

**Supplementary Table S1****Bouwman et al.***BRCA1 variants used to validate the functional complementation assay.*

<b>Mutation</b>	<b>BIC classification<sup>a</sup></b>	<b>BIC reports<sup>a</sup></b>	<b>IARC class<sup>b</sup></b>	<b>Align GVD<sup>c</sup></b>
185delAG	deleterious	1988	5	NA
C61G	deleterious	230	5	C65
Y105C	neutral	18	1	C15
R866C	neutral	24	1	C65
E1250K	neutral	20	1	C0
R1699W	deleterious	14	5	C65
A1708E	deleterious	45	5	C65
5382insC	deleterious	1069	5	NA

<sup>a</sup><http://research.nhgri.nih.gov/bic/>.<sup>b</sup><http://brca.iarc.fr/LOVD/>.<sup>c</sup><http://agvgd.iarc.fr/>.

**Supplementary Table S2****Bouwman et al.***Low BRCA1 VUS protein levels are associated with structural instability.*

<b>Variant</b>	<b>Literature</b>	<b>Align GV-GD</b>
V1688del	less stable <sup>a</sup>	NA
G1706E	less stable <sup>b</sup>	C65
A1708E	less stable <sup>b,c</sup>	C65
L1764P	less stable <sup>b,c</sup>	C35
G1770V	no data	C0
A1789T	no data	C55
W1837R	less stable <sup>b,c</sup>	C65

<sup>a</sup>De Nicolo et al., Cancer Res. 2009;69:7030–7.<sup>b</sup>Lee et al., Cancer Res. 2010;70:4880–90.<sup>c</sup>Rowling et al., J. Biol. Chem. 2010;285:20080–7.

Results of the proliferation and cisplatin sensitivity assays for all tested BRCA1 variants.

Variants <sup>a</sup>	Series	Growth <sup>b</sup>	Cisplatin sensitivity assay			
			RSE	IC <sub>50c</sub>	Pval <sub>c</sub>	Classification <sup>c</sup>
WT_1A	1	+	0,0345	1,1079	0,0000	Neutral
WT_1B	1	+	0,0753	0,3063	0,0005	Neutral
WT_1C	2	+	0,0860	0,5562	0,0000	Neutral
WT_1D	2	+	0,0626	0,8580	0,0000	Neutral
WT_2A	3	+	0,0723	1,0549	0,0000	Neutral
WT_2B	3	+	0,0589	0,3593	0,0001	Neutral
WT_1E	4	+	0,0950	0,5643	0,0000	Neutral
WT_2C	4	+	<b>0,1108</b>	0,8499	0,0000	Neutral
WT_3A	5	+	0,0490	0,7071	0,0000	Neutral
WT_3B	6	+	0,0628	0,7071	0,0000	Neutral
WT_1F	7	+	0,0828	0,5547	0,0000	Neutral
WT_2D	7	+	<b>0,1340</b>	0,6877	0,0000	Neutral
WT_3C	7	+	0,0508	0,8790	0,0000	Neutral
WT_1H	9	+	0,0538	0,6846	0,0000	Neutral
WT_2F	9	+	0,0595	1,1495	0,0000	Neutral
WT_3E	9	+	0,0863	0,2872	0,0007	Neutral
Vector_1A	1	-	0,0592	-0,4033	1,0000	Deleterious
Vector_1B	1	-	0,0532	-1,0109	1,0000	Deleterious
Vector_1C	2	-	0,0606	-0,5466	1,0000	Deleterious
Vector_1D	2	-	0,0893	-0,8677	1,0000	Deleterious
Vector_2A	3	-	0,0915	-0,3294	1,0000	Deleterious
Vector_2B	3	-	0,0745	-1,0848	1,0000	Deleterious
Vector_1E	4	-	<b>0,1810</b>	-0,6018	1,0000	Deleterious
Vector_2C	4	-	0,0615	-0,8124	1,0000	Deleterious
Vector_3A	5	-	0,0400	-0,7071	1,0000	Deleterious
Vector_3B	6	-	0,0332	-0,7071	1,0000	Deleterious
Vector_1F	7	-	0,0402	-0,5778	1,0000	Deleterious
Vector_2D	7	-	0,0515	-0,8994	1,0000	Deleterious
Vector_3C	7	-	0,0865	-0,6442	1,0000	Deleterious
Vector_1H	9	-	0,0816	-1,1100	1,0000	Deleterious
Vector_2F	9	-	0,0738	-0,6389	1,0000	Deleterious
Vector_3E	9	-	0,0930	-0,3724	1,0000	Deleterious
S4F_A	5	+	0,0647	0,1232	0,0409	Neutral
S4F_B	6	+/-	0,0544	-0,6589	1,0000	Deleterious
S4F_C	7	+	0,1083	0,0950	0,0781	Deleterious
S4F_E	9	+/-	0,0552	0,7112	0,0000	Neutral
M18T_A	1	-	0,0885	-1,0506	1,0000	Deleterious
M18T_B	4	-	<b>0,1061</b>	-2,0627	1,0000	Deleterious
M18T_C	7	-	0,0642	-0,9694	1,0000	Deleterious
185delAG_A	1	-	0,0394	-0,8973	1,0000	Deleterious
185delAG_B	4	-	0,0858	-2,0947	1,0000	Deleterious
K45Q_A	1	+	0,0790	2,9466	0,0000	Neutral
C61G_A	3	+/-	0,0600	-0,0888	1,0000	Deleterious
C61G_B	4	+/-	0,0469	-1,2589	1,0000	Deleterious

Variants <sup>a</sup>	Series	Growth <sup>b</sup>	Cisplatin sensitivity assay			
			RSE	IC <sub>50c</sub>	Pval <sub>c</sub>	Classification <sup>c</sup>
C61G_C	6	-	0,0965	-1,1279	1,0000	Deleterious
C64G_A	5	-	0,0886	-1,3934	1,0000	Deleterious
C64G_1B	6	-	<b>0,1202</b>	-0,1074	1,0000	Deleterious
C64G_1C	7	-	<b>0,1575</b>	-0,5623	1,0000	Deleterious
C64G_2B	9	-	0,0564	-0,8290	1,0000	Deleterious
D67Y_A	1	+	0,0818	1,4549	0,0000	Neutral
Y105C_A	1	+	0,0381	1,3694	0,0000	Neutral
N132K_A	3	+	0,0381	1,7084	0,0000	Neutral
P142H_A	1	+	0,0518	1,8785	0,0000	Neutral
L147F_A	1	+	0,0362	1,4328	0,0000	Neutral
L165P_A	1	+	0,0505	1,2680	0,0000	Neutral
R170W_A	5	+	0,0754	2,4403	0,0000	Neutral
R170W_B	6	+	0,0460	1,3542	0,0000	Neutral
S186Y_A	1	+	0,0638	1,7449	0,0000	Neutral
V191I_A	5	+	0,0861	2,1697	0,0000	Neutral
V191I_B	6	+	0,0394	2,5241	0,0000	Neutral
T231M_A	1	+	0,0584	0,8223	0,0000	Neutral
D245V_A	1	+	0,0341	1,8975	0,0000	Neutral
L246V_A	1	+	0,0352	1,7224	0,0000	Neutral
V271L_A	1	+	0,0507	3,5869	0,0000	Neutral
V271L_B	4	+	<b>0,1512</b>	3,1220	0,0000	Neutral
V271L_C	7	+	0,0960	1,4044	0,0000	Neutral
S308A_A	3	+	<b>0,1251</b>	2,8371	0,0000	Neutral
S308A_B	7	+	<b>0,1280</b>	1,5743	0,0000	Neutral
R358LXCXE_A	3	+	0,0368	2,4925	0,0000	Neutral
L668F_A	2	+	0,0342	2,0243	0,0000	Neutral
D695N_A	2	+	0,0642	0,7509	0,0000	Neutral
D695N_B	4	+	0,0660	2,4188	0,0000	Neutral
P798L_A	1	+	0,0677	0,9712	0,0000	Neutral
N810Y_A	1	+	0,0466	0,8292	0,0000	Neutral
T826K_A	1	+	0,0372	1,7506	0,0000	Neutral
R841Q_A	2	+	0,0501	0,6357	0,0000	Neutral
R841Q_B	4	+	0,0570	3,0412	0,0000	Neutral
Y856H_A	2	+	0,0644	1,1639	0,0000	Neutral
R866C_A	1	+	0,0471	1,4701	0,0000	Neutral
S988A_A	1	+	0,0686	1,7358	0,0000	Neutral
M1008I_A	1	+	0,0691	1,6555	0,0000	Neutral
E1060A_A	2	+	0,0696	1,9215	0,0000	Neutral
S1101N_A	3	+	0,0477	0,9973	0,0000	Neutral
K1110del_A	3	+	<b>0,1055</b>	0,9948	0,0000	Neutral
K1110del_B	7	+	0,0793	1,2176	0,0000	Neutral
S1140G_A	1	+	0,0478	1,7748	0,0000	Neutral
E1214K_A	1	+	0,0589	1,5939	0,0000	Neutral
N1236K_A	3	+	0,0668	2,2793	0,0000	Neutral
E1250K_A	1	+	0,0381	0,6524	0,0000	Neutral
E1250K_B	4	+	<b>0,2051</b>	2,6733	0,0000	Neutral
E1250K_C	7	+	<b>0,1007</b>	0,2484	0,0020	Neutral
L1267S_A	3	+	0,0350	2,7494	0,0000	Neutral
E1282V_A	1	+	0,0489	0,8747	0,0000	Neutral
S1297del_A	3	+	0,0593	1,2943	0,0000	Neutral
S1301R_A	3	+	0,0979	1,1843	0,0000	Neutral

Variants <sup>a</sup>	Series	Growth <sup>b</sup>	Cisplatin sensitivity assay			
			RSE	IC <sub>50c</sub>	Pval <sub>c</sub>	Classification <sup>c</sup>
E1346K_A	1	+	0,0509	0,8768	0,0000	Neutral
V1378I_A	3	+	0,0557	1,7250	0,0000	Neutral
M1400V_A	3	+	0,0816	1,6125	0,0000	Neutral
L1407P_A	2	+	0,0842	0,4587	0,0000	Neutral
L1407P_B	4	+	<b>0,1380</b>	0,3290	0,0003	Neutral
L1407P_C	7	+	<b>0,1040</b>	-0,0580	1,0000	Deleterious
M1411T_A	2	+	0,0525	1,0698	0,0000	Neutral
R1443G_A	3	+	0,0584	0,9479	0,0000	Neutral
S1448G_A	3	+	0,0889	2,4780	0,0000	Neutral
S1486C_A	5	+	0,0346	0,6437	0,0000	Neutral
S1486C_B	6	+	0,0354	0,7585	0,0000	Neutral
S1497A_A	2	+	0,0430	1,5440	0,0000	Neutral
V1534M_A	3	+	0,0746	0,6665	0,0000	Neutral
R1589P_A	5	+	0,0507	0,3069	0,0005	Neutral
R1589P_B	6	+	0,0390	1,7003	0,0000	Neutral
M1628T_A	2	+	0,0492	2,1699	0,0000	Neutral
S1651P_1A	5	-	0,0869	-1,4827	1,0000	Deleterious
S1651P_1B	6	-	0,0985	-1,6377	1,0000	Deleterious
S1651P_2B	9	+	0,0665	0,1257	0,0389	Neutral
S1651F_A	5	+/-	0,0916	-1,0131	1,0000	Deleterious
S1651F_B	6	+	0,0238	0,8010	0,0000	Neutral
S1651F_C	7	+	0,0453	0,3853	0,0001	Neutral
S1651F_E	9	+	0,0478	0,4712	0,0000	Neutral
M1652I_A	2	+	0,0575	0,8336	0,0000	Neutral
S1655F_1A	2	+/-	0,0585	0,1120	0,0530	Deleterious
S1655F_1B	4	+/-	0,0557	-0,5597	1,0000	Deleterious
S1655F_1D	9	-	0,0545	-0,7457	1,0000	Deleterious
S1655F_2A	5	+/-	0,0966	-0,0019	0,5829	Deleterious
S1655F_2C	9	+/-	0,0644	-0,3953	1,0000	Deleterious
H1686R_A	2	-	0,0702	-0,8099	1,0000	Deleterious
H1686R_B	4	+/-	<b>0,1181</b>	-2,2835	1,0000	Deleterious
H1686R_C	7	+/-	0,0556	-0,5733	1,0000	Deleterious
H1686Q_1A	5	-	0,0831	-1,2761	1,0000	Deleterious
H1686Q_1B	6	-	0,0758	-1,0652	1,0000	Deleterious
H1686Q_2B	9	-	0,0828	-1,0395	1,0000	Deleterious
V1688del_A	2	-	0,0571	-0,8492	1,0000	Deleterious
V1688del_B	4	+/-	<b>0,1295</b>	-1,6687	1,0000	Deleterious
V1688del_C	7	+/-	0,0989	-0,6382	1,0000	Deleterious
T1691I_A	5	-	<b>0,1028</b>	-1,7344	1,0000	Deleterious
T1691I_B	6	-	0,0708	-1,8155	1,0000	Deleterious
T1691I_C	7	-	<b>0,1040</b>	-0,5493	1,0000	Deleterious
R1699Q_A	2	+/-	0,0901	-0,6949	1,0000	Deleterious
R1699Q_B	4	+	0,0651	-0,3181	1,0000	Deleterious
R1699Q_C	7	+	<b>0,1089</b>	-0,2861	1,0000	Deleterious
R1699W_A	2	-	0,0579	-0,7304	1,0000	Deleterious
R1699W_B	4	+/-	0,0932	-1,6656	1,0000	Deleterious
G1706E_A	2	-	0,0512	-0,2735	1,0000	Deleterious
G1706E_B	4	+/-	<b>0,1413</b>	-1,1738	1,0000	Deleterious
G1706E_C	7	+/-	0,0387	-0,5879	1,0000	Deleterious
G1706A_A	2	+	0,0560	1,5162	0,0000	Neutral
A1708E_A	2	-	0,0632	-0,3318	1,0000	Deleterious

Variants <sup>a</sup>	Series	Growth <sup>b</sup>	Cisplatin sensitivity assay			
			RSE	IC <sub>50c</sub>	Pval <sub>c</sub>	Classification <sup>c</sup>
A1708E_B	4	-	<b>0,1226</b>	-1,4028	1,0000	Deleterious
A1708E_C	7	+/-	0,0390	-0,3277	1,0000	Deleterious
W1718C_1A	5	-	0,0622	-1,2632	1,0000	Deleterious
W1718C_1B	6	-	0,0628	-1,6730	1,0000	Deleterious
W1718C_2B	9	-	0,0559	-0,4434	1,0000	Deleterious
T1720A_A	2	+	0,0593	1,7747	0,0000	Neutral
E1735K_A	5	-	<b>0,1285</b>	-1,6796	1,0000	Deleterious
E1735K_B	6	-	0,0842	-1,8444	1,0000	Deleterious
E1735K_C	7	-	<b>0,1234</b>	-0,8332	1,0000	Deleterious
V1736A_A	5	+/-	0,0713	-0,4206	1,0000	Deleterious
V1736A_B	6	+/-	0,0300	0,2465	0,0020	Neutral
V1736A_D	9	+/-	0,0631	0,1519	0,0209	Neutral
D1739V_A	2	-	0,0620	0,1062	0,0604	Deleterious
D1739V_B	4	+/-	0,0905	-1,0330	1,0000	Deleterious
D1739V_D	9	-	0,0783	-0,9813	1,0000	Deleterious
D1739G_1A	2	-	0,0742	-0,7609	1,0000	Deleterious
D1739G_1B	4	-	0,0762	-1,8849	1,0000	Deleterious
D1739G_2A	5	-	0,0546	-1,1529	1,0000	Deleterious
H1746Q_1A	5	-	0,0670	-1,1908	1,0000	Deleterious
H1746Q_1B	6	-	0,0551	-0,9436	1,0000	Deleterious
H1746Q_2B	9	+	0,0608	0,2019	0,0061	Neutral
R1753T_A	5	+	0,0358	0,9632	0,0000	Neutral
R1753T_B	6	+/-	0,0436	-0,0791	1,0000	Deleterious
R1753T_C	7	-	<b>0,1037</b>	-0,5898	1,0000	Deleterious
R1753T_E	9	+/-	0,0746	-0,0704	1,0000	Deleterious
5382insC_A	2	+/-	0,0754	0,5319	0,0000	Neutral
5382insC_B	4	-	0,0407	-1,1736	1,0000	Deleterious
5382insC_D	9	-	0,0547	-0,7466	1,0000	Deleterious
L1764P_A	2	+/-	0,0501	0,0010	0,5596	Deleterious
L1764P_B	4	-	0,0776	-1,5545	1,0000	Deleterious
L1764P_D	9	-	0,0364	-0,8385	1,0000	Deleterious
C1767S_A	5	+	0,0619	2,4716	0,0000	Neutral
C1767S_B	6	+	0,0427	0,4970	0,0000	Neutral
G1770V_A	3	+/-	0,0575	-0,0695	1,0000	Deleterious
G1770V_B	4	+/-	0,0899	-0,3865	1,0000	Deleterious
G1770V_D	9	-	0,0454	-0,8780	1,0000	Deleterious
W1782C_A	2	+	0,0646	0,7391	0,0000	Neutral
A1789T_1A	5	-	0,0348	-1,4200	1,0000	Deleterious
A1789T_1B	6	-	0,0788	-1,2525	1,0000	Deleterious
A1789T_2B	9	-	0,0635	-0,9476	1,0000	Deleterious
E1794D_A	2	+	0,0744	1,3308	0,0000	Neutral
V1804D_A	2	+	0,0582	1,0883	0,0000	Neutral
P1812R_A	3	+	0,0316	1,8815	0,0000	Neutral
W1837R_A	5	-	0,0592	-1,3334	1,0000	Deleterious
W1837R_B	6	-	0,0653	-1,0818	1,0000	Deleterious
H1862L_A	3	+	0,0787	1,5076	0,0000	Neutral

<sup>a</sup>Data include biological repeat experiments (A-H) and independently transfected replicas if applicable (1-3).

<sup>b</sup>The ability to support growth is indicated by + (as BRCA1 wild-type controls or more), +/- (between BRCA1 wild-type controls and empty RMCE vector controls) or - (as

empty RMCE vector controls or less).

°Functional classification is based on the corrected p value for cisplatin sensitivity. WT = BRCA1 wild-type, Vector = empty RMCE vector, RSE = residual square error (values above 0.1 indicated in bold),  $IC_{50c}$  = corrected cisplatin  $IC_{50}$  value, and  $Pval_c$  = p value for classification.

**Supplementary Table S4**

**Bouwman et al.**

*Comparison of in silico and literature predictions with the classification of all BRCA1 variants analyzed.*

Variant	DNA change	Type of mutation <sup>a</sup>	Align GVGD <sup>b</sup>	Predicted splice effect <sup>c</sup>	Literature predictions <sup>d</sup>	Growth <sup>e</sup>	IC <sub>50c</sub> (a.u.)	Classification
S4F	c.11C>T	VUS <sup>f</sup>	C0	No	ND	+/- to +	-0.66 to 0.71	Not Clear
M18T	c.53T>C	VUS <sup>f,g</sup>	C45	No	No consensus	-	-1.05 to -0.97	Deleterious
185delAG	c.68_69delAG	Deleterious control <sup>h</sup>	ND	ND	Known deleterious <sup>l</sup>	-	-2.09 to -0.90	Deleterious <sup>n</sup>
K45Q	c.133A>C	VUS <sup>f</sup>	C0	No <sup>k</sup>	Neutral	+	2.95	Neutral
C61G	c.181T>G	Deleterious control <sup>h</sup>	C65	No	Known deleterious <sup>l</sup>	- to +/-	-1.26 to -0.09	Deleterious
C64G	c.190T>G	VUS <sup>f</sup>	C65	Yes	Deleterious <sup>m</sup>	-	-1.40 to -0.83	Deleterious <sup>n</sup>
D67Y	c.199G>T	VUS <sup>f,g</sup>	C0	No	Neutral	+	1.45	Neutral
Y105C	c.314A>G	Neutral control <sup>f,g</sup>	C15	No	Known neutral <sup>l</sup>	+	1.37	Neutral
N132K	c.396C>A	VUS <sup>f,g</sup>	C0	No	No consensus	+	1.71	Neutral
P142H	c.425C>A	VUS <sup>g</sup>	C0	No	No consensus	+	1.88	Neutral
L147F	c.441G>C	VUS <sup>f</sup>	C0	Yes <sup>k</sup>	ND	+	1.43	Neutral
L165P	c.494T>C	VUS <sup>f</sup>	C25	No	ND	+	1.27	Neutral
R170W	c.508C>T	VUS <sup>f</sup>	C25	No	ND	+	1.35 to 2.44	Neutral
S186Y	c.557C>A	VUS <sup>g</sup>	C15	No	Predicted neutral	+	1.74	Neutral
V191I	c.571G>A	VUS <sup>f,g</sup>	C0	No	Predicted neutral	+	2.17 to 2.52	Neutral
T231M	c.692C>T	VUS <sup>f</sup>	C0	No	ND	+	0.82	Neutral
D245V	c.734A>T	VUS <sup>f</sup>	C0	No	ND	+	1.90	Neutral
L246V	c.736T>G	VUS	C0	No	No consensus	+	1.72	Neutral
V271L	c.811G>C	VUS <sup>f</sup>	C0	No	Predicted neutral	+	1.40 to 3.59	Neutral
S308A	c.922A>G; c.923G>C	Artificial <sup>h</sup>	ND	ND	Predicted deleterious <sup>h</sup>	+	NS	Not Clear
R358LXCXE	c.1073T>G; c.1078T>C; c.1084G>C; c.1086G>T	Artificial <sup>h</sup>	ND	ND	Neutral <sup>h</sup>	+	2.49	Neutral
L668F	c.2002C>T	VUS <sup>f,g</sup>	C0	No	Predicted neutral	+	2.02	Neutral
D695N	c.2083G>A	VUS <sup>f</sup>	C0	No	Neutral	+	0.75 to 2.42	Neutral



Variant	DNA change	Type of mutation <sup>a</sup>	Align GVD <sup>b</sup>	Predicted splice effect <sup>c</sup>	Literature predictions <sup>d</sup>	Growth <sup>e</sup>	IC <sub>50c</sub> (a.u.)	Classification
P798L	c.2393C>T	VUS <sup>f</sup>	C0	No	ND	+	0.97	Neutral
N810Y	c.2428A>T	VUS <sup>g</sup>	C0	No	No consensus	+	0.83	Neutral
T826K	c.2477C>A	VUS <sup>f</sup>	C0	No	Neutral	+	1.75	Neutral
R841Q	c.2522G>A	VUS <sup>f</sup>	C0	No	ND	+	0.64 to 3.04	Neutral
Y856H	c.2566T>C	VUS <sup>f</sup>	C0	No	Neutral	+	1.16	Neutral
R866C	c.2596C>T	Neutral control <sup>f,g</sup>	C65	No	Known neutral <sup>l</sup>	+	1.47	Neutral
S988A	c.2962T>G	Artificial <sup>h</sup>	C0	No	Neutral <sup>h</sup>	+	1.74	Neutral
M1008I	c.3024G>A	VUS <sup>f</sup>	C0	No	Neutral	+	1.66	Neutral
E1060A	c.3179A>C	VUS <sup>f</sup>	C0	No	Deleterious	+	1.92	Neutral
S1101N	c.3302G>A	VUS <sup>f,g</sup>	C0	No	Neutral	+	1.00	Neutral
K1110del	c.3328_3330 delAAG	VUS <sup>f</sup>	ND	ND	ND	+	1.22	Neutral
S1140G	c.3418A>G	VUS <sup>f</sup>	C0	No	Neutral	+	1.77	Neutral
E1214K	c.3640G>A	VUS <sup>f,g</sup>	C0	No	Neutral	+	1.59	Neutral
N1236K	c.3708T>G	VUS <sup>f</sup>	C0	No	Neutral	+	2.28	Neutral
E1250K	c.3748G>A	Neutral control <sup>f</sup>	C0	No	Known neutral <sup>l</sup>	+	0.65	Neutral
L1267S	c.3800T>C	VUS <sup>f</sup>	C0	No	ND	+	2.75	Neutral
E1282V	c.3845A>T	VUS <sup>f</sup>	C0	Yes	ND	+	0.87	Neutral
S1297del	c.3891_3893 delTTC	VUS <sup>f</sup>	ND	ND	ND	+	1.29	Neutral
S1301R	c.3903T>A	VUS <sup>f</sup>	C0	No	ND	+	1.18	Neutral
E1346K	c.4036G>A	VUS <sup>f</sup>	C0	No	Neutral	+	0.88	Neutral
V1378I	c.4132G>A	VUS <sup>f</sup>	C0	No	Neutral	+	1.72	Neutral
M1400V	c.4198A>G	VUS <sup>i</sup>	C0	No	Deleterious	+	1.61	Neutral
L1407P	c.4220T>C	VUS <sup>i</sup>	C65	No	Deleterious	+	0.46	Neutral <sup>n</sup>
M1411T	c.4232T>C	VUS <sup>i</sup>	C65	No	Deleterious <sup>i</sup>	+	1.07	Neutral
R1443G	c.4327C>G	VUS <sup>f</sup>	C0	No	Inconclusive	+	0.95	Neutral
S1448G	c.4342A>G	VUS <sup>f</sup>	C0	No	ND	+	2.48	Neutral
S1486C	c.4456A>T	VUS <sup>f</sup>	C0	No	ND	+	0.64 to 0.76	Neutral
S1497A	c.4489T>G	Artificial <sup>h</sup>	C0	Yes	Deleterious <sup>d,h</sup>	+	1.54	Neutral
V1534M	c.4600G>A	VUS <sup>g</sup>	C0	No	Neutral	+	0.67	Neutral

Variant	DNA change	Type of mutation <sup>a</sup>	Align GVGDb <sup>b</sup>	Predicted splice effect <sup>c</sup>	Literature predictions <sup>d</sup>	Growth <sup>e</sup>	IC <sub>50c</sub> (a.u.)	Classification
R1589P	c.4766G>C	VUS <sup>f</sup>	C0	No	ND	+	0.31 to 1.70	Neutral
M1628T	c.4883T>C	VUS <sup>f</sup>	C0	No	Neutral	+	2.17	Neutral
S1651P	c.4951T>C	VUS <sup>f</sup>	C0	No	ND	- to +	-1.64 to 0.13	Not Clear
S1651F	c.4952C>T	VUS <sup>fj</sup>	C0	No	Neutral	+/- to +	-1.01 to 0.80	Not Clear
M1652I	c.4956G>A	VUS <sup>hj</sup>	C0	No	No consensus	+	0.83	Neutral
S1655F	c.4964C>T	VUS <sup>i</sup>	C25	No	Deleterious	- to +/-	-0.75 to 0.03	Deleterious <sup>n</sup>
H1686R	c.5057A>G	VUS <sup>f</sup>	C25	No	ND	- to +/-	-0.81 to -0.57	Deleterious
H1686Q	c.5058T>A	VUS <sup>f</sup>	C15	No	ND	-	-1.28 to -1.04	Deleterious
V1688del	c.5062_5064 delGTT	VUS <sup>g</sup>	ND	ND	Deleterious <sup>g</sup>	- to +/-	-0.85 to -0.64	Deleterious
T1691I	c.5072C>T	VUS <sup>fj</sup>	C65	Yes <sup>k</sup>	Deleterious	-	-1.82	Not Clear
R1699W	c.5095C>T	Deleterious control <sup>l</sup>	C65	No	Known deleterious <sup>l</sup>	- to +/-	-1.67 to -0.73	Deleterious <sup>n</sup>
R1699Q	c.5096G>A	VUS <sup>fj</sup>	C35	No	No consensus	+	-0.69 to -0.32	Deleterious <sup>n</sup>
G1706E	c.5117G>A	VUS <sup>gj</sup>	C65	No	Deleterious	- to +/-	-0.59 to -0.27	Deleterious <sup>n</sup>
G1706A	c.5117G>C	VUS <sup>fj</sup>	C55	No	No consensus	+	1.52	Neutral
A1708E	c.5123C>A	Deleterious control <sup>h,gj</sup>	C65	No	Known deleterious <sup>l</sup>	- to +/-	-0.33 to -0.33	Deleterious
W1718C	c.5154G>T	VUS <sup>i</sup>	C65	No <sup>k</sup>	Deleterious	-	-1.67 to -0.44	Deleterious
T1720A	c.5158A>G	VUS <sup>f,gj</sup>	C0	No	Neutral	+	1.77	Neutral
E1735K	c.5203G>A	VUS <sup>f</sup>	C55	No	ND	-	-1.84	Not Clear
V1736A	c.5207T>C	VUS <sup>i</sup>	C65	No	No consensus	+/-	-0.42 to 0.25	Not Clear <sup>n</sup>
D1739G	c.5216A>G	VUS <sup>fj</sup>	C65	Yes	Deleterious	-	-1.88 to -0.76	Deleterious
D1739V	c.5216A>T	VUS <sup>fj</sup>	C65	No	Deleterious	- to +/-	-1.03 to 0.11	Deleterious
H1746Q	c.5238C>G	VUS <sup>f</sup>	C15	No	ND	- to +	-1.19 to 0.20	Not Clear
R1753T	c.5258G>C	VUS <sup>fj</sup>	C65	No	Deleterious	- to +	-0.08 to 0.96	Not Clear <sup>n</sup>
5382insC	c.5266dupC	Deleterious control <sup>h</sup>	ND	ND	Known deleterious <sup>l</sup>	- to +/-	-1.17 to 0.53	Not Clear <sup>n</sup>
L1764P	c.5291T>C	VUS <sup>fj</sup>	C25	No	No consensus	- to +/-	-1.55 to 0.00	Deleterious <sup>n</sup>
C1767S	c.5300G>C	VUS <sup>f</sup>	C0	No	ND	+	0.50 to 2.47	Neutral
G1770V	c.5309G>T	VUS <sup>f</sup>	C0	No	ND	- to +/-	-0.88 to -0.07	Deleterious <sup>n</sup>
W1782C	c.5346G>T	VUS <sup>f</sup>	C15	No	ND	+	0.74	Neutral
A1789T	c.5365G>A	VUS <sup>f</sup>	C55	Yes	Neutral	-	-1.42 to -0.95	Deleterious

Variant	DNA change	Type of mutation <sup>a</sup>	Align GVD <sup>b</sup>	Predicted splice effect <sup>c</sup>	Literature predictions <sup>d</sup>	Growth <sup>e</sup>	IC <sub>50c</sub> (a.u.)	Classification
E1794D	c.5382G>C	VUS <sup>fj</sup>	C0	No	Neutral	+	1.33	Neutral
V1804D	c.5411T>A	VUS <sup>hj</sup>	C0	No	No consensus	+	1.09	Neutral
P1812R	c.5435C>G	VUS <sup>f</sup>	C15	No	ND	+	1.88	Neutral
W1837R	c.5509T>C	VUS <sup>fj</sup>	C65	No	No consensus	-	-1.33 to -1.08	Deleterious
H1862L	c.5585A>T	VUS <sup>f</sup>	C0	No	ND	+	1.51	Neutral

<sup>a</sup> Type of mutation indicates if variants are a VUS according to the BIC database (<http://research.nhgri.nih.gov/bic/>).

<sup>b</sup> Align GVD score (<http://agvgd.iarc.fr/>).

<sup>c</sup> Splice effect predictions are derived from information on the IARC website (<http://brca.iarc.fr/>), the predicted chance that missense mutations create or damage splice sites is indicated with yes (moderate or increased probability) or no (null, weak or low probability).

<sup>d</sup> Literature predictions are derived from the Leiden Open Variation Database ([http://chromium.liacs.nl/LOVD2/cancer/home.php?select\\_db=BRCA1](http://chromium.liacs.nl/LOVD2/cancer/home.php?select_db=BRCA1)), unless indicated otherwise.

<sup>e</sup> The ability to support growth is indicated by + (as BRCA1 wild-type controls or more), +/- (between BRCA1 wild-type controls and empty RMCE vector controls) or - (as empty RMCE vector controls or less).

<sup>f</sup> Dutch/Belgian VUS.

<sup>g</sup> Easton et al., *Am. J. Hum. Genet.* 2007;81:873–83.

<sup>h</sup> Chang et al., *J. Clin. Invest.* 2009;119:3160–71.

<sup>i</sup> Sy et al., *Proc. Natl. Acad. Sci. U.S.A.* 2009;106:7155–60.

<sup>j</sup> Lee et al., *Cancer Res.* 2010;70:4880–90.

<sup>k</sup> Mutation in a 5' or 3' consensus splice site.

<sup>l</sup> Classified in the BIC database.

<sup>m</sup> Predicted deleterious according to Morris et al., *Hum. Mol. Genet.* 2006;15:599–606 and Ransburgh et al., *Cancer Res.* 2010;70:988–95.

<sup>n</sup> Functionally impaired in the DR-GFP and/or combined PARP inhibitor/cisplatin sensitivity assay.

IC<sub>50c</sub> = corrected cisplatin IC<sub>50</sub> value, ND = Not Determined, NS = Not Significant because of RSE>0.1.