR, 1.47; 95% CI, 0.38-5.73; $P = .58$; nab-paclitaxel/carboplatin: OR, 1.00; 95% CI, 0.24-4.20; $P = 1.0$). There was an indication for a deleterious effect of *PIK3CA*-tPVs, however, the CI values were wide ($n = 22$; all: pCR rate 18.2%; OR, 0.28; 95% CI, 0.07-1.08; $P = .06$; gemcitabine: pCR rate 20%; OR, 0.48; 95% CI, 0.06-4.26; $P = .51$; carboplatin: pCR rate 16.7%; OR, 0.25; 95% CI, 0.05-1.27; $P = .09$). For details see eTable 5.

Survival in other genetic subgroups:

In multivariable modelling, *TP53*- and *PIK3CA*-tPVs were associated with worse invasive disease-free survival (IDFS) than the respective wildtype (WT) populations (*TP53*-tPVs: 74.0% vs. *TP53*-WT: 87.4%; *PIK3CA*-tPVs: 56.1% vs. *PIK3CA*-WT: 77.6%). The statistically significant risk increase of *TP53*-tPVs compared with WT in the entire cohort (Hazard ratio (HR) adj., 2.81; 95% CI, 1.02-7.78; $P = .046$) was more pronounced in the gemcitabine-arm (HR adj., 3.70; 95% CI: 0.89-15.43, $P = .07$), whereas the risk increase was smaller in the carboplatin-arm (HR adj., 1.94; 95% CI, 0.46-8.25; $P = .37$).

For *PIK3CA*-tPVs, this unfavorable association was independent of the treatment arm (all: HR adj., 1.61; 95% CI, 0.79-3.28; $P = .19$; gemcitabine: HR adj., 1.64; 95% CI, 0.58-4.68; $P = .35$; carboplatin: HR adj., 1.65; 95% CI, 0.62-4.42; $P = .32$).

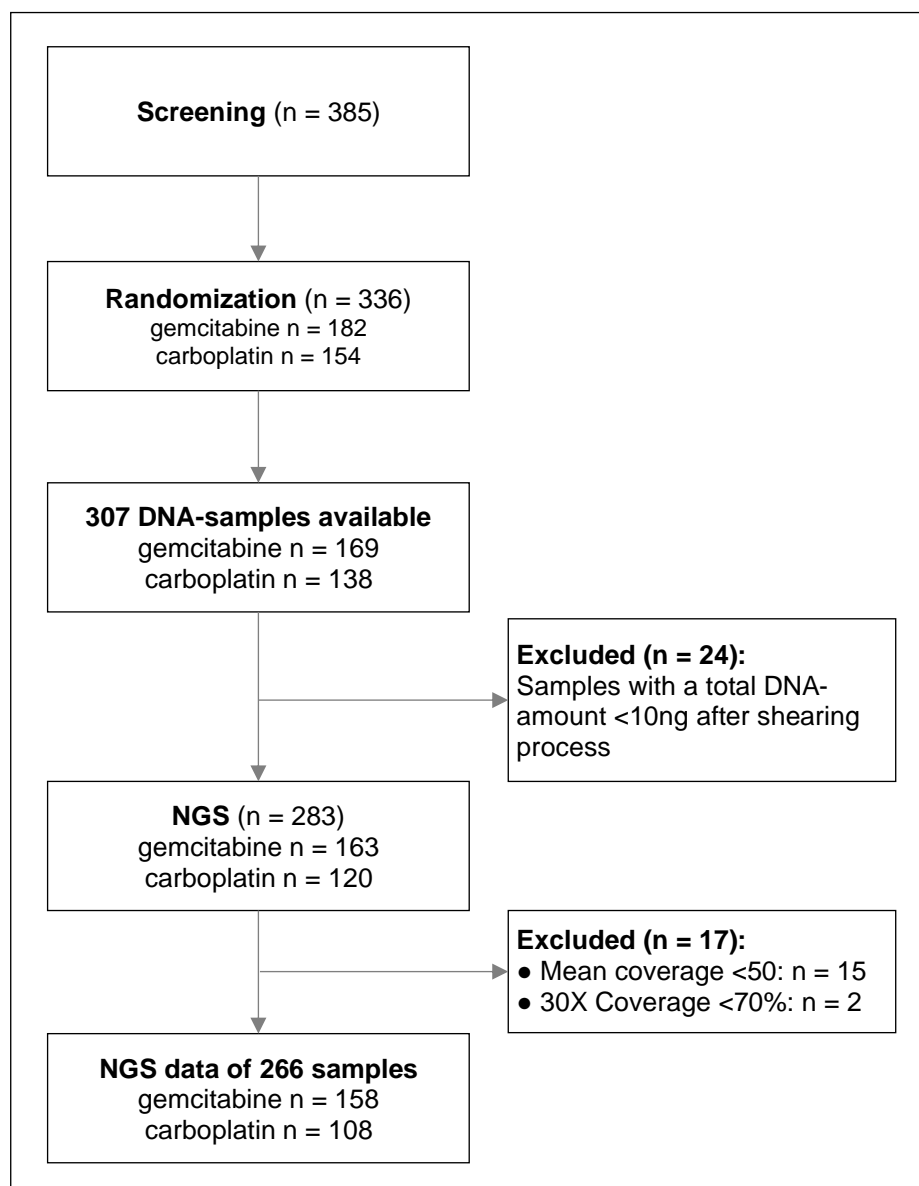
For overall survival (OS), the associations were similar but less distinct. Worse OS was seen for the *TP53*-tPV cohort, e.g. after gemcitabine (HR adj., 2.43; 95% CI, 0.57-10.35; $P = .23$).

The OS differences between *PIK3CA*-tPV and *PIK3CA*-WT groups were statistically less pronounced (all: HR adj., 1.49; 95% CI, 0.63-3.54; $P = .37$) and largest in the carboplatin-arm (HR adj., 1.83; 95% CI, 0.60-5.54; $P = .29$).

Within the heterogeneous group with tPVs in rarely mutated cancer predisposition genes (RCP genes; $n = 20$, including one sample with additional *BRCA1*-tPV), no survival event was observed in the carboplatin-arm. Combining this cohort with the *BRCA1/2*-tPV carriers, a numerical benefit for IDFS and OS after carboplatin was observed (IDFS: 91.0% vs. 72.1%, HR adj., 0.29; 95% CI, 0.07-1.22; $P = .09$; OS: 95.8% vs. 74.9%; HR adj., 0.22; 95% CI, 0.03-1.65; $P = .14$), when compared with the cohort without tPVs in *BRCA1/2* and/or RCP genes. No survival benefit was seen after gemcitabine (IDFS: 74.9% vs. 75.6%, HR adj., 1.12; 95% CI, 0.54-2.32; $P = .75$; OS: 79.7% vs. 83.4%; HR adj., 1.17; 95% CI, 0.49-2.82; $P = .72$).

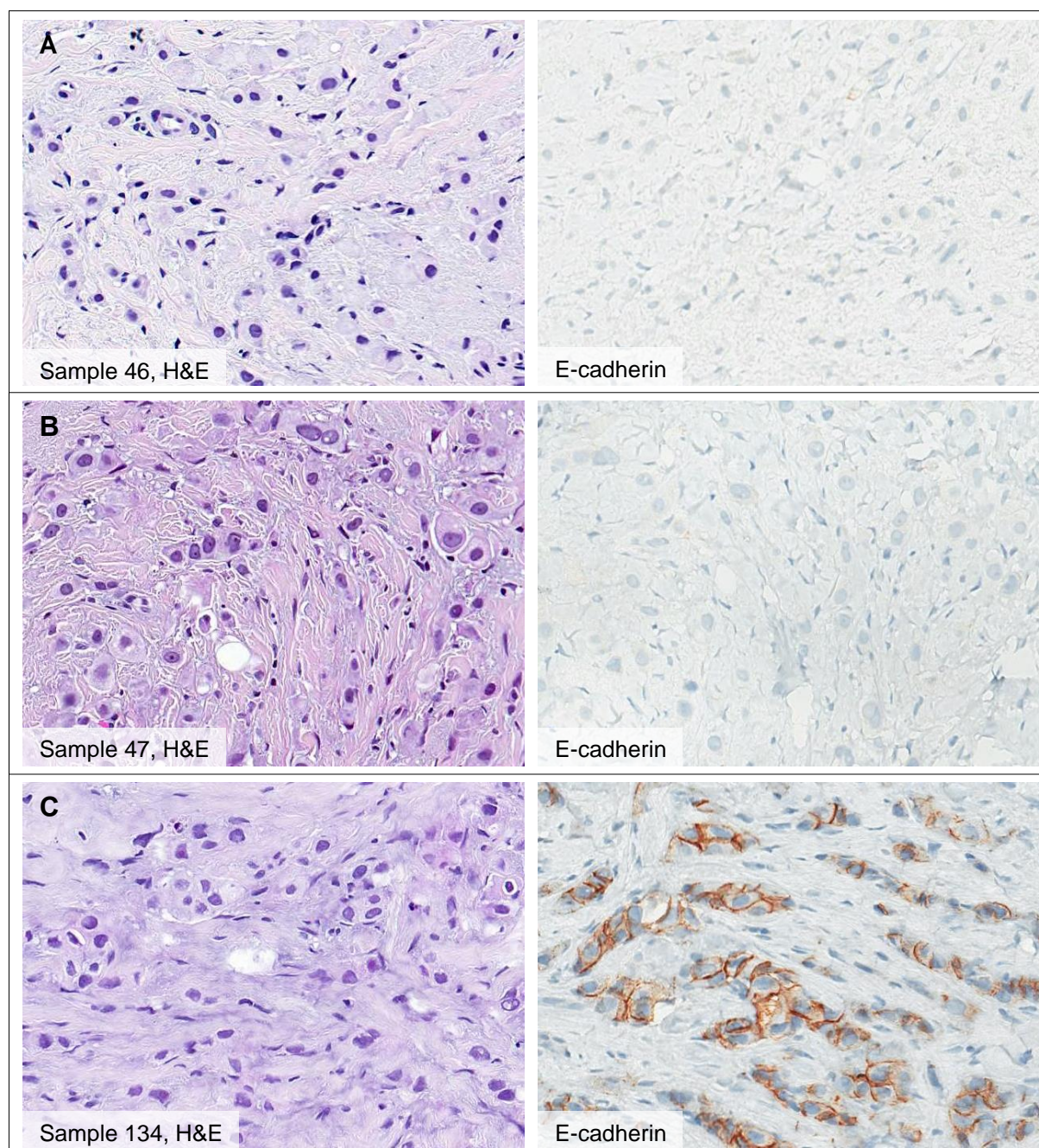
For overview, see eTable 5.

eFigure 1. Flow Diagram of Samples Analyzed in the Study



eFigure 1: Consort-like flow diagram of the ADAPT-TN-trial and the sample processing. The mean read coverage of successfully analyzed samples was 538x (range: 51x-2,885x).
carboplatin = nab-paclitaxel/carboplatin, gemcitabine = nab-paclitaxel/gemcitabine, NGS = next generation sequencing

eFigure 2. Immunohistochemical E-Cadherin Staining



eFigure 2: Hematoxylin and eosin staining (H&E) on the left side; E-cadherin staining on the right side of the two pretreatment biopsies with invasive-lobular cancer (A and B) and a TNBC sample with a NST (invasive carcinoma of no special type) histology and a basal-like PAM50-subtype for comparison (C). (A) and (B) display a *CDH1*-tPV. Sample 46 (A) did not show a *TP53*-tPV and had a luminal A PAM50-subtype. In Sample 47 (B), a *TP53*-tPV and a normal-like subtype were observed. TNBC = triple-negative breast cancer, tPV = tumor pathogenic variant

eTable 1. Baseline Characteristics of Patients With and Without Available Tumor Pathogenic Variant Assessment

	Not in tPV analysis (n = 70)	In tPV analysis (n = 266)	Total (n = 336)	p-value
Age at registration				.59 ^c
Median	50	51	50	
Mean (range)	50.6 (26.0–73.0)	51.5 (26.0–76.0)	51.3 (26.0–76.0)	
Menopausal status				.46 ^b
Postmenopausal	30 (42.9)	127 (47.7)	157 (46.7)	
Premenopausal	38 (54.3)	125 (47.0)	163 (48.5)	
Unknown/unclear	2 (2.9)	14 (5.3)	16 (4.8)	
Clinical tumor size (cT)				.35 ^b
1	21 (30.0)	104 (39.1)	125 (37.2)	
2	43 (61.4)	145 (54.5)	188 (56.0)	
3–4	6 (8.6)	17 (6.4)	23 (6.8)	
Clinical nodal status (cN)				.98 ^b
0	52 (74.3)	196 (73.7)	248 (73.8)	
1	16 (22.9)	61 (22.9)	77 (22.9)	
2–3	2 (2.9)	9 (3.4)	11 (3.3)	
Grade (central)				.18 ^a
2	7 (10)	15 (6)	22 (7)	
3	61 (90)	251 (94)	312 (93)	
Missing	2	0	2	
Ki67 (primary, central) [%]				< .001 ^c
Median	65	75	72.5	
Mean (range)	58.1 (15-90)	68.4 (10-100)	66.37 (10-100)	
Missing	6	6	12	
Histology (central)				.18 ^a
NST	65 (96)	262 (99)	327 (98)	
Medullary	0 (0)	1 (0)	1 (0)	
Invasive-lobular	1 (1)	2 (1)	3 (1)	
Metaplastic	1 (1)	1 (0)	2 (1)	
Apocrine carcinoma	1 (1)	0 (0)	1 (0)	
Missing	2	0	2	
PAM50-subtype				.04 ^a
Basal	25 (69.4)	225 (85.2)	250 (83.3)	
HER2-E	4 (11.1)	15 (5.7)	19 (6.3)	
Lum A	2 (5.6)	3 (1.1)	5 (1.7)	
Normal	5 (13.9)	21 (8.0)	26 (8.7)	
Missing	34	2	36	
Treatment arm				< .001 ^b
gemcitabine	24 (34.3)	158 (59.4)	182 (54.2)	
carboplatin	46 (65.7)	108 (40.6)	154 (45.8)	
pCR (ypT0, ypN0)				.65 ^b
No	37 (63.8)	178 (66.9)	215 (66.4)	
Yes	21 (36.2)	88 (33.1)	109 (33.6)	
Missing	12	0	12	
pCR (ypT0/is, ypN0)				.79 ^b
No	36 (62.1)	170 (63.9)	206 (63.6)	
Yes	22 (37.9)	96 (36.1)	118 (36.4)	
Missing	12	0	12	

eTable 1: Comparison of baseline characteristics of patients with available tumor panel sequencing data (n = 266) compared to the patients without (n = 70). Data are displayed as No. (%), unless otherwise indicated. Following statistical test were applied according to samples size and variable category: a) Fisher's exact test, b) Pearson Chi-square test, c) Wilcoxon test. Statistically significant p-values (< .05) are displayed in bold.

carboplatin = nab-paclitaxel/carboplatin, gemcitabine = nab-paclitaxel/gemcitabine, HER2-E = human epidermal growth factor 2 (HER2)-enriched, Lum A = Luminal A, NST = invasive carcinoma of no special type, pCR = pathologic complete response, tPV = tumor pathogenic variants

eTable 2. Overview of the Detected Tumor Pathogenic Variants in All 266 Samples

ID	gene	transcript	HGVS (nucleotide)	HGVS (protein)	genomic position (hg38)	VF	total reads	consequence	IARC-class	histology	PAM 50
1	<i>BARD1</i> <i>TP53</i>	NM_000465	c.1569-1G>C	p.?	chr2:g.214752556	0.83	96	splicing	4	NST	basal-like
		NM_000546	c.839G>C	p.(Arg280Thr)	chr17:g.7673781	0.59	131	missense	4		
2	<i>BARD1</i> <i>TP53</i> <i>PTEN</i>	NM_000466	c.1872del	p.(Leu625Serfs*7)	chr2:g.214745098	0.91	256	frameshift	5	NST	basal-like
		NM_000546	c.203_204insCAGC	p.(Glu68Aspfs*82)	chr17:g.7676165_7676166	0.83	546	frameshift	5		
		NM_000314	c.720C>G	p.(Tyr240*)	chr10:g.87957938	0.8	385	stop gained	5		
3	<i>BARD1</i> <i>TP53</i>	NM_000467	c.295A>T	p.(Arg99*)	chr2:g.214792366	0.46	1269	stop gained	5	NST	basal-like
		NM_000546	c.838A>G	p.(Arg280Gly)	chr17:g.7673782	0.48	2438	missense	4		
4	<i>BRCA1</i> <i>TP53</i>	NM_007294	c.1155G>A	p.(Trp385*)	chr17:g.43094376	0.42	287	stop gained	5	NST	basal-like
		NM_000546	c.742C>T	p.(Arg248Trp)	chr17:g.7674221	0.34	447	missense	4		
5	<i>BRCA1</i> <i>TP53</i> <i>PTEN</i>	NM_007294	c.121C>T	p.(His41Tyr)	chr17:g.43115739	0.42	177	missense	4	NST	HER2-E
		NM_000546	c.377A>G	p.(Tyr126Cys)	chr17:g.7675235	0.6	158	missense	4		
		NM_000314	c.209+2T>C	p.?	chr10:g.87925559	0.54	74	splicing	4		
6	<i>BRCA1</i> <i>BRCA1</i> <i>TP53</i>	NM_007294	c.1600C>T	p.(Gln534*)	chr17:g.43093931	0.79	1026	stop gained	5	NST	basal-like
		NM_007294	c.4088C>G	p.(Ser1363*)	chr17:g.43091443	0.13	780	stop gained	5		
		NM_000546	c.998del	p.(Arg333Leufs*12)	chr17:g.7670711	0.45	1317	frameshift	4		
7	<i>BRCA1</i> <i>TP53</i>	NM_007294	c.1600C>T	p.(Gln534*)	chr17:g.43093931	0.79	699	stop gained	5	NST	basal-like
		NM_000546	c.329G>C	p.(Arg110Pro)	chr17:g.7676040	0.45	654	missense	4		
8	<i>BRCA1</i> <i>TP53</i>	NM_007294	c.1600del	p.(Gln534Argfs*12)	chr17:g.43093931	0.35	186	frameshift	5	NST	basal-like
		NM_000546	c.488A>G	p.(Tyr163Cys)	chr17:g.7675124	0.35	426	missense	4		
9	<i>BRCA1</i> <i>TP53</i>	NM_007294	c.1621C>T	p.(Gln541*)	chr17:g.43093910	0.83	230	stop gained	5	NST	basal-like
		NM_000546	c.965del	p.(Pro322Hisfs*23)	chr17:g.7673563	0.68	167	frameshift	5		
10	<i>BRCA1</i> <i>TP53</i>	NM_007294	c.181T>G	p.(Cys61Gly)	chr17:g.43106487	0.6	136	missense	5	NST	basal-like
		NM_000546	c.517G>T	p.(Val173Leu)	chr17:g.7675095	0.15	1137	missense	4		
11	<i>BRCA1</i> <i>TP53</i>	NM_007294	c.181T>G	p.(Cys61Gly)	chr17:g.43106487	0.7	142	missense	5	NST	basal-like
		NM_000546	c.586C>T	p.(Arg196*)	chr17:g.7674945	0.46	470	stop gained	5		
12	<i>BRCA1</i> <i>TP53</i>	NM_007294	c.181T>G	p.(Cys61Gly)	chr17:g.43106487	0.77	370v	missense	5	NST	basal-like
		NM_000546	c.329G>C	p.(Arg110Pro)	chr17:g.7676040	0.33	440	missense	4		
13	<i>BRCA1</i> <i>TP53</i>	NM_007294	c.1958_1961del	p.(Lys653Serfs*47)	chr17:g.43093570_43093573	0.43	101	frameshift	5	NST	basal-like
		NM_000546	c.742del	p.(Arg248Glyfs*97)	chr17:g.7674221	0.29	195	frameshift	5		
14	<i>BRCA1</i> <i>TP53</i>	NM_007294	c.2338C>T	p.(Gln780*)	chr17:g.43093193	0.71	1641	stop gained	5	NST	basal-like
		NM_000546	c.659A>G	p.(Tyr220Cys)	chr17:g.7674872	0.49	1324	missense	4		
15	<i>BRCA1</i> <i>TP53</i>	NM_007294	c.2479G>T	p.(Glu827*)	chr17:g.43093052	0.37	937	stop gained	5	NST	basal-like
		NM_000546	c.811G>T	p.(Glu271*)	chr17:g.7673809	0.37	1881	stop gained	5		

ID	gene	transcript	HGVS (nucleotide)	HGVS (protein)	genomic position (hg38)	VF	total reads	consequence	IARC-class	histology	PAM 50
16	<i>BRCA1</i> <i>TP53</i>	NM_007294 NM_000546	c.2679_2682del c.637C>T	p.(Lys893Asnfs*106) p.(Arg213*)	chr17:g.43092849_43092852 chr17:g.7674894	0.49 0.57	106 203	frameshift stop gained	5 5	NST	basal-like
17	<i>BRCA1</i> <i>TP53</i>	NM_007294 NM_000546	c.273del c.240del	p.(Cys91Trpfs*28) p.(Thr81Hisfs*42)	chr17:g.43104896 chr17:g.7676129	0.38 0.34	210 361	frameshift frameshift	5 5	NST	basal-like
18	<i>BRCA1</i> <i>TP53</i>	NM_007294 NM_000546	c.3700_3704del c.659A>G	p.(Val1234Glnfs*8) p.(Tyr220Cys)	chr17:g.43091827_43091831 chr17:g.7674872	0.54 0.4	179 343	frameshift missense	5 4	NST	basal-like
19	<i>BRCA1</i> <i>BRCA2</i> <i>TP53</i>	NM_007294 NM_000059 NM_000546	c.3718C>T c.6781G>T c.840A>T	p.(Gln1240*) p.(Glu2261*) p.(Arg280Ser)	chr17:g.43091813 chr13:g.32341136 chr17:g.7673780	0.38 0.48 0.15	1611 2131 2517	stop gained stop gained missense	5 5 4	NST	basal-like
20	<i>BRCA1</i> <i>TP53</i>	NM_007294 NM_000546	c.4072G>T c.818G>A	p.(Glu1358*) p.(Arg273His)	chr17:g.43091459 chr17:g.7673802	0.82 0.56	194 429	stop gained missense	5 5	NST	basal-like
21	<i>BRCA1</i>	NM_007294	c.4689C>G	p.(Tyr1563*)	chr17:g.43071225	0.11	839	stop gained	5	NST	basal-like
22	<i>BRCA1</i> <i>TP53</i> <i>PIK3CA</i>	NM_007294 NM_000546 NM_006218	c.4986+3G>C c.1006G>T c.353-9_360del	p.? p.(Glu336*) p.?	chr17:g.43070925 chr17:g.7670703 chr3:g.179199681_179199697	0.73 0.41 0.14	2949 3106 1716	splicing stop gained splicing	4 4 4	NST	basal-like
23	<i>BRCA1</i> <i>TP53</i>	NM_007294 NM_000546	c.5008A>T c.743G>A	p.(Arg1670*) p.(Arg248Gln)	chr17:g.43067674 chr17:g.7674220	0.32 0.29	50 153	stop gained missense	5 5	NST	basal-like
24	<i>BRCA1</i> <i>TP53</i>	NM_007294 NM_000546	c.5033del c.723del	p.(Asn1678Ilefs*2) p.(Cys242Alafs*5)	chr17:g.43067649 chr17:g.7674240	0.5 0.42	165 431	frameshift frameshift	5 5	NST	basal-like
25	<i>BRCA1</i>	NM_007294	c.5096G>A	p.(Arg1699Gln)	chr17:g.43063930	0.48	106	missense	5	NST	basal-like
26	<i>BRCA1</i> <i>TP53</i>	NM_007294 NM_000546	c.5153-2del c.809T>C	p.? p.(Phe270Ser)	chr17:g.43063375 chr17:g.7673811	0.91 0.86	323 828	splicing missense	4 4	NST	basal-like
27	<i>BRCA1</i> <i>STK11</i> <i>TP53</i>	NM_007294 NM_000455 NM_000546	c.5177_5180del c.763_772del c.743G>A	p.(Arg1726Lysfs*3) p.(Phe255Thrfs*29) p.(Arg248Gln)	chr17:g.43063346_43063349 chr19:g.1221241_1221250 chr17:g.7674220	0.59 0.05 0.32	62 136 395	frameshift frameshift missense	5 5 5	NST	basal-like
28	<i>BRCA1</i> <i>TP53</i> <i>TP53</i>	NM_007294 NM_000546 NM_000546	c.5266dup c.524G>A c.700T>A	p.(Gln1756Profs*74) p.(Arg175His) p.(Tyr234Asn)	chr17:g.43057063 chr17:g.7675088 chr17:g.7674263	0.48 0.17 0.38	500 1121 653	frameshift missense missense	5 4 4	NST	basal-like
29	<i>BRCA1</i> <i>TP53</i>	NM_007294 NM_000546	c.5266dup c.321C>A	p.(Gln1756Profs*74) p.(Tyr107*)	chr17:g.43057063 chr17:g.7676048	0.76 0.5	1161 2410	frameshift stop gained	5 5	NST	basal-like
30	<i>BRCA1</i> <i>TP53</i>	NM_007294 NM_000546	c.5266dup c.700T>A	p.(Gln1756Profs*74) p.(Tyr234Asn)	chr17:g.43057063 chr17:g.7674263	0.7 0.55	374 469	frameshift missense	5 4	NST	basal-like
31	<i>BRCA1</i> <i>TP53</i>	NM_007294 NM_000546	c.5266dup c.1015G>T	p.(Gln1756Profs*74) p.(Glu339*)	chr17:g.43057063 chr17:g.7670694	0.77 0.46	89 129	frameshift stop gained	5 5	NST	basal-like
32	<i>BRCA1</i> <i>TP53</i>	NM_007294 NM_000546	c.5266dup c.770T>G	p.(Gln1756Profs*74) p.(Leu257Arg)	chr17:g.43057063 chr17:g.7674193	0.7 0.35	53 81	frameshift missense	5 4	NST	basal-like

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33	<i>BRCA1</i>	NM_007294	c.5266dup	p.(Gln1756Profs*74)	chr17:g.43057063	0.53	339	frameshift	5	NST	basal-like
	<i>BRCA2</i>	NM_000059	c.7913_7917del	p.(Phe2638*)	chr13:g.32362630_32362634	0.42	485	stop gained	5		
	<i>TP53</i>	NM_000546	c.324_341del	p.(Phe109_Leu114del)	chr17:g.7676028_7676045	0.11	559	inframe deletion	4		
34	<i>BRCA1</i>	NM_007294	c.5267_5268del	p.(Gln1756Argfs*73)	chr17:g.43057061_43057062	0.67	629	Frameshift	5	NST	basal-like
	<i>TP53</i>	NM_000546	c.287_288del	p.(Ser96Cysfs*52)	chr17:g.7676081_7676082	0.32	1958	frameshift	5		
35	<i>BRCA1</i>	NM_007294	c.5277+1G>A	p.?	chr17:g.43057051	0.13	130	splicing	5	NST	basal-like
36	<i>BRCA1</i>	NM_007294	c.5278-1G>A	p.?	chr17:g.43051118	0.77	123	splicing	4	NST	basal-like
	<i>TP53</i>	NM_000546	c.723del	p.(Cys242Alafs*5)	chr17:g.7674240	0.51	314	frameshift	5		
37	<i>BRCA1</i>	NM_007294	c.5330del	p.(Thr1777Lysfs*16)	chr17:g.43051065	0.56	82	frameshift	5	NST	basal-like
	<i>TP53</i>	NM_000546	c.298C>T	p.(Gln100*)	chr17:g.7676071	0.59	119	stop gained	5		
38	<i>BRCA1</i>	NM_007294	c.5345G>A	p.(Trp1782*)	chr17:g.43049182	0.72	317	stop gained	5	NST	basal-like
	<i>TP53</i>	NM_000546	c.524G>A	p.(Arg175His)	chr17:g.7675088	0.53	2213	missense	4		
39	<i>BRCA1</i>	NM_007294	c.5503C>T	p.(Arg1835*)	chr17:g.43045767	0.72	2450	stop gained	5	NST	basal-like
	<i>TP53</i>	NM_000546	c.775G>T	p.(Asp259Tyr)	chr17:g.7674188	0.44	3424	missense	4		
40	<i>BRCA1</i>	NM_007294	c.5503C>T	p.(Arg1835*)	chr17:g.43045767	0.31	64	stop gained	5	NST	normal-like
	<i>TP53</i>	NM_000546	c.713G>A	p.(Cys238Tyr)	chr17:g.7674250	0.25	71	missense	4		
41	<i>BRCA1</i>	NM_007294	c.5510G>A	p.(Trp1837*)	chr17:g.43045760	0.74	176	stop gained	5	NST	basal-like
	<i>TP53</i>	NM_000546	c.428T>C	p.(Val143Ala)	chr17:g.7675184	0.62	190	missense	4		
42	<i>BRCA1</i>	NM_007294	c.685del	p.(Ser229Leufs*5)	chr17:g.43094846	0.88	154	frameshift	5	NST	basal-like
	<i>TP53</i>	NM_000546	c.536A>G	p.(His179Arg)	chr17:g.7675076	0.54	1149	missense	4		
43	<i>BRCA2</i>	NM_000059	c.3847_3848del	p.(Val1283Lysfs*2)	chr13:g.32338202_32338203	0.73	352	frameshift	5	NST	basal-like
	<i>TP53</i>	NM_000546	c.659A>G	p.(Tyr220Cys)	chr17:g.7674872	0.56	1605	missense	4		
44	<i>BRCA2</i>	NM_000059	c.7894dup	p.(Ala2632Glyfs*9)	chr13:g.32362611	0.4	274	frameshift	5	NST	basal-like
	<i>TP53</i>	NM_000546	c.329G>C	p.(Arg110Pro)	chr17:g.7676040	0.51	451	missense	4		
45	<i>BRCA2</i>	NM_000059	c.7980T>A	p.(Tyr2660*)	chr13:g.32363182	0.37	565	stop gained	5	NST	basal-like
	<i>TP53</i>	NM_000546	c.723del	p.(Cys242Alafs*5)	chr17:g.7674240	0.18	2360	frameshift	5		
46	<i>CDH1</i>	NM_004360	c.1565+1G>T	p.?	chr16:g.68815760	0.15	471	splicing	4	inv-lobular	Lum A
47	<i>CDH1</i>	NM_004360	c.2389_2390delinsG	p.(Tyr797Valfs*19)	chr16:g.68829747_68829748	0.19	362	frameshift	5	inv-lobular	normal-like
	<i>TP53</i>	NM_000546	c.371dup	p.(Cys124Trpfs*25)	chr17:g.7675998	0.18	366	frameshift	5		
48	<i>CHEK2</i>	NM_007194	c.1100del	p.(Thr367Metfs*15)	chr22:g.28695869	0.48	114	frameshift	5	NST	basal-like
	<i>TP53</i>	NM_000546	c.949dup	p.(Gln317Profs*20)	chr17:g.7673579	0.24	177	frameshift	5		
49	<i>CHEK2</i>	NM_007194	c.592+3A>T	p.?	chr22:g.28724974	0.77	173	splicing	4	NST	basal-like
	<i>TP53</i>	NM_000546	c.810del	p.(Phe270Leufs*75)	chr17:g.7673810	0.48	658	frameshift	5		
50	<i>FANCM</i>	NM_020937	c.1491dup	p.(Gln498Thrfs*7)	chr14:g.45159190	0.73	242	frameshift	5	NST	basal-like
	<i>TP53</i>	NM_000546	c.711G>A	p.(Met237Ile)	chr17:g.7674252	0.60	493	missense	4		

ID	gene	transcript	HGVS (nucleotide)	HGVS (protein)	genomic position (hg38)	VF	total reads	consequence	IARC-class	histology	PAM 50
51	FANCM TP53	NM_020937	c.1972C>T	p.(Arg658*)	chr14:g.45167133	0.49	755	stop gained	5	NST	basal-like
		NM_000546	c.993+2T>C	p.?	chr17:g.7673533	0.2	271	splicing	4		
52	FANCM TP53	NM_020937	c.1972C>T	p.(Arg658*)	chr14:g.45167133	0.61	257	stop gained	5	NST	basal-like
		NM_000546	c.344_356dup	p.(Lys120Phefs*33)	chr17:g.7676013_7676025	0.32	1684	frameshift	5		
53	PALB2 PALB2	NM_024675	c.1046del	p.(Asn349Ilefs*7)	chr16:g.23635500	0.41	436	frameshift	5	NST	basal-like
		NM_024675	c.3256C>T	p.(Arg1086*)	chr16:g.23607958	0.39	684	stop gained	5		
54	PALB2 TP53	NM_024675	c.172_175del	p.(Gln60Argfs*7)	chr16:g.23637886	0.72	250	frameshift	5	NST	HER2-E
		NM_000546	c.743G>A	p.(Arg248Gln)	chr17:g.7674220	0.58	316	missense	5		
55	PALB2 TP53	NM_024675	c.1724G>A	p.(Trp575*)	chr16:g.23630430	0.82	148	stop gained	5	NST	basal-like
		NM_000546	c.316_320del	p.(Ser106Argfs*41)	chr17:g.7676049_7676053	0.74	305	frameshift	5		
56	PALB2	NM_024675	c.3201+2dup	p.?	chr16:g.23614002	0.38	350	splicing	4	NST	basal-like
57	PALB2	NM_024675	c.509_510del	p.(Arg170Ilefs*14)	chr16:g.23636036_23636037	0.61	1249	frameshift	5	NST	basal-like
58	RAD50 TP53 PTEN	NM_005732	c.934C>T	p.(Gln312*)	chr5:g.132587972	0.23	71	stop gained	5	NST	basal-like
		NM_000546	c.328del	p.(Arg110Valfs*13)	chr17:g.7676041	0.27	233	frameshift	5		
		NM_000314	c.278del	p.(His93Leufs*6)	chr10:g.87933037	0.25	80	frameshift	5		
59	RAD51C TP53	NM_058216	c.653_654del	p.(Glu218Valfs*33)	chr17:g.58703277_58703278	0.78	280	frameshift	5	NST	basal-like
		NM_000546	c.754_762del	p.(Leu252_Ile254del)	chr17:g.7674201_7674209	0.57	375	inframe deletion	4		
60	RAD51D TP53	NM_002878	c.138_144+8del	p.?	chr17:g.35119103_35119117	0.49	433	splicing	5	NST	basal-like
		NM_000546	c.400T>G	p.(Phe134Val)	chr17:g.7675212	0.62	687	missense	4		
61	XRCC2 TP53	NM_005431	c.96del	p.(Phe32Leufs*30)	chr7:g.152660726	0.67	557	frameshift	5	NST	basal-like
		NM_000546	c.761T>A	p.(Ile254Asn)	chr17:g.7674202	0.38	1099	missense	4		
62	TP53 MAP3K1	NM_000546	c.706dup	p.(Tyr236Leufs*4)	chr17:g.7674257	0.44	551	frameshift	5	NST	basal-like
		NM_005921	c.407C>A	p.(Ser136*)	chr5:g.56815980	0.23	526	stop gained	5		
63	TP53 PIK3CA	NM_000546	c.323del	p.(Gly108Valfs*15)	chr17:g.7676046	0.5	552	frameshift	5	NST	normal-like
		NM_006218	c.1345_1356del	p.(Pro449_Leu452del)	chr3:g.179210279_179210290	0.25	1033	inframe deletion	4		
64	TP53 PIK3CA	NM_000546	c.404G>A	p.(Cys135Tyr)	chr17:g.7675208	0.23	1703	missense	4	NST	basal-like
		NM_006218	c.308_313del	p.(Glu103_Pro104del)	chr3:g.179199133_179199138	0.26	2877	inframe deletion	4		
65	TP53 PIK3CA	NM_000546	c.497C>G	p.(Ser166*)	chr17:g.7675115	0.21	225	stop gained	5	NST	basal-like
		NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.46	185	missense	5		
66	TP53 PIK3CA	NM_000546	c.528_536del	p.(Pro177_His179del)	chr17:g.7675076_7675084	0.05	172	inframe deletion	4	NST	normal-like
		NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.17	182	missense	5		
67	TP53 PIK3CA	NM_000546	c.536A>G	p.(His179Arg)	chr17:g.7675076	0.19	1201	missense	4	NST	basal-like
		NM_006218	c.1636C>G	p.(Val105_Gly106del)	chr3:g.179199136_179199143	0.07	231	inframe insertion	4		
68	TP53 PIK3CA	NM_000546	c.581T>G	p.(Leu194Arg)	chr17:g.7674950	0.19	1443	missense	4	NST	HER2-E
		NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.25	2438	missense	5		

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69	TP53 PIK3CA	NM_000546	c.659A>G	p.(Tyr220Cys)	chr17:g.7674872	0.42	1326	missense	4	NST	HER2-E
		NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.43	1114	missense	5		
70	TP53 PIK3CA	NM_000546	c.686_687del	p.(Cys229Tyrfs*10)	chr17:g.7674276_7674277	0.3	1808	frameshift	5	NST	basal-like
		NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.2	2342	missense	5		
71	TP53 PIK3CA	NM_000546	c.722C>A	p.(Ser241Tyr)	chr17:g.7674241	0.38	210	missense	4	NST	basal-like
		NM_006218	c.1636C>G	p.(Gln546Glu)	chr3:g.179218306	0.32	118	missense	4		
72	TP53 PIK3CA	NM_000546	c.742C>T	p.(Arg248Trp)	chr17:g.7674221	0.39	302	missense	4	NST	basal-like
		NM_006218	c.3141T>A	p.(His1047Gln)	chr3:g.179234298	0.39	265	missense	4		
73	TP53 PIK3CA	NM_000546	c.743G>T	p.(Arg248Leu)	chr17:g.7674220	0.34	743	missense	4	NST	basal-like
		NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.37	966	missense	5		
74	TP53 PIK3CA	NM_000546	c.818G>A	p.(Arg273His)	chr17:g.7673802	0.42	865	missense	5	NST	normal-like
		NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.37	940	missense	5		
75	TP53 PIK3CA	NM_000546	c.859G>T	p.(Glu287*)	chr17:g.7673761	0.3	1528	stop gained	5	NST	HER2-E
		NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.2	1653	missense	5		
76	TP53 PIK3CA PIK3CA PTEN	NM_000546	c.524G>A	p.(Arg175His)	chr17:g.7675088	0.37	2486	missense	4	NST	HER2-E
		NM_006218	c.1234C>T	p.(Arg412*)	chr3:g.179209683	0.16	2483	stop gained	5		
		NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.32	2577	missense	5		
		NM_000314	c.618_627del	p.(Phe206Leufs*12)	chr10:g.87952243_87952252	0.22	2214	frameshift	5		
77	TP53 PIK3CA PTEN	NM_000546	c.427G>A	p.(Val143Met)	chr17:g.7675185	0.34	1214	missense	4	NST	HER2-E
		NM_006218	c.3140A>T	p.(His1047Leu)	chr3:g.179234297	0.29	915	missense	5		
		NM_000314	c.686C>G	p.(Ser229*)	chr10:g.87957904	0.35	718	stop gained	5		
78	TP53 PIK3CA PTEN	NM_000546	c.626_627del	p.(Arg209Lysfs*6)	chr17:g.7674904_7674905	0.08	175	frameshift	5	NST	normal-like
		NM_006218	c.3145G>C	p.(Gly1049Arg)	chr3:g.179234302	0.12	318	missense	4		
		NM_000314	c.388C>T	p.(Arg130*)	chr10:g.87933147	0.14	394	stop gained	5		
79	TP53 PIK3CA PTEN	NM_000546	c.747G>T	p.(Arg249Ser)	chr17:g.7674216	0.25	777	missense	4	NST	HER2-E
		NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.29	570	missense	5		
		NM_000314	c.70G>T	p.(Asp24Tyr)	chr10:g.878464539	0.23	888	missense	4		
80	TP53 PIK3CA PTEN	NM_000546	c.839G>A	p.(Arg280Lys)	chr17:g.7673781	0.17	541	missense	4	NST	HER2-E
		NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.15	421	missense	5		
		NM_000314	c.900del	p.(Ile300Metfs*7)	chr10:g.87960992	0.22	293	frameshift	5		
81	TP53 PTEN	NM_000546	c.672G>A	p.?	chr17:g.7674859	0.16	287	splicing	4	NST	normal-like
		NM_000314	c.432dup	p.(Phe145Ilefs*35)	chr10:g.87933191	0.12	99	frameshift	5		
82	TP53 PTEN	NM_000546	c.700T>G	p.(Tyr234Asp)	chr17:g.7674263	0.23	1258	missense	4	NST	HER2-E
		NM_000314	c.998_1001dup	p.(Arg335Glnfs*9)	chr10:g.87961092_87961095	0.14	1149	missense	5		
83	TP53 PTEN	NM_000546	c.713G>T	p.(Cys238Phe)	chr17:g.7674250	0.41	246	missense	4	NST	basal-like
		NM_000314	c.80A>G	p.(Tyr27Cys)	chr10:g.87894025	0.37	310	missense	4		

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84	TP53 PTEN	NM_000546	c.821T>C	p.(Val274Ala)	chr17:g.7673799	0.4	1346	missense	4	NST	basal-like
		NM_000314	c.511C>T	p.(Gln171*)	chr10:g.87952136	0.24	1220	stop gained	5		
85	TP53 PTEN	NM_000546	c.916C>T	p.(Arg306*)	chr17:g.7673704	0.38	2506	stop gained	5	NST	basal-like
		NM_000314	c.955_958del	p.(Thr319*)	chr10:g.87961047_87961050	0.32	1275	stop gained	5		
86	TP53 PTEN	NM_000546	c.920-2A>G	p.?	chr17:g.7673610	0.66	381	splicing	4	NST	basal-like
		NM_000314	c.578_588del	p.(Leu193Glnfs*5)	chr10:g.87952203_87952213	0.61	359	frameshift	5		
87	TP53	NM_000546	c.1004del	p.(Arg335Leufs*10)	chr17:g.7670705	0.36	1720	frameshift	5	NST	basal-like
88	TP53	NM_000546	c.1024C>T	p.(Arg342*)	chr17:g.7670685	0.7	166	stop gained	5	NST	basal-like
89	TP53	NM_000546	c.1024C>T	p.(Arg342*)	chr17:g.7670685	0.21	1586	stop gained	5	NST	basal-like
90	TP53	NM_000546	c.1024C>T	p.(Arg342*)	chr17:g.7670685	0.77	480	stop gained	5	NST	basal-like
91	TP53	NM_000546	c.1024C>T	p.(Arg342*)	chr17:g.7670685	0.42	2065	stop gained	5	NST	basal-like
92	TP53	NM_000546	c.1025G>C	p.(Arg342Pro)	chr17:g.7670684	0.23	170	missense	4	NST	basal-like
93	TP53	NM_000546	c.1045G>T	p.(Glu349*)	chr17:g.7670664	0.23	177	stop gained	5	NST	basal-like
94	TP53	NM_000546	c.132del	p.(Met44Ilefs*79)	chr17:g.7676237	0.4	392	frameshift	5	NST	basal-like
95	TP53	NM_000546	c.217dup	p.(Val73Glyfs*76)	chr17:g.7676152	0.48	562	frameshift	5	NST	basal-like
96	TP53	NM_000546	c.228del	p.(Pro77Glnfs*46)	chr17:g.7676141	0.4	1771	frameshift	4	NST	basal-like
97	TP53	NM_000546	c.228del	p.(Pro77Glnfs*46)	chr17:g.7676141	0.56	1297	frameshift	4	NST	basal-like
98	TP53	NM_000546	c.267del	p.(Ser90Profs*33)	chr17:g.7676102	0.17	3154	frameshift	5	NST	basal-like
99	TP53	NM_000546	c.310_325del	p.(Gln104Serfs*14)	chr17:g.7676044_7676059	0.26	1165	frameshift	5	NST	basal-like
100	TP53	NM_000546	c.318_321del	p.(Ser106Argfs*16)	chr17:g.7676048_7676051	0.15	1786	frameshift	5	NST	basal-like
101	TP53	NM_000546	c.321C>A	p.(Tyr107*)	chr17:g.7676048	0.18	284	stop gained	5	NST	basal-like
102	TP53	NM_000546	c.321C>A	p.(Tyr107*)	chr17:g.7676048	0.6	508	stop gained	5	NST	basal-like
103	TP53	NM_000546	c.321C>G	p.(Tyr107*)	chr17:g.7676048	0.34	852	stop gained	5	NST	basal-like
104	TP53	NM_000546	c.321C>G	p.(Tyr107*)	chr17:g.7676048	0.33	493	stop gained	5	NST	basal-like
105	TP53	NM_000546	c.322delinsCT	p.(Gly108Valfs*41)	chr17:g.7676047	0.65	2105	frameshift	5	NST	basal-like
106	TP53	NM_000546	c.323_329dup	p.(Leu111Phefs*40)	chr17:g.7676040_7676046	0.21	2196	frameshift	5	NST	basal-like
107	TP53	NM_000546	c.327_328dup	p.(Arg110Profs*14)	chr17:g.7676041_7676042	0.45	467	frameshift	5	NST	basal-like
108	TP53	NM_000546	c.328del	p.(Arg110Valfs*13)	chr17:g.7676041	0.56	404	frameshift	5	NST	basal-like
109	TP53	NM_000546	c.328del	p.(Arg110Valfs*13)	chr17:g.7676041	0.44	230	frameshift	5	NST	basal-like
110	TP53	NM_000546	c.328del	p.(Arg110Valfs*13)	chr17:g.7676041	0.5	407	frameshift	5	NST	basal-like
111	TP53	NM_000546	c.328dup	p.(Arg110Profs*39)	chr17:g.7676041	0.24	130	frameshift	5	NST	basal-like
112	TP53	NM_000546	c.329G>C	p.(Arg110Pro)	chr17:g.7676040	0.33	167	missense	4	NST	basal-like
113	TP53	NM_000546	c.329G>C	p.(Arg110Pro)	chr17:g.7676040	0.29	1322	missense	4	medullary	basal-like

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114	TP53	NM_000546	c.329G>C	p.(Arg110Pro)	chr17:g.7676040	0.4	1037	missense	4	NST	basal-like
115	TP53	NM_000546	c.341T>A	p.(Leu114*)	chr17:g.7676028	0.48	528	stop gained	5	NST	basal-like
116	TP53	NM_000546	c.351del	p.(Thr118Glnfs*5)	chr17:g.7676018	0.63	943	frameshift	5	NST	basal-like
117	TP53	NM_000546	c.365_366del	p.(Val122Aspfs*26)	chr17:g.7676003_7676004	0.7	945	frameshift	5	NST	basal-like
118	TP53	NM_000546	c.367_371del	p.(Thr123Hisfs*24)	chr17:g.7675998_7676002	0.51	488	frameshift	5	NST	basal-like
119	TP53	NM_000546	c.374_375insCACG	p.(Tyr126Hisfs*24)	chr17:g.7675994_7675995	0.39	1549	frameshift	5	NST	basal-like
120	TP53	NM_000546	c.374_375insTTGGCT	p.(Thr125_Tyr126insTrpLeu)	chr17:g.7675994_7675995	0.38	161	inframe insertion	4	NST	basal-like
121	TP53	NM_000546	c.374C>G	p.(Thr125Arg)	chr17:g.7675995	0.79	669	missense	4	NST	basal-like
122	TP53	NM_000546	c.374C>G	p.(Thr125Arg)	chr17:g.7675995	0.28	386	missense	4	NST	basal-like
123	TP53	NM_000546	c.375+1del	p.?	chr17:g.7675993	0.26	143	splicing	5	NST	basal-like
124	TP53	NM_000546	c.375+1del	p.?	chr17:g.7675993	0.5	331	splicing	4	NST	basal-like
125	TP53	NM_000546	c.375+1dup	p.?	chr17:g.7675993	0.25	554	splicing	4	NST	basal-like
126	TP53	NM_000546	c.375+1G>A	p.?	chr17:g.7675993	0.28	1234	splicing	4	NST	basal-like
127	TP53	NM_000546	c.376-3C>G	p.?	chr17:g.7675239	0.72	504	splicing	4	NST	basal-like
128	TP53	NM_000546	c.376T>G	p.(Tyr126Asp)	chr17:g.7675236	0.42	1146	missense	4	NST	missing
129	TP53	NM_000546	c.393_395del	p.(Asn131del)	chr17:g.7675217_7675219	0.32	325	inframe deletion	4	NST	basal-like
130	TP53	NM_000546	c.395A>G	p.(Lys132Arg)	chr17:g.7675217	0.73	287	missense	4	NST	normal-like
131	TP53	NM_000546	c.396G>C	p.(Lys132Asn)	chr17:g.7675216	0.21	2030	frameshift	4	NST	HER2-E
132	TP53	NM_000546	c.398del	p.(Met133Serfs*37)	chr17:g.7675214	0.54	1404	missense	5	NST	basal-like
133	TP53	NM_000546	c.445dup	p.(Ser149Phefs*32)	chr17:g.7675167	0.63	1012	frameshift	5	NST	basal-like
134	TP53	NM_000546	c.445dup	p.(Ser149Phefs*32)	chr17:g.7675167	0.45	2546	frameshift	5	NST	basal-like
135	TP53	NM_000546	c.455del	p.(Pro152Argfs*18)	chr17:g.7675157	0.16	702	frameshift	5	NST	basal-like
136	TP53	NM_000546	c.462del	p.(Thr155Profs*15)	chr17:g.7675150	0.08	2470	frameshift	5	NST	basal-like
137	TP53	NM_000546	c.476C>T	p.(Ala159Val)	chr17:g.7675136	0.66	612	missense	4	NST	basal-like
138	TP53	NM_000546	c.476C>T	p.(Ala159Val)	chr17:g.7675136	0.6	272	missense	4	NST	basal-like
139	TP53	NM_000546	c.476C>T	p.(Ala159Val)	chr17:g.7675136	0.33	1318	missense	4	NST	basal-like
140	TP53	NM_000546	c.488A>G	p.(Tyr163Cys)	chr17:g.7675124	0.21	2596	missense	4	NST	basal-like
141	TP53	NM_000546	c.488A>G	p.(Tyr163Cys)	chr17:g.7675124	0.44	521	missense	4	NST	basal-like
142	TP53	NM_000546	c.499_500del	p.(Gln167Alafs*13)	chr17:g.7675112_7675113	0.64	257	frameshift	5	NST	basal-like
143	TP53	NM_000546	c.499C>T	p.(Gln167*)	chr17:g.7675113	0.3	408	stop gained	5	NST	basal-like
144	TP53	NM_000546	c.517G>A	p.(Val173Met)	chr17:g.7675095	0.1	2173	missense	4	NST	normal-like
145	TP53	NM_000546	c.524G>A	p.(Arg175His)	chr17:g.7675088	0.69	2591	missense	4	NST	basal-like

ID	gene	transcript	HGVS (nucleotide)	HGVS (protein)	genomic position (hg38)	VF	total reads	consequence	IARC-class	histology	PAM 50
146	TP53	NM_000546	c.524G>A	p.(Arg175His)	chr17:g.7675088	0.7	255	missense	4	NST	basal-like
147	TP53	NM_000546	c.524G>A	p.(Arg175His)	chr17:g.7675088	0.35	2025	missense	4	NST	basal-like
148	TP53	NM_000546	c.524G>A	p.(Arg175His)	chr17:g.7675088	0.26	2494	missense	4	NST	basal-like
149	TP53	NM_000546	c.524G>A	p.(Arg175His)	chr17:g.7675088	0.3	2422	missense	4	NST	basal-like
150	TP53	NM_000546	c.524G>A	p.(Arg175His)	chr17:g.7675088	0.22	369	missense	4	NST	basal-like
151	TP53	NM_000546	c.524G>A	p.(Arg175His)	chr17:g.7675088	0.36	661	missense	4	NST	basal-like
152	TP53	NM_000546	c.524G>A	p.(Arg175His)	chr17:g.7675088	0.32	505	missense	4	NST	basal-like
153	TP53	NM_000546	c.527G>A	p.(Cys176Tyr)	chr17:g.7675085	0.29	2294	missense	4	NST	basal-like
154	TP53	NM_000546	c.527G>A	p.(Cys176Tyr)	chr17:g.7675085	0.31	2479	missense	4	NST	basal-like
155	TP53	NM_000546	c.529_546del	p.(Pro177_Cys182del)	chr17:g.7675066_7675083	0.21	736	inframe deletion	4	NST	basal-like
156	TP53	NM_000546	c.535C>T	p.(His179Tyr)	chr17:g.7675077	0.41	1423	missense	4	NST	basal-like
157	TP53	NM_000546	c.536A>G	p.(His179Arg)	chr17:g.7675076	0.52	1225	missense	4	NST	basal-like
158	TP53	NM_000546	c.536A>T	p.(His179Leu)	chr17:g.7675076	0.35	2664	missense	4	NST	basal-like
159	TP53	NM_000546	c.551_554del	p.(Asp184Alafs*62)	chr17:g.7675058_7675061	0.46	1070	frameshift	5	NST	basal-like
160	TP53	NM_000546	c.559+1G>T	p.?	chr17:g.7675052	0.34	241	splicing	4	NST	basal-like
161	TP53	NM_000546	c.560-1G>A	p.?	chr17:g.7674972	0.5	1004	splicing	4	NST	basal-like
162	TP53	NM_000546	c.574C>T	p.(Gln192*)	chr17:g.7674957	0.56	372	stop gained	5	NST	basal-like
163	TP53	NM_000546	c.574C>T	p.(Gln192*)	chr17:g.7674957	0.65	346	stop gained	5	NST	basal-like
164	TP53	NM_000546	c.581T>G	p.(Leu194Arg)	chr17:g.7674950	0.71	249	missense	4	NST	basal-like
165	TP53	NM_000546	c.584T>A	p.(Ile195Asn)	chr17:g.7674947	0.22	1008	missense	4	NST	basal-like
166	TP53	NM_000546	c.584T>C	p.(Ile195Thr)	chr17:g.7674947	0.35	450	missense	4	NST	basal-like
167	TP53	NM_000546	c.586C>T	p.(Arg196*)	chr17:g.7674945	0.47	555	stop gained	5	NST	basal-like
168	TP53	NM_000546	c.586C>T	p.(Arg196*)	chr17:g.7674945	0.14	195	stop gained	5	NST	normal-like
169	TP53	NM_000546	c.586C>T	p.(Arg196*)	chr17:g.7674945	0.93	1002	stop gained	5	NST	basal-like
170	TP53	NM_000546	c.610G>T	p.(Glu204*)	chr17:g.7674921	0.24	1082	stop gained	5	NST	basal-like
171	TP53	NM_000546	c.626_627del	p.(Arg209Lysfs*6)	chr17:g.7674904_7674905	0.87	442	frameshift	5	metaplastic	basal-like
172	TP53	NM_000546	c.635_636del	p.(Phe212Serfs*3)	chr17:g.7674895_7674896	0.26	156	frameshift	5	NST	basal-like
173	TP53	NM_000546	c.637C>T	p.(Arg213*)	chr17:g.7674894	0.12	2194	stop gained	5	NST	basal-like
174	TP53	NM_000546	c.637C>T	p.(Arg213*)	chr17:g.7674894	0.71	1770	stop gained	5	NST	basal-like
175	TP53	NM_000546	c.637C>T	p.(Arg213*)	chr17:g.7674894	0.42	931	stop gained	5	NST	basal-like
176	TP53	NM_000546	c.637C>T	p.(Arg213*)	chr17:g.7674894	0.42	1048	stop gained	5	NST	basal-like
177	TP53	NM_000546	c.637C>T	p.(Arg213*)	chr17:g.7674894	0.28	1130	stop gained	5	NST	basal-like

ID	gene	transcript	HGVS (nucleotide)	HGVS (protein)	genomic position (hg38)	VF	total reads	consequence	IARC-class	histology	PAM 50
178	TP53	NM_000546	c.637C>T	p.(Arg213*)	chr17:g.7674894	0.38	2122	stop gained	5	NST	basal-like
179	TP53	NM_000546	c.637C>T	p.(Arg213*)	chr17:g.7674894	0.14	107	stop gained	5	NST	basal-like
180	TP53	NM_000546	c.637C>T	p.(Arg213*)	chr17:g.7674894	0.42	568	stop gained	5	NST	basal-like
181	TP53	NM_000546	c.646G>A	p.(Val216Met)	chr17:g.7674885	0.59	481	missense	4	NST	basal-like
182	TP53	NM_000546	c.647T>A	p.(Val216Glu)	chr17:g.7674884	0.71	578	missense	4	NST	basal-like
183	TP53	NM_000546	c.653T>G	p.(Val218Gly)	chr17:g.7674878	0.64	168	missense	4	NST	basal-like
184	TP53	NM_000546	c.659A>G	p.(Tyr220Cys)	chr17:g.7674872	0.65	443	missense	4	NST	basal-like
185	TP53	NM_000546	c.659A>G	p.(Tyr220Cys)	chr17:g.7674872	0.39	312	missense	4	NST	basal-like
186	TP53	NM_000546	c.659A>G	p.(Tyr220Cys)	chr17:g.7674872	0.37	848	missense	4	NST	basal-like
187	TP53	NM_000546	c.659A>G	p.(Tyr220Cys)	chr17:g.7674872	0.45	557	missense	4	NST	basal-like
188	TP53	NM_000546	c.659A>G	p.(Tyr220Cys)	chr17:g.7674872	0.66	902	missense	4	NST	basal-like
189	TP53	NM_000546	c.676_679del	p.(Gly226Leufs*20)	chr17:g.7674284_7674287	0.42	405	frameshift	5	NST	basal-like
190	TP53	NM_000546	c.683_686del	p.(Asp228Valfs*18)	chr17:g.7674277_7674280	0.27	1775	frameshift	5	NST	basal-like
191	TP53	NM_000546	c.688_689del	p.(Thr230Hisfs*9)	chr17:g.7674274_7674275	0.43	376	frameshift	5	NST	basal-like
192	TP53	NM_000546	c.722C>A	p.(Ser241Tyr)	chr17:g.7674241	0.53	2628	missense	4	NST	basal-like
193	TP53	NM_000546	c.723del	p.(Cys242Alafs*5)	chr17:g.7674240	0.35	1115	frameshift	5	NST	basal-like
194	TP53	NM_000546	c.723del	p.(Cys242Alafs*5)	chr17:g.7674240	0.23	535	frameshift	5	NST	basal-like
195	TP53	NM_000546	c.724T>A	p.(Cys242Ser)	chr17:g.7674239	0.3	1431	missense	4	NST	basal-like
196	TP53	NM_000546	c.726C>A	p.(Cys242*)	chr17:g.7674237	0.71	1476	stop gained	5	NST	basal-like
197	TP53	NM_000546	c.730_738dup	p.(Gly244_Met246dup)	chr17:g.7674225_7674233	0.25	934	inframe insertion	4	NST	basal-like
198	TP53	NM_000546	c.733_734delinsTT	p.(Gly245Phe)	chr17:g.7674229_7674230	0.17	597	missense	4	NST	basal-like
199	TP53	NM_000546	c.733G>C	p.(Gly245Arg)	chr17:g.7674230	0.46	764	missense	4	NST	basal-like
200	TP53	NM_000546	c.734G>A	p.(Gly245Asp)	chr17:g.7674229	0.38	198	missense	4	NST	basal-like
201	TP53	NM_000546	c.734G>A	p.(Gly245Asp)	chr17:g.7674229	0.22	118	missense	4	NST	basal-like
202	TP53	NM_000546	c.742C>T	p.(Arg248Trp)	chr17:g.7674221	0.53	210	missense	4	NST	basal-like
203	TP53	NM_000546	c.742C>T	p.(Arg248Trp)	chr17:g.7674221	0.13	1677	missense	4	NST	basal-like
204	TP53	NM_000546	c.742C>T	p.(Arg248Trp)	chr17:g.7674221	0.19	537	missense	4	NST	basal-like
205	TP53	NM_000546	c.742C>T	p.(Arg248Trp)	chr17:g.7674221	0.73	157	missense	4	NST	basal-like
206	TP53	NM_000546	c.743G>A	p.(Arg248Gln)	chr17:g.7674220	0.41	528	missense	5	NST	basal-like
207	TP53	NM_000546	c.743G>A	p.(Arg248Gln)	chr17:g.7674220	0.55	1065	missense	5	NST	basal-like
208	TP53	NM_000546	c.743G>A	p.(Arg248Gln)	chr17:g.7674220	0.2	149	missense	5	NST	basal-like
209	TP53	NM_000546	c.743G>A	p.(Arg248Gln)	chr17:g.7674220	0.44	481	missense	5	NST	basal-like

ID	gene	transcript	HGVS (nucleotide)	HGVS (protein)	genomic position (hg38)	VF	total reads	consequence	IARC-class	histology	PAM 50
210	TP53	NM_000546	c.752T>G	p.(Ile251Ser)	chr17:g.7674211	0.35	2350	missense	4	NST	basal-like
211	TP53	NM_000546	c.757A>C	p.(Thr253Pro)	chr17:g.7674206	0.7	187	missense	4	NST	basal-like
212	TP53	NM_000546	c.763dup	p.(Ile255Asnfs*9)	chr17:g.7674200	0.51	1202	frameshift	5	NST	basal-like
213	TP53	NM_000546	c.770_771del	p.(Leu257Argfs*6)	chr17:g.7674192_7674193	0.47	1325	frameshift	5	NST	basal-like
214	TP53	NM_000546	c.770del	p.(Leu257Argfs*88)	chr17:g.7674193	0.57	99	frameshift	5	NST	basal-like
215	TP53	NM_000546	c.770T>C	p.(Leu257Pro)	chr17:g.7674193	0.19	222	missense	4	NST	basal-like
216	TP53	NM_000546	c.785G>T	p.(Gly262Val)	chr17:g.7673835	0.41	699	missense	4	NST	basal-like
217	TP53	NM_000546	c.796G>C	p.(Gly266Arg)	chr17:g.7673824	0.59	698	missense	4	NST	basal-like
218	TP53	NM_000546	c.797G>A	p.(Gly266Glu)	chr17:g.7673823	0.31	502	missense	4	NST	basal-like
219	TP53	NM_000546	c.808T>A	p.(Phe270Ile)	chr17:g.7673812	0.13	98	missense	4	NST	missing
220	TP53	NM_000546	c.811G>T	p.(Glu271*)	chr17:g.7673809	0.11	1971	stop gained	5	NST	basal-like
221	TP53	NM_000546	c.817C>T	p.(Arg273Cys)	chr17:g.7673803	0.67	838	missense	4	NST	basal-like
222	TP53	NM_000546	c.817C>T	p.(Arg273Cys)	chr17:g.7673803	0.78	4233	missense	4	NST	HER2-E
223	TP53	NM_000546	c.817C>T	p.(Arg273Cys)	chr17:g.7673803	0.68	1856	missense	4	NST	basal-like
224	TP53	NM_000546	c.818G>A	p.(Arg273His)	chr17:g.7673802	0.47	567	missense	5	NST	basal-like
225	TP53	NM_000546	c.818G>A	p.(Arg273His)	chr17:g.7673802	0.29	235	missense	5	NST	basal-like
226	TP53	NM_000546	c.818G>A	p.(Arg273His)	chr17:g.7673802	0.64	153	missense	5	NST	basal-like
227	TP53	NM_000546	c.818G>A	p.(Arg273His)	chr17:g.7673802	0.25	2125	missense	5	NST	basal-like
228	TP53	NM_000546	c.818G>C	p.(Arg273Pro)	chr17:g.7673802	0.69	460	missense	4	NST	basal-like
229	TP53	NM_000546	c.821T>C	p.(Val274Ala)	chr17:g.7673799	0.55	2176	missense	4	NST	basal-like
230	TP53	NM_000546	c.827C>A	p.(Ala276Asp)	chr17:g.7673793	0.51	148	missense	4	NST	HER2-E
231	TP53	NM_000546	c.833C>G	p.(Pro278Arg)	chr17:g.7673787	0.24	515	missense	4	NST	normal-like
232	TP53	NM_000546	c.837_843dup	p.(Arg282Glufs*26)	chr17:g.7673777_7673783	0.1	1563	frameshift	5	NST	basal-like
233	TP53	NM_000546	c.838A>G	p.(Arg280Gly)	chr17:g.7673782	0.26	467	missense	4	NST	basal-like
234	TP53	NM_000546	c.839G>A	p.(Arg280Lys)	chr17:g.7673781	0.55	720	missense	4	NST	basal-like
235	TP53	NM_000546	c.844C>T	p.(Arg282Trp)	chr17:g.7673776	0.37	257	missense	4	NST	basal-like
236	TP53	NM_000546	c.856G>A	p.(Glu286Lys)	chr17:g.7673764	0.42	1029	missense	4	NST	basal-like
237	TP53	NM_000546	c.916C>T	p.(Arg306*)	chr17:g.7673704	0.61	2348	stop gained	5	NST	basal-like
238	TP53	NM_000546	c.957del	p.(Lys320Argfs*25)	chr17:g.7673571	0.24	690	frameshift	5	NST	normal-like
239	TP53	NM_000546	c.957del	p.(Lys320Argfs*25)	chr17:g.7673571	0.31	1182	frameshift	5	NST	normal-like
240	TP53	NM_000546	c.983dup	p.(Thr329Hisfs*8)	chr17:g.7673545	0.27	233	frameshift	5	NST	basal-like
241	PIK3CA	NM_006218	c.1633G>A	p.(Glu545Lys)	chr3:g.179218303	0.35	81	missense	5	NST	Lum A

ID	gene	transcript	HGVS (nucleotide)	HGVS (protein)	genomic position (hg38)	VF	total reads	consequence	IARC-class	histology	PAM 50
242	PIK3CA	NM_006218	c.1633G>A	p.(Glu545Lys)	chr3:g.179218303	0.25	208	missense	5	NST	normal-like
243	PIK3CA	NM_006218	c.3140A>G	p.(His1047Arg)	chr3:g.179234297	0.12	253	missense	5	NST	normal-like
244	PTEN	NM_000314	c.1006_1007del	p.(Tyr336Leufs*6)	chr10:g.87961098_87961099	0.12	168	frameshift	5	NST	normal-like
245	X									NST	basal-like
246	X									NST	basal-like
247	X									NST	basal-like
248	X									NST	basal-like
249	X									NST	HER2-E
250	X									NST	normal-like
251	X									NST	basal-like
252	X									NST	basal-like
253	X									NST	basal-like
254	X									NST	normal-like
255	X									NST	basal-like
256	X									NST	Lum A
257	X									NST	normal-like
258	X									NST	normal-like
259	X									NST	basal-like
260	X									NST	basal-like
261	X									NST	basal-like
262	X									NST	normal-like
263	X									NST	basal-like
264	X									NST	basal-like
265	X									NST	basal-like
266	X									NST	HER2-E

eTable 2: The detected tPVs (tumor pathogenic variants) with their exact genomic position (hg38) and consequence on nucleotide and protein level according to the HGVS nomenclature⁶, and the respective IARC-class¹ (4 = likely deleterious, 5 = deleterious variant) are shown. The variant fraction and total reads of the respective variant are given. Additionally histology and PAM50-subtype are displayed.
HER2-E = human epidermal growth factor 2 (HER2)-enriched, IARC = International Agency for Researchers on Cancer, Lum A = Luminal A, NST = invasive carcinoma of no special type, tPV = tumor pathogenic variants, VF = variant fraction, X = no tPV detected

eTable 3. Pathologic Complete Response Rate of Patients With Tumor Pathogenic Variants in Non-*BRCA1/2* Genes

A)			
tPV in following gene	pCR rate overall [%]	pCR rate gemcitabine [%]	pCR rate carboplatin [%]
<i>TP53</i> (n = 233)	37.3 (87/233)	27.9 (38/136)	50.5 (49/97)
<i>PIK3CA</i> (n = 22)	18.2 (4/22)	20 (2/10)	16.7 (2/12)
<i>PTEN</i> (n = 15)	26.7 (4/15)	12.5 (1/8)	42.9 (3/7)
<i>PALB2</i> (n = 5)	0 (0/5)	0 (0/2)	0 (0/3)
<i>BARD1</i> (n = 3)	66.7 (2/3)	0 (0/1)	100 (2/2)
<i>FANCM</i> (n = 3)	100 (3/3)	NA	100 (3/3)
<i>CDH1</i> (n = 2)	0 (0/2)	0 (0/2)	NA
<i>CHEK2</i> (n = 2)	50 (1/2)	50 (1/2)	NA
<i>RAD50</i> (n = 1)	0 (0/1)	0 (0/1)	NA
<i>RAD51C</i> (n = 1)	0 (0/1)	0 (0/1)	NA
<i>RAD51D</i> (n = 1)	0 (0/1)	0 (0/1)	NA
<i>STK11</i> (n = 1)	0 (0/1)	0 (0/1)	NA
<i>XRCC2</i> (n = 1)	0 (0/1)	NA	0 (0/1)
<i>MAP3K1</i> (n = 1)	0 (0/1)	0 (0/1)	NA

eTable 3: pCR rate in percentage [%] and in parenthesis No. of patients with pCR per total No. of patients with a tPV (tumor pathogenic variant) in the respective gene. The rate is shown overall and for each treatment arm.

As some tumors showed multiple tPVs and are shown with each respective gene, multiple referencing is possible.

NA = not applicable; carboplatin = nab-paclitaxel/carboplatin, gemcitabine = nab-paclitaxel/gemcitabine, pCR = pathologic complete response, tPV = tumor pathogenic variants, WT = wildtype

eTable 4. Clinical Parameters Included in the Multivariable Model

A) pCR		all		gemcitabine		carboplatin	
parameter		OR [95% CI]	p-value	OR [95% CI]	p-value	OR [95% CI]	p-value
Age ≥ 50 years		_ ^a		2.03 [0.89–4.64]	.09	_ ^a	
cT > 1		0.50 [0.28–0.88]	.02	0.47 [0.21–1.02]	.06	_ ^a	
cN > 0		_ ^a		_ ^a		_ ^a	
Grade 3		_ ^a		_ ^a		_ ^a	
Ki67 ≥ 75%		4.26 [2.36–7.70]	<.001	5.40 [2.19–13.34]	<.001	4.61 [2.02–10.53]	<.001
carboplatin-arm		3.08 [1.75–5.44]	<.001	NA		NA	
B) IDFS							
parameter		HR [95% CI]	p-value	HR [95% CI]	p-value	HR [95% CI]	p-value
Age ≥ 50 years		_ ^a		_ ^a		_ ^a	
cT > 1		_ ^a		_ ^a		_ ^a	
cN > 0		3.35 [2.04–5.49]	<.001	2.72 [1.42–5.21]	.002	4.58 [2.08–10.07]	<.001
Grade 3		_ ^a		_ ^a		_ ^a	
Ki67 ≥ 75%		_ ^a		_ ^a		_ ^a	
carboplatin-arm		_ ^a		NA		NA	
C) OS							
parameter		HR [95% CI]	p-value	HR [95% CI]	p-value	HR [95% CI]	p-value
Age ≥ 50 years		_ ^a		_ ^a		_ ^a	
cT > 1		_ ^a		_ ^a		_ ^a	
cN > 0		4.68 [2.57–8.52]	<.001	3.27 [1.49–7.20]	.003	7.40 [2.81–19.51]	<.001
Grade 3		_ ^a		_ ^a		_ ^a	
Ki67 ≥ 75%		_ ^a		_ ^a		_ ^a	
carboplatin-arm		_ ^a		NA		NA	

eTable 4: Overview of the clinical parameters included into multivariable analyses for the complete cohort and separated in both treatment arms with estimates (Odds ratio (OR) or Hazard ratio (HR) as appropriate) and 95% confidence intervals (CI) and p-values for the multivariable modelling in relevant clinical parameters. A) Pathologic complete response (pCR) with six patients excluded due to missing Ki67 assessments; B) invasive-disease free survival (IDFS); C) overall survival (OS).

a = parameter not selected, carboplatin = nab-paclitaxel/carboplatin, cN = clinical nodal status, cT = clinical tumor size, gemcitabine = nab-paclitaxel/gemcitabine, NA = not applicable

eTable 5. Multivariable Modeling of Genetic Subgroups for Pathologic Complete Response, Invasive Disease–Free Survival, and Overall Survival

A) pCR		overall		gemcitabine		carboplatin	
tPV		OR [95% CI]	p-value	OR [95% CI]	p-value	OR [95% CI]	p-value
<i>BRCA1/2</i> (n = 41)		1.87 [0.87–4.00]	.11	2.34 [0.88–6.19]	.09	1.47 [0.41–5.21]	.55
RCP genes (n = 20)		0.67 [0.22–2.02]	.47	0.26 [0.03–2.33]	.23	1.14 [0.28–4.65]	.85
<i>BRCA1/2</i> + RCP genes (n = 60)		1.40 [0.72–2.71]	.32	1.48 [0.61–3.60]	.39	1.36 [0.50–3.69]	.54
<i>TP53</i> (n = 231)		1.25 [0.47–3.30]	.66	1.47 [0.38–5.73]	.58	1.00 [0.24–4.20]	1.0
<i>PTEN</i> (n = 13)		0.48 [0.12–1.89]	.29	NA		0.91 [0.17–4.79]	.91
<i>PIK3CA</i> (n = 21)		0.28 [0.07–1.08]	.06	0.48 [0.06–4.26]	.51	0.25 [0.05–1.27]	.09
B) IDFS							
tPV		HR [95% CI]	p-value	HR [95% CI]	p-value	HR [95%CI]	p-value
<i>BRCA1/2</i> (n = 42)		1.06 [0.52–2.15]	.88	1.18 [0.52–2.70]	.69	0.78 [0.18–3.38]	.74
RCP genes (n = 20)		0.42 [0.13–1.35]	.14	0.91 [0.27–3.01]	.87	NA	
<i>BRCA1/2</i> + RCP genes (n = 61)		0.75 [0.40–1.40]	.37	1.12 [0.54–2.32]	.75	0.29 [0.07–1.22]	.09
<i>TP53</i> (n = 233)		2.81 [1.02–7.78]	.046	3.70 [0.89–15.43]	.07	1.94 [0.46–8.25]	.37
<i>PTEN</i> (n = 15)		1.02 [0.37–2.82]	.97	0.89 [0.21–3.70]	.87	1.28 [0.30–5.44]	.74
<i>PIK3CA</i> (n = 22)		1.61 [0.79–3.28]	.19	1.64 [0.58–4.68]	.35	1.65 [0.62–4.42]	.32
C) OS							
tPV		HR [95% CI]	p-value	HR [95% CI]	p-value	HR [95% CI]	p-value
<i>BRCA1/2</i> (n = 42)		1.00 [0.42–2.39]	.99	1.21 [0.45–3.24]	.70	0.57 [0.08–4.36]	.59
RCP genes (n = 20)		0.44 [0.11–1.84]	.26	0.98 [0.23–4.23]	.97	NA	
<i>BRCA1/2</i> + RCP genes (n = 61)		0.74 [0.34–1.59]	.44	1.17 [0.49–2.82]	.72	0.22 [0.03–1.65]	.14
<i>TP53</i> (n = 233)		2.03 [0.72–5.70]	.18	2.43 [0.57–10.35]	.23	1.49 [0.34–6.49]	.59
<i>PTEN</i> (n = 15)		0.76 [0.19–3.16]	.71	0.68 [0.09–5.06]	.71	0.91 [0.12–6.82]	.93
<i>PIK3CA</i> (n = 22)		1.49 [0.63–3.54]	.37	1.12 [0.26–4.80]	.88	1.83 [0.60–5.54]	.29

eTable 5: Odds ratio (OR) or Hazard ratio (HR), as appropriate, and 95% confidence intervals (CI) and p-values for the multivariable modelling according to the genetic subgroup.

A) Pathologic complete response rate (pCR), six patients excluded due to missing Ki67 assessments; B) invasive-disease free survival (IDFS); C) overall survival (OS).

Statistically significant ($p < .05$) and model relevant findings ($p < .157$) are displayed in bold letters. carboplatin = nab-paclitaxel/carboplatin, gemcitabine = nab-paclitaxel/gemcitabine, NA = not applicable; no estimation possible due to sparse data, RCP genes = rarely mutated cancer predisposition genes (*BARD1*, *CHEK2*, *CDH1*, *FANCM*, *PALB2*, *RAD50*, *RAD51C*, *RAD51D*, *STK11*, *XRCC2*), combined for statistical analyses due to sparse cases, tPV = tumor pathogenic variants

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