Supplementary Tables

Supplementary Table S1. RNA-seq analyses of global exon splicing events. *BRCA1* exon 11 mutant cell lines expressed higher mRNA and protein levels of the *BRCA1-Δ11q* alternative splice variant compared with cell lines with *BRCA1* mutations located outside of exon 11 (Fig. 1C). To investigate the possibility that *BRCA1-Δ11q* expression was higher in exon 11 mutant cell lines because of a global increase in alternative exon splicing, we carried out RNA-seq analyses and measured the number of unique exon-exon junctions (predicted to be a result of alternative exon splicing) in comparisons of cell lines with exon 11 mutations (SUM149PT, UWB1.289) versus those with mutations located outside of exon 11 (HCC1395, MDA-MB-436). Table 1 show comparisons carried out and the number of unique splicing events found in each cell line in that particular comparison. In conclusion, there were no differences in the number of unique events in comparisons between cell lines with *BRCA1* mutations inside versus outside of exon 11. Therefore, we do not believe the cell lines with exon 11 mutations have an overall increased level of global splicing.

Comparisons	Unique in exon 11	Unique in non-exon 11
SUM149PT vs HCC1395	775	772
SUM149PT vs MDA-MB-436	592	411
UWB1.289 vs HCC1395	601	719
UWB1.289 vs MDA-MB-436	405	309
Total events	2373	2211

Supplementary Table S2. Cell line therapy sensitivities. Mean LC50 values (n = 3) for cell lines treated with rucaparib, olaparib, cisplatin and taxol shown in Fig. 2B, were used to calculate fold changes in sensitivity, compared to MDA-MB-231 cells. Additionally, mean LC50 values (n = 3) for SUM149PT and UWB1.289 cells with non-target (NT), BRCA1 shRNA #1 and #2 treated with rucaparib or cisplatin from Fig. 2E, were used to calculate fold changes in sensitivity compared to respective NT cells. *P* values (unpaired *t*-test) are provided in parenthesis.

Cell lines	Rucaparib (nM)	Olaparib (nM)	Cisplatin (ng/ml)	Taxol (nM)
MDA-MB-231	1	1	1	1
MCF7	1.2 (0.389)	1.6 (0.067)	1.8 (0.0185)	2.1 (0.1056)
MDA-MB-468	1.5 (0.1808)	1.4 (0.0791)	2 (0.0096)	2.7 (0.0496)
L56Br-C1	4.9 (0.0043)	1.7 (0.031)	3.2 (0.0037)	0.6 (0.0323)
SUM149PT	7.2 (0.003)	8.2 (0.0008)	5.9 (0.0013)	0.4 (0.0102)
UWB1.289	9.1 (0.0027)	10.3 (0.0005)	4.2 (0.0021)	1.1 (0.7379)
SUM1315	95.3 (0.0017)	3326.7 (0.0003)	10.3 (0.001)	1.1 (0.6838)
HCC1395	200.5 (0.0016)	4216.9 (0.0003)	11.5 (0.0009)	0.4 (0.0072)
MDA-MB-436	173.2 (0.0016)	11976 (0.0003)	21.4 (0.0008)	0.6 (0.0715)
SUM149PT+NT	1		1	
SUM149PT+B1#1	12.2 (0.0082)		2.1 (0.0455)	
SUM149PT+B1#2	34.5 (0.0064)		3.7 (0.0206)	
UWB1.289+NT	1		1	
UWB1.289+B1#1	14.3 (0.0201)		2.2 (0.0246)	
UWB1.289+B1#2	26.7 (0.0177)		2.7 (0.0153)	

Supplementary Table S3. Hazard ratios for survival of patients with serous ovarian carcinomas associated with *BRCA1* mutation, age at diagnosis and stage (Fig. 5A). Data were evaluated for 1,712 participants and grouped according to whether mutations were located inside versus outside exon 11 (missense and intronic variants were excluded from the analyses). In a Cox regression model, adjusted for age at diagnosis, stage, study and year of diagnosis, the hazard ratio for participants with *BRCA1* frameshift mutations outside of exon 11 was 0.76 (95% CI, 0.61-0.94; $P = 0.01$) and the hazard ratio for participants with frameshift mutations inside of exon 11 was 0.79 (95% CI, 0.57-1.09; $P = 0.15$).

	HR	95% CI	*P* Value
BRCA 1 mutation			
Noncarriers	1	Referent	
FS outside of exon 11	0.76	0.61 – 0.94	0.01
FS inside of exon 11	0.79	0.57 – 1.09	0.15
Stage			
Early	1	Referent	
Advanced	3.26	2.47 – 4.30	<0.001
Grade			
Low	1	Referent	
High	2.18	1.60 – 2.98	<0.001
Age at diagnosis	1.02	1.02 – 1.03	<0.001

Supplementary Table S4. Characteristics of studies included in survival analysis from Fig. 5A.

Study	Study	Country	Noncarrier	*BRCA1*	Total	Reference
Belgium Ovarian Cancer Study	BEL	Belgium	12	8	20	(9)
Spanish National Cancer Centre	CNO	Spain	11	4	15	(10)
Meir Hospital - Sapir Medical Center	ISR	Israel	32	9	41	(11)
Kathleen Cuningham Consortium for Research into Familial Breast Cancer	KCO	Australia	28	56	84	(12)
MALOVA	MAL	Denmark	255	12	267	(13)
National Cancer Institute	NCI	USA	1	12	13	(14)
Royal Marsden Hospital	RMH	UK	41	15	56	(15)
Western General Hospital, Edinburgh	SCO	UK	26	10	36	(16)
The National Israeli Study of Ovarian Cancer	SIE	Israel	355	120	475	(17)
Swedish Breast Cancer Study	SWE	Sweden	13	19	32	(18)
The Cancer Genome Atlas	TCG	USA	268	22	290	(19)
University of California San Francisco	UCS	USA	8	7	15	(20)
UK Gilda Radner Familial Ovarian Cancer Registries	UKF	UK	45	34	79	(21)
Women's Cancer Program at Cedars Sinai Medical Center	WCR	USA	238	51	289	(22)
Total			1,333	379	1,712	