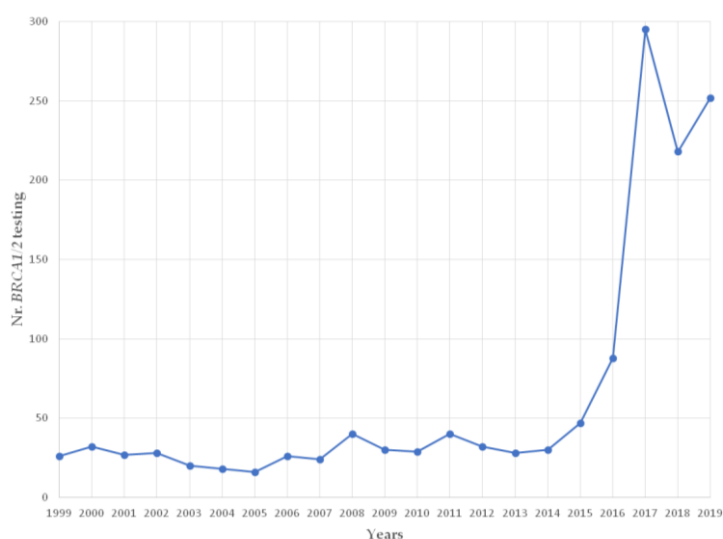
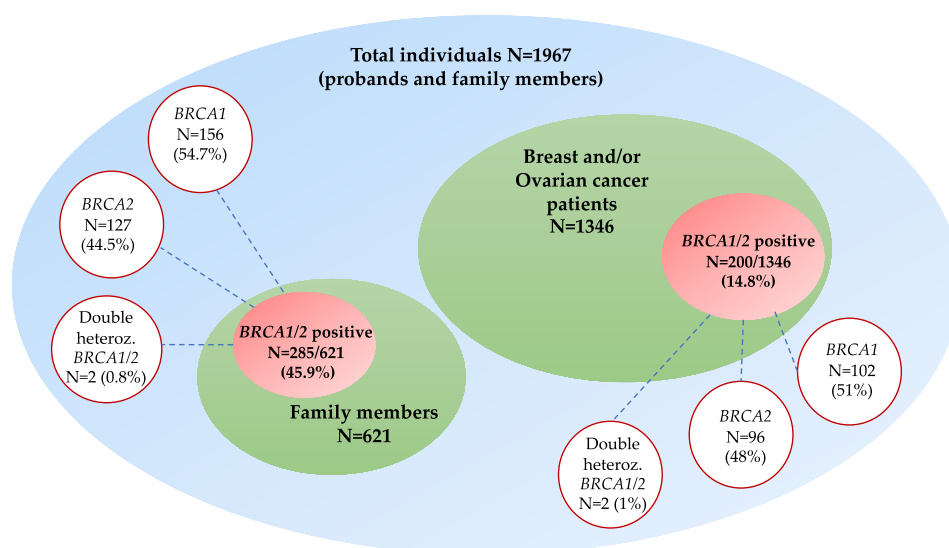


# Hereditary Breast and Ovarian Cancer in Families from Southern Italy (Sicily) – Prevalence and Geographic Distribution of Pathogenic Variants in *BRCA1/2* Genes

Lorena Incorvaia, Daniele Fanale, Giuseppe Badalamenti, Marco Bono, Valentina Calò, Daniela Cancelliere, Marta Castiglia, Alessia Fiorino, Alessia Pivetti, Nadia Barraco, Sofia Cutaia and Antonio Russo and Viviana Bazan



**Figure S1.** Number of genetic testing for *BRCA1/2* genes performed on HBOC patients every year at our Centre (1999-2019).



**Figure S2.** Total number of individuals included in the Hereditary Breast/Ovarian Cancer (HBOC) study (1999-2019). Considering both probands and family members, overall 1967 individuals were genetically tested for *BRCA1/2* PVs. Our analysis showed that 485 (24.6%) out of 1967 subjects (proband and family members) harbour a germline *BRCA1/2* PV. 200 (14.8%) out of 1346 were HBOC patients and 285 (45.9%) out of 621 were family members harbouring a *BRCA1/2* PV.

**Table S1.** Other Pathogenic Variants (class V) and Variants of Uncertain Significance (class III) detected in *BRCA1* gene.

GENE	BIC NOMENCLATURE	HGVS NOMENCLATURE	VARIANT CLASSIFICATION	CANCER PATIENTS	CARRIERS (patients and family members)
<i>BRCA1</i>	3663C>T (Q1182X)*	c.3544C>T (p.Gln1182Ter)*	V	3	5
	5242C>A (A1708E)	c.5123C>A (p.Ala1708Glu)	V	1	4
	1103insC	c.984_985insC (p.Asn329fs)	V	1	4
	185insA	c.66dupA (p.Glu23Argfs)	V	1	4
	IVS8+2T>A	c.547+2T>A	V	1	4
	185delAG	c.66_67AG[1] (p.Glu23fs)	V	1	3
	1001delA (D295fs)	c.882del (p.Asp295fs)	V	1	3
	236delTG	c.115_116TG[1] (p.Cys39_Asp40delinsTer)	V	1	2
	3385delT (L1042fs)	c.3266del (p.Leu1089fs)	V	1	2
	290delG (P58fs)	c.171del (p.Pro58fs)	V	1	2
	2388delG (V757fs)	c.2269del (p.Val757fs)	V	1	2
	1135delA (K292fs)	c.1016del (p.Lys339fs)	V	1	2
	5190insA	c.5071dupA (p.Thr1691Asnfs)	V	1	1
	5215G>A (R1699Q)	c.5096G>A (p.Arg1699Gln)	V	1	1
	3486G>T (D1123Y)	c.3367G>T (p.Asp1123Tyr)	III	1	1
	2000C/G	c.1881C>G (p.Val627=)	III	2	2
	K1487R	c.4460A>G (p.Lys1487Arg)	III	1	1
	IVS11+3A>G	c.4096+3A>G	III	1	1
	E1352K	c.4054G>A (p.Glu1352Lys)	III	2	2
	S1580F	c.4739C>T (p.Ser1580Phe)	III	1	1
IVS7+36C>T	c.441+36C>T	III	1	1	
M297L	c.889A>C (p.Met297Leu)	III	1	1	
N1355del	c.4063_4065delAAT (p.Asn1355del)	III	1	1	
E23Q	c.67G>C (p.Glu23Gln)	III	1	1	
R1634G	c.4900A>G (p.Arg1634Gly)	III	1	1	
T248P	c.742A>C (p.Thr248Pro)	III	1	1	

\* This PV is present together with the PV IVS13-2A>T (HGVS: c.7008-2A>T) (reported in Table S2) in one of two probands showing double heterozygosity for *BRCA1* and *BRCA2*, therefore the total number of *BRCA1* PV cancer patients is 104 and the total number of *BRCA2* cancer patients is 98.

**Table S2.** Other Pathogenic Variants (class V) and Variants of Uncertain Significance (class III) detected in *BRCA2* gene.

GENE				
BIC NOMENCLATURE	HGVS NOMENCLATURE	VARIANT CLASSIFICATION	CANCER PATIENTS	CARRIERS (patients and family members)
2041delA (I605fs)	c.1813del (p.Ile605fs)	V	3	4
IVS13-2A>T*	c.7008-2A>T*	V	3	4
IVS18+2T>C**	c.8331+2T>C**	V	2	4
3386T>G (L1053X)	c.3158T>G (p.Leu1053Ter)	V	2	4
7218del5 (I2330fs)	c.6990_6994del (p.Ile2330fs)	V	2	4
6252insG	c.6024dupG (p.Gln2009Alafs)	V	2	4
6187C>T (Q1987X)	c.5959C>T (p.Gln1987Ter)	V	2	4
5946delCTCT	c.5718_5719CT[2] (p.Leu1908fs)	V	2	4
7708C>T (R2494X)	c.7480C>T (p.Arg2494Ter)	V	2	4
983del4	c.751_754ACAG[1] (p.Asp252fs)	V	2	4
IVS5-2A>G	c.476-2A>G	V	2	3
2881del4 (D885fs)	c.2653_2656del (p.Asp885fs)	V	2	3
9481insA	c.9253dupA (p.Thr3085Asnfs)	V	2	3
5823delAT	c.5593_5594AT[1] (p.Phe1866fs)	V	2	3
9376C>T (Q3050X)	c.9148C>T (p.Gln3050Ter)	V	2	3
9683delAG	c.9453_9454AG[1] (p.Glu3152fs)	V	2	3
6503delITT (L2092fs)	c.6275_6276del (p.Leu2092fs)	V	1	3
5991delT (F1921fs)	c.5763del (p.Phe1921fs)	V	1	3
6352C>T (Q2042X)	c.6124C>T (p.Gln2042Ter)	V	1	2
5302insA	c.5073dupA (p.Trp1692Metfs)	V	1	2
V1756E	c.5267T>A (p.Val1756Glu)	III	1	1
K100E	c.298A>G (p.Lys100Glu)	III	1	1
S2697R	c.8091C>A (p.Ser2697Arg)	III	1	1
R3384G	c.10150C>G (p.Arg3384Gly)	III	2	2
S2807P	c.8419T>C (p.Ser2807Pro)	III	1	1
K1517R	c.4550A>G (p.Lys1517Arg)	III	1	1

T1426I	c.4277C>A (p.Thr1426Ile)	III	1	1
I1173F	c.3517A>T (p.Ile1173Phe)	III	1	1
8490T>G (H2754Q)	c.8262T>G (p.His2754Gln)	III	1	1
I1831T	c.5492T>C (p.Ile1831Thr)	III	2	2
P2798R	c.8393C>G (p.Pro2798Arg)	III	1	1
10067C>A (P3280H)	c.9839C>A (p.Pro3280His)	III	1	1
M1890T	c.5669T>C (p.Met1890Thr)	III	1	1
T567I	c.1700C>T (p.Thr567Ile)	III	1	1
692G>C (R115T)	c.464G>C (p.Arg155Thr)	III	1	1
L3101P	c.9302T>C (p.Leu3101Pro)	III	1	1
P2767S	c.8299C>T (p.Pro2767Ser)	III	1	1
E1254D	c.3762G>T (p.Glu1254Asp)	III	1	1
1997T>G (F590C)	c.1769T>G (p.Phe590Cys)	III	1	1
5656G>A (V1810I)	c.5428G>A (p.Val1810Ile)	III	1	1
3209C>T (A994V)	c.2981C>T (p.Ala994Val)	III	1	1
K1888R	c.5663A>G (p.Lys1888Arg)	III	1	1
F1506L	c.4516T>C (p.Phe1506Leu)	III	1	1

\* This PV is present together with the PV 3663C>T (HGVS: c.3544C>T; p.Gln1182Ter) (reported in Table S1) in one of two probands showing double heterozygosity for *BRCA1* and *BRCA2*. \*\* This PV is present together with the PV 300T>G (HGVS: c.181T>G; p.Cys61Gly) (reported in Table 3) in one of two probands showing double heterozygosity for *BRCA1* and *BRCA2*. Therefore, the total number of *BRCA1* PV cancer patients is 104 and the total number of *BRCA2* cancer patients is 98.