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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Garcia-Pelaez J, Barbosa-Matos R, Lobo S, et al. Genotype-first approach to identify associations between *CDH1* germline variants and cancer phenotypes: a multicentre study by the European Reference Network on Genetic Tumour Risk Syndromes. *Lancet Oncol* 2022; published online Nov 24. https://doi.org/10.1016/S1470-2045(22)00643-X.

Supplementary Appendix

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HDGC guidelines from 1999 to 2020 and Yale criteria (Lerner et al., 2022).

Disease-focus	Caldas et al., 1999[1]	Fitzgerald et al., 2010[2]	Van der Post et al., 2015[3]	Blair et al., 2020[4]	Lerner et al., 2022[5]
GC-centered	≥2 confirmed DGC in 1st/2nd degree relatives, one <50	≥2 GC, one confirmed DGC <50	≥2 GC, one confirmed DGC regardless of age	≥2 GC, one confirmed DGC regardless of age	≥2 GC, one one <50
	≥3 confirmed DGC in 1st/2nd degree relatives, regardless of age	≥3 confirmed DGC in 1st/2nd degree relatives, regardless of age			≥2 GC, one confirmed DGC regardless of age
		Isolated DGC case <40	Isolated DGC case <40	Isolated DGC case <50	Isolated DGC at any age
			Personal or family history of CL/P in a patient with DGC	Personal or family history of CL/P in a patient with DGC regardless of age	
			Gastric in situ signet ring cells and/or pagetoid spread of signet ring cells	Gastric *in situ* signet ring cells and/or pagetoid spread of signet ring cells <50	
				Isolated case of DGC regardless of age (in individuals of Māori ethnicity)	
DGC- plus LBC-centered		Personal or family history of DGC+LBC, at least one <50	Personal or family history of DGC+LBC, at least one <50	≥1 case of DGC regardless of age and ≥1 case of LBC <70 years in different relatives	
				History of DGC and LBC, both <70 years old	
LBC-centered			*Bilateral LBC or family history (≥2 LBC, <50)*	≥2 cases of LBC in relatives <50 years old	
				Bilateral LBC <70 years old	
BC-centered					NCCN HBOC criteria[6]

Van der Post et al 2015 suggested to use the criteria in italics above, however these were not formal criteria for testing. DGC – Diffuse gastric cancer; LBC – Lobular breast cancer; GC – Gastric cancer; HBOC – Hereditary breast and ovarian cancer

Dataset in numbers regarding family history, phenotypical distribution and age of onset.

Cohort characteristics	**Number (n)**	**Frequency (%)**
Cohort details (total number of patients)	**1875**	100
Probands	854	46
Relatives	1021	54
Cancer history (total number of families)	**854**	100
Familial history of cancer	484	56·7
Personal history of cancer	348	40·7
No familial/personal cancer history	14	1·6
Unknown	8	1
Cancer history of GC/BC (total number of families)	**832**	100
Familial history of GC	101	12·1
Personal history of GC	54	6·5
Familial history of BC	245	29·4
Personal history of BC	196	23·6
Familial history of GC+BC	98	11·8
Personal history of GC+BC	3	0·4
Familial history of OTHER cancer	40	4·8
Personal history of OTHER cancer	95	11·4
Phenotypic presentations in 854 probands	**950**	100
Diffuse/signet ring cells GC (DGC)	176	18·5
Intestinal type GC (IGC)	6	0·6
Mixed GC (MGC)	1	0·1
GC unknown histotype (GC)	13	1·4
Lobular BC (LBC)	58	6·1
Ductal BC (DBC)	32	3·4
Mixed BC (MBC)	1	0·1
BC unknown histotype (BC)	398	41·9
Colorectal cancer (CRC)	36	3·8
Ovarian cancer (OC)	100	10·5
Other phenotypes (OTH)	80	8·4
No cancer in carriers (Healthy)	49	5·2
Phenotypic presentations in relatives	**1021**	100
Diffuse/signet ring cells GC (DGC)	143	14
Intestinal type GC (IGC)	2	0·2
Mixed GC (MGC)	1	0·1
GC unknown histotype (GC)	224	22
Lobular BC (LBC)	33	3·2
Ductal BC (DBC)	7	0·7
Mixed BC (MBC)	0	0
BC unknown histotype (BC)	429	42
Colorectal cancer (OTH)	42	4·1
Ovarian cancer (OC)	30	2·9
Other phenotypes (OTH)	109	10·7
No cancer in carriers (Healthy)	1	0·1
Age of cancer onset and carrier status	**Number**	**Average age of onset ± SD**
Age of diagnosis in affected probands with carrier status known (age range 1 to 93)	950 [ages available of 761]	47·59±13·50
First diagnosis in affected probands with carrier status known (age range 1 to 85)	854 [ages available of 678]	46·7±13·34
First diagnosis in affected relatives with carrier status unknown (age range 17 to 90)	1021 [ages available of 830]	50·97±14·11

GC – gastric cancer; BC – Breast cancer

Distribution and abbreviation for OTHER phenotypes

Other phenotypes (abbreviation)	Number of cases (n)
Abdominal cancer (AC)	1
Acute lymphocytic leukemia (ALL)	1
Adenomatous polyposis (AP)	1
Bladder cancer (BDC)	8
Brain tumour (BRC)	6
Bowel cancer (BWC)	3
Chondrosarcoma (CHOND)	1
Colorectal polyposis (Co-po)	15
Cardiac tumour (CT)	1
Cervix Cancer (CXC)	1
Endometrial cancer (EC)	3
Familial adenomatous polyposis (FAP)	1
Fundic polyps (FP)	2
Gynecologic adenocarcinoma (G-ADK)	1
Gall bladder cancer (GLLBC)	1
Hepatic cancer (HC)	1
Kidney cancer (KC)	3
Lung cancer (LC)	13
Leukemia (LEU)	3
Li-Fraumeni syndrome (LFS)	1
Lymphoma no Hodgkin (LNHL)	1
Laryngeal cancer (LRYC)	1
Liver cancer (LVC)	1
Hodgkin lymphoma (Mb Hodgkin)	1
Melanoma (MEL)	11
Malignant melanoma (MM)	2
Myeloma (MYE)	1
Neuroblastoma (NBL)	1
Neurofibromatosis type II (NFMII)	2
Oesophagus cancer (OEC)	2
Oesophageus polyps (OEP)	1
Osteoclastoma (OST)	1
Osteogenesis imperfecta (OSTEO IMP)	1
Pancreatic cancer (PC)	33
Prostatic cancer (PRSC)	15
Renal cancer (RC)	1
Skin cancer (SKC)	1
Serous tubal intraepithelial carcinoma (STIC)	3
Tongue cancer (TC)	1
Type II diabetes (TIIDB)	13
Uterine sarcoma (US)	1
Uterine cancer (UTC)	5
Uveal melanoma (uveal MEL)	1
Unknown (NA, OTHC, UC, UP)	22
No cancer in carriers (Healthy)	50
Total	**239**

Summary of contributions for the dataset of 854 families carrying rare *CDH1* germline variants by affiliation and country.

Submitting authors	Institution of submitting authors	Country	No. of families referred per country
Genevieve Michils; Hilde Brems	UZ leuven, Leuven	Belgium	274
Karim Dahan; Damien Feret	Center for Medical Genetics, Gosseiles		
Vincent bours	Collège belge de Génétique, Liège		
Robin de Putter	Center for Medical Genetics, Ghent		
Lisa Golmard; Maud Blanluet ; Chrystelle Colas	Institute Curie, Paris	France	163
Patrick Benusiglio; Camille Desseignés; Coulet Florence	GH Pitié- Salpêtrière, Sorbonne Université		
Daniele Calistri; Gianluca Tedaldi	IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola	Italy	138
Guglielmina Nadia Ranzani	University of Pavia, Pavia		
Maurizio Genuardi	Catholic University of the Sacred Heart, Rome		
Joan Brunet Vidal; Conxi Lázaro; Gabriel Capellá	Instituto Catalán de Oncologia, Barcelona	Spain	82
Judith Balmaña	Vall d'Hebron Institute of Oncology, Barcelona		
José Luis Soto	Elche University Hospital, Elche		
Ana Patiño-García	Universidad de Navarra-Navarra, Pamplona		
Cristina Martínez-Bouzas; Mª Isabel Tejada; María Garcia-Barcina; Sergio Carrera; Sonia Merino	Hospital Universitario Cruces, Baracaldo		
Elena Domínguez-Garrido	Rioja Salud Foundation, La Rioja		
Stefan Aretz; Isabel Spier; Robert Hüneburg	Universität Bonn, Bonn	Germany	52
Karl Hackmann; Evelin Schröck	Institut für Klinische Genetik (TUD), Dresden		
Elke Holinski-Feder; Verena Steinke	Medical Genetics Center, Munich		
Marc Tischkowitz	Cambridge University Hospitals NHS Foundation Trust, Cambridge	UK	43
Gareth Evans; Emma R Woodward	Manchester Centre for Genomic Medicine, Manchester		
Helen Hanson	St George's University Hospital, London		
Nicoline Hoogerbrugge; Marjolijn Ligtenberg	Radboud University Medical Centre, Nijmegen	The Netherlands	36
Conceição Egas	Innovation Biocant - Center in Biotechnology, Cantanhede	Portugal	33
Carla Oliveira; Sérgio Castedo	Institute of Molecular Pathology and Immunology of the University of Porto (Ipatimup diagnostics) and Centro Hospitalar e Universitario de S. Joao (CHUSJ), Porto		
Catarina Silveira; Inês Silva	GENOMED, Lisbon		
Manuel Teixeira	Intituto Português de Oncologia do Porto (IPO-Porto), Porto		
Srdjan Novakovic; Ana Blatnik; Mateja Krajc	Institute of Oncology Ljubljana, Ljubljana	Slovenia	29
Kristina Lagerstedt-Robinson; Svetlana Bajalica-Lagercrantz	Karolinska University Hospital, Stockholm	Sweden	4
52 submitters	**29 institutions**	**10 countries**	**854 families**

No. – Number

Description and classification of the variant(s) presented by each family, HDGC criteria fulfillment, phenotypical information and affiliation in the dataset used.

Family _ID	Nucelotide Change (HGVS) (NM_004360.4; LRG_301)	Molecular classification	Variant group/predicted consequence	ACMG/AMP *CDH1* criteria	ACMG/AMP *CDH1* classification for analysis	2015 HDGC Criteria	2020 HDGC Criteria	Yale criteria	2020 HDGC Criteria + LBC-centred criteria (LBC-expanded criteria)	Cancer history	GC and/or BC history	Country of diagnosis
F524	c.-71C>G	5'-UTR SNV	Non-coding	BA1; BP2_Supporting	LBV/BV	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F507	c.-63C>A	5'-UTR SNV	Non-coding	-	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F508	c.-63C>A	5'-UTR SNV	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F525	c.-54G>C	5'-UTR SNV	Non-coding	BS1; PS4_Supporting; PM2	LBV/BV	1	1	DGC	1	Familial history of cancer	GC-only	Portugal
F509	c.-44G>A	5'-UTR SNV	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F526	c.-29C>G	5'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F571	c.-29C>G	5'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F572	c.-29C>G	5'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F001	g.(?_68737292)_(68737463_?)del [EX1del]	Large deletion	Coding truncating	PVS1; PM2	PV/LPV	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	France
F003	g.(?_68737292)_(68738411_?)del [EX1_2del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	no criteria	3	HBOC	3	Familial history of cancer	BC-only	UK
F011	g.(?_68737292)_(68738411_?)del [EX1_2del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	Belgium
F005	g.(?_68737292)_(68738411_?)del [EX1_2del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	Spain
F014	g.(?_68737292)_(68835537_?)del [EX1_16del]	Large deletion	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F004	g.(?_68737292)_(68738411_?)del [EX1_2del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F007	g.(?_68737292)_(68738411_?)del [EX1_2del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Slovenia
F002	g.(?_68737292)_(68738411_?)del [EX1_2del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F008	g.(?_68737292)_(68738411_?)del [EX1_2del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Germany

F009	g.(?_68737292)_(68738411_?)del [EX1_2del]	Large deletion	Coding truncating	PVS1; PS4; PM3	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy
F012	g.(?_68737292)_(68835537_?)del [EX1_16del]	Large deletion	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F006	g.(?_68737292)_(68738411_?)del [EX1_2del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Slovenia
F013	g.(?_68737292)_(68835537_?)del [EX1_16del]	Large deletion	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	UK
F010	g.(?_68737292)_(68738411_?)del [EX1_2del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	3	7	DGC	7	Personal history of cancer	GC+BC	Spain
F016	c.2T>C	Start codon loss	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	3	2	HBOC	2	Familial history of cancer	GC+BC	Slovenia
F015	c.2T>C	Start codon loss	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	Portugal
F017	c.3G>A	Start codon loss	Coding truncating	PVS1; PS4_Supporting; PM2; PP1_Moderate	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F187	c.8C>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Germany
F188	c.8C>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F189	c.8C>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F190	c.8C>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Germany
F191	c.8C>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Germany
F192	c.8C>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Germany
F193	c.19A>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F529	c.27G>A	Synonymous	Synonymous	-	VUS	no criteria	no criteria	no criteria	no criteria	Unknown	-	Belgium
F018	c.31del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	no criteria	3	HBOC	3	Familial history of cancer	GC+BC	Italy
F194	c.31_32insTGCTGC	In-frame variants	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Italy
F019	c.45_46insT	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	UK
F195	c.44_46dup	In-frame variants	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Spain
F196	c.41_46dup	In-frame variants	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium

F020	c.48G>A	Splice-site	Coding truncating	PVS1_Moderate; PS3; PS4_Supporting; PM2; PP1_Supporting	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	Spain
F021	c.48+1G>A	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2; PP1_Moderate	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F530	c.48+5C>G	Intronic SNVs	Non-coding	BA1; BP2_Strong	LBV/BV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F531	c.48+41C>T	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	Belgium
F532	c.48+52C>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F533	c.48+63T>C	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F534	c.48+83C>T	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F022	c.49-2A>G	Splice-site	Coding truncating	PVS1_Strong; PS3_Moderate; PS4; PM2; PP1	PV/LPV	2	4	DGC	4	Familial history of cancer	GC-only	UK
F023	c.49-1G>C	Splice-site	Coding truncating	PVS1_Strong; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F197	c.53C>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F024	c.55_74del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	The Netherlands
F198	c.56C>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F025	c.59G>A	Nonsense	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	no criteria	4	DGC	4	Personal history of cancer	GC-only	UK
F199	c.61C>G	Missense	Coding non-truncating	PS4_Supporting; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F200	c.61C>G	Missense	Coding non-truncating	PS4_Supporting; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F026	c.67C>T	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F535	c.69G>A	Synonymous	Synonymous	PM2; BS2_Supporting; BP7	LBV/BV	1	1	DGC	1	Familial history of cancer	GC-only	Portugal
F201	c.79C>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	GC-only	Belgium
F202	c.83G>A	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F203	c.83G>A	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium

F204	c.83G>A	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F027	c.86dup	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	Germany
F205	c.87C>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F206	c.87C>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F434	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Germany
F436	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	no criteria	4	DGC	4	Familial history of cancer	GC+BC	The Netherlands
F437	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	History of GC+BC, 1 LBC regardless of age	Familial history of cancer	GC+BC	The Netherlands
F439	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F440	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F441	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F442	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F443	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F444	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Germany
F445	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Germany
F438	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	1	1	DGC	1	Familial history of cancer	GC-only	Portugal
F433	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	2	4	DGC	4	Personal history of cancer	GC-only	Italy
F435	c.88C>A	Missense	Coding non-truncating	BA1; BS2	LBV/BV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F207	c.89C>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F208	c.103G>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F209	c.103G>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium

F549	c.150C>A	Synonymous	Synonymous	PM2; BS2; BP7; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Unknown	-	Belgium
F210	c.160A>G	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F211	c.160A>G	Missense	Coding non-truncating	BS2_Supporting	VUS	1	1	DGC	1	Familial history of cancer	GC-only	France
F028	c.129_163+9dup	Large duplication	Coding truncating	PS4_Supporting; PM2	VUS	1	1	DGC	1	Familial history of cancer	GC-only	France
F550	c.163+14G>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F551	c.163+75A>T	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F552	c.163+81G>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F553	c.163+81G>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F554	c.163+90T>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F555	c.163+115A>T	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F510	chr16:68767553 -68771266_del3713	Intronic deletion	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Germany
F511	chr16:68795089-68799711_del4622	Intronic deletion	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Germany
F512	chr16:68795089-68799711_del4622	Intronic deletion	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Germany
F029	c.(163+1_164-1)_(387+1_388-1)del [EX3del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	Spain
F032	c.(163+1_164-1)_(387+1_388-1)del [EX3del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy
F212	c.164T>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France
F213	c.164T>C	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F033	c.(163+1_164-1)_(1137+1_1138-1)del [EX3_8del]	Large deletion	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	Germany
F030	c.(163+1_164-1)_(387+1_388-1)del [EX3del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	Spain
F031	c.(163+1_164-1)_(387+1_388-1)del [EX3del]	Large deletion	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F034	c.187C>T	Nonsense	Coding truncating	PVS1; PS4; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	Spain

F038	c.187C>T	Nonsense	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	UK
F036	c.187C>T	Nonsense	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F035	c.187C>T	Nonsense	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	DGC	1	Personal history of cancer	GC-only	Italy
F037	c.187C>T	Nonsense	Coding truncating	PVS1; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	Spain
F039	c.208dup	Frameshift	Coding truncating	PVS1; PS4_MODERATE; PM2	PV/LPV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	GC-only	UK
F556	c.213C>T	Synonymous	Synonymous	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F214	c.214G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F215	c.214G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F216	c.214G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France
F041	c.220C>T	Nonsense	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	no criteria	no criteria	DGC	no criteria	Personal history of cancer	GC-only	France
F040	c.220C>T	Nonsense	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	Italy
F042	c.220C>T	Nonsense	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	no criteria	4	DGC	4	Familial history of cancer	GC+BC	UK
F217	c.233G>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F218	c.244G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F219	c.244G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F220	c.244G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F221	c.244G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F222	c.244G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F557	c.249T>C	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F223	c.257A>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F224	c.269G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy

F225	c.269G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F226	c.269G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F227	c.271T>C	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	DGC	no criteria	Personal history of cancer	GC-only	Sweden
F043	c.281_283delinsGT	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy
F044	c.283C>T	Nonsense	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	UK
F558	c.303C>T	Synonymous	Synonymous	BP7	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F559	c.303C>T	Synonymous	Synonymous	BP7	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F228	c.304G>A	Missense	Coding non-truncating	BS1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F045	c.308G>A	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy
F046	c.322del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F527	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Italy
F576	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F577	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F578	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F579	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F580	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F581	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F582	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F583	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F584	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	France
F585	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy

F590	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	GC-only	Italy
F591	c.324A>G	Synonymous	Synonymous	BA1; BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F047	c.326del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	Spain
F048	c.336del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Spain
F229	c.337A>G	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F573	c.345G>A	Synonymous	Synonymous	BA1; BP2_Strong	LBV/BV	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F049	c.360del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy
F231	c.371G>A	Missense	Coding non-truncating	PS4_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F230	c.371G>A	Missense	Coding non-truncating	PS4_Supporting	VUS	2	4	DGC	4	Personal history of cancer	GC-only	Italy
F574	c.375C>T	Synonymous	Synonymous	BP7	VUS	no criteria	4	DGC	4	Personal history of cancer	GC-only	Italy
F050	c.377del	Frameshift	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	The Netherlands
F232	c.377C>T	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F051	c.385C>T	Nonsense	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F052	c.385C>T	Nonsense	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	UK
F053	c.387+1G>A	In-frame Exon skipping	Coding non-truncating	PVS1_Moderate, PS3_Supporting, BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Spain
F513	c.387+5G>A	Intronic SNVs	Non-coding	BS2; BS3; BP2_Strong	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	France
F528	c.387+27C>T	Intronic SNVs	Non-coding	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F592	c.387+27C>T	Intronic SNVs	Non-coding	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F593	c.387+27C>T	Intronic SNVs	Non-coding	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F594	c.387+27C>T	Intronic SNVs	Non-coding	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F595	c.387+27C>T	Intronic SNVs	Non-coding	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium

F596	c.387+27C>T	Intronic SNVs	Non-coding	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F597	c.387+27C>T	Intronic SNVs	Non-coding	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F598	c.387+27C>T	Intronic SNVs	Non-coding	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F599	c.387+27C>T	Intronic SNVs	Non-coding	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F575	c.387+76C>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F536	c.388-44G>A	Intronic SNVs	Non-coding	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F600	c.388-44G>A	Intronic SNVs	Non-coding	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F601	c.388-44G>A	Intronic SNVs	Non-coding	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F602	c.388-44G>A	Intronic SNVs	Non-coding	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F603	c.388-44G>A	Intronic SNVs	Non-coding	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F604	c.388-44G>A	Intronic SNVs	Non-coding	BA1; BS2_Supporting	LBV/BV	3	2	HBOC	2	Familial history of cancer	GC+BC	Spain
F537	c.388-21C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F605	c.388-21C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	GC-only	Belgium
F606	c.388-21C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F607	c.388-21C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F608	c.388-21C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F609	c.388-21C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F610	c.388-21C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F611	c.388-21C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F514	c.388-14T>G	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F586	c.388-8C>T	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France

F054	c.(387+1_388-1)_(1711+1_1712-1)dup [EX_4_11dup]	Large duplication	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	France
F587	c.393C>T	Synonymous	Synonymous	PS4_Supporting; BP4; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F588	c.393C>T	Synonymous	Synonymous	PS4_Supporting; BP4; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F055	c.415del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	Spain
F233	c.437C>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F056	c.479_480del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	3	2	DGC	2	Familial history of cancer	GC+BC	France
F057	c.489C>A	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	The Netherlands
F058	c.497dup	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	Belgium
F234	c.499G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F235	c.499G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F236	c.519A>C	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F059	c.521del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	3	2	DGC	2	Familial history of cancer	GC+BC	Germany
F060	c.521dup	Frameshift	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Sweden
F061	c.521dup	Frameshift	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	France
F062	c.531+1G>T	Splice-site	Coding truncating	PVS1_Strong; PS4_Supporting; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	Slovenia
F237	c.531+3A>G	Splice-site &	Coding truncating &	PM2; BS3	VUS	no criteria	no criteria	DGC	no criteria	Personal history of cancer	GC+BC	Belgium
F589	c.532-25T>C	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F613	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	2	4	HBOC	4	Familial history of cancer	GC+BC	Germany
F617	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	2	4	DGC	4	Personal history of cancer	GC-only	Italy
F538	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F612	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy

F614	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F615	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	GC-only	Spain
F616	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Unknown	-	Spain
F619	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	personal history of cancer	BC-only	Italy
F621	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F622	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F623	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F624	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F629	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F630	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F631	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F632	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F633	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F634	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F635	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	GC-only	Spain
F636	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F637	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F638	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	Other cancer	Spain
F639	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	Other cancer	Spain
F640	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	Other cancer	Spain
F641	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain

F642	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F643	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F620	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	1	1	HBOC	1	Familial history of cancer	GC+BC	Germany
F618	c.532-18C>T	Intronic SNVs	Non-coding	BA1; BS2	LBV/BV	1	1	HBOC	1	Familial history of cancer	GC+BC	France
F063	c.570C>A	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	3	2	HBOC	2	Familial history of cancer	GC+BC	Portugal
F064	c.639del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F065	c.641T>C	Missense	Coding non-truncating	PS4_Supporting; PM2	VUS	1	1	DGC	1	Familial history of cancer	GC-only	UK
F238	c.650C>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Slovenia
F239	c.659T>G	Missense	Coding non-truncating	PS4_Supporting; PM2	VUS	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F242	c.670C>T	Missense	Coding non-truncating	BS2	LBV/BV	1	1	DGC	1	Familial history of cancer	GC-only	Portugal
F240	c.670C>T	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Germany
F241	c.670C>T	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F243	c.670C>T	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F244	c.670C>T	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F245	c.670C>T	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F246	c.670C>T	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F247	c.671G>A	Missense	Coding non-truncating	BP2_Strong; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F248	c.671G>A	Missense	Coding non-truncating	BP2_Strong; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F249	c.674T>C	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F250	c.674T>C	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F251	c.677C>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium

F066	c.684C>G	Nonsense	Coding truncating	PVS1; PM2	PV/LPV	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	Slovenia
F539	c.687+66A>G	Intronic SNVs	Non-coding	BS2_Supporting; BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F644	c.687+66A>G	Intronic SNVs	Non-coding	BS2_Supporting; BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F645	c.687+66A>G	Intronic SNVs	Non-coding	BS2_Supporting; BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F646	c.687+66A>G	Intronic SNVs	Non-coding	BS2_Supporting; BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F647	c.687+66A>G	Intronic SNVs	Non-coding	BS2_Supporting; BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F650	c.687+66A>G	Intronic SNVs	Non-coding	BS2_Supporting; BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F625	c.688-53C>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F626	c.688-53C>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F067	c.688-1G>C	Splice-site	Coding truncating	PVS1_Strong; PS3_Moderate; PS4_Suportive; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	Italy
F068	c.696_697del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	no criteria	4	DGC	4	Familial history of cancer	GC+BC	UK
F069	c.696_697del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	France
F515	c.699C>T	Synonymous	Synonymous	BP7	VUS	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	France
F252	c.712A>C	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F253	c.712A>C	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Italy
F254	c.719A>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F255	c.752C>T	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F627	c.759C>T	Synonymous	Synonymous	BP7	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F256	c.764A>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F257	c.764A>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F070	c.781G>T	Nonsense	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy

F071	c.781G>T	Nonsense	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy
F258	c.808T>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Germany
F259	c.808T>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F260	c.808T>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F261	c.808T>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	Other cancer	France
F072	c.811_812delinsTTAAGGGATATA	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	The Netherlands
F074	c.832+1G>T	Splice-site	Coding truncating	PVS1_Strong; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	France
F073	c.832+1G>A	Splice-site	Coding truncating	PVS1_Strong; PS4_Supporting; PM2	PV/LPV	no criteria	no criteria	HBOC	History of GC+BC, 1 LBC regardless of age	Familial history of cancer	GC+BC	Slovenia
F628	c.833-34T>C	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F075	c.833-476_1138-463del [EX7_8del]	Large deletion	Coding truncating	PVS1; PM2	PV/LPV	no criteria	no criteria	HBOC	Isolated LBC <55	Personal history of cancer	BC-only	Italy
F076	c.834A>G	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Germany
F077	c.834A>G	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	Isolated LBC <55	Personal history of cancer	BC-only	Germany
F262	c.835A>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	France
F263	c.854C>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F264	c.866C>T	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F265	c.866C>T	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F266	c.892G>C	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	France
F267	c.892G>C	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F268	c.892G>C	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	France
F446	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy

F447	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F448	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F449	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F450	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F451	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	GC-only	The Netherlands
F452	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F453	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F454	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F455	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F456	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France
F457	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F458	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Unknown	-	Belgium
F459	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	History of GC+BC, 1 LBC regardless of age	Familial history of cancer	GC+BC	France
F460	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	Isolated LBC <55	Personal history of cancer	BC-only	Belgium
F461	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F462	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F463	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F464	c.892G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F648	c.894C>T	Synonymous	Synonymous	BP4; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F649	c.894C>T	Synonymous	Synonymous	BP4; BP7	LBV/BV	no criteria	no criteria	DGC	no criteria	Personal history of cancer	GC-only	Italy

F269	c.896C>G	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F270	c.901G>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F540	c.906C>T	Synonymous	Synonymous	BS2_Supporting; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F670	c.906C>T	Synonymous	Synonymous	BS2_Supporting; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F671	c.906C>T	Synonymous	Synonymous	BS2_Supporting; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F651	c.924T>C	Synonymous	Synonymous	PM2; BP7	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F541	c.933C>G	Synonymous	Synonymous	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F672	c.933C>G	Synonymous	Synonymous	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F673	c.933C>G	Synonymous	Synonymous	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F674	c.933C>G	Synonymous	Synonymous	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F652	c.957T>A	Synonymous	Synonymous	-	VUS	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	France
F271	c.963G>C	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F272	c.966C>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F078	c.971del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	The Netherlands
F079	c.977T>A	Missense	Coding non-truncating	PS4_Supporting; PM2; PP1_Supporting	VUS	1	1	DGC	1	Familial history of cancer	GC-only	Spain
F083	c.1003C>T	Nonsense	Coding truncating	PVS1; PS4; PP1_Strong	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	Belgium
F082	c.1003C>T	Nonsense	Coding truncating	PVS1; PS4; PP1_Strong	PV/LPV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F080	c.1003C>T	Nonsense	Coding truncating	PVS1; PS4; PP1_Strong	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	Italy
F081	c.1003C>T	Nonsense	Coding truncating	PVS1; PS4; PP1_Strong	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	The Netherlands
F084	c.1003C>T	Nonsense	Coding truncating	PVS1; PS4; PP1_Strong	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	UK
F273	c.1004G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain

F274	c.1004G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F085	c.1008+2T>G	Splice-site	Coding truncating	PVS1_STRONG; PS4_Moderate; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	UK
F086	c.1008+2T>G	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	UK
F653	c.1008+47T>C	Intronic SNVs	Non-coding	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F654	c.1009-32G>A	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F655	c.1009-32G>A	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F656	c.1009-14C>T	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F087	c.1009_1010del	Frameshift	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	no criteria	no criteria	no criteria	Isolated LBC <55	Personal history of cancer	BC-only	Belgium
F088	c.(1008+1_1009-1)_(1711+1_1712-1)del [EX8_11del]	Large deletion	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	Germany
F275	c.1018A>G	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	The Netherlands
F277	c.1018A>G	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F276	c.1018A>G	Missense	Coding non-truncating	BA1	LBV/BV	1	1	DGC	1	Familial history of cancer	GC-only	Portugal
F657	c.1020G>A	Synonymous	Synonymous	BS1; BP2; PS4_Supporting	LBV/BV	2	4	DGC	4	Personal history of cancer	GC-only	The Netherlands
F089	c.1036C>T	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Sweden
F090	c.1056del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Spain
F658	c.1083T>G	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F091	c.1108G>A	Missense	Coding non-truncating	PS4_Supporting; PM2	VUS	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F659	c.1119G>A	Synonymous	Synonymous	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F278	c.1127A>G	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F279	c.1127A>G	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F280	c.1127A>G	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium

F281	c.1127A>G	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F092	c.1135_1137+5delinsTTAGA	Splice-site	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F282	c.1136C>T	Splice-site &	Coding truncating &	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F283	c.1136C>T	Splice-site &	Coding truncating &	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F094	c.1137G>A	Splice-site	Coding truncating	PVS1_Moderate; PS3; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Portugal
F093	c.1137G>A	Splice-site	Coding truncating	PVS1_MODERATE; PS3; PS4; PM2	PV/LPV	2	4	DGC	4	Familial history of cancer	GC+BC	Italy
F095	c.1137G>A	Splice-site	Coding truncating	PVS1_Moderate; PS3; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F284	c.1137+4A>G	Splice-site &	Coding truncating &	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F660	c.1137+9A>G	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F661	c.1137+81C>T	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F542	c.1137+86T>G	Intronic SNVs	Non-coding	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F677	c.1137+86T>G	Intronic SNVs	Non-coding	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F678	c.1137+86T>G	Intronic SNVs	Non-coding	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F662	c.1137+106A>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F663	c.1137+114A>C	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F664	c.1138-22G>T	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F854	c.1138-13C>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F665	c.1138-10T>C	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F285	c.1138-3C>T	Intronic SNVs	Non-coding	BS1; BP4	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F096	c.1141A>T	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	no criteria	3	HBOC	3	Familial history of cancer	GC+BC	France
F097	c.1141A>T	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	no criteria	no criteria	HBOC	History of GC+BC, 1 LBC	Familial history of cancer	GC+BC	France

									regardless of age			
F286	c.1143G>C	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	France
F098	c.1147C>T	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	France
F287	c.1149G>C	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F666	c.1161C>T	Synonymous	Synonymous	-	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	France
F667	c.1170C>T	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F288	c.1171G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F289	c.1171G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F290	c.1171G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F291	c.1171G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F292	c.1174G>A	Missense	Coding non-truncating	BS2; BP2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Unknown	-	Belgium
F293	c.1174G>A	Missense	Coding non-truncating	BS2; BP2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	GC-only	France
F668	c.1194G>A	Synonymous	Synonymous	PM2; BP7	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F099	c.1220del	Frameshift	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Spain
F294	c.1222G>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F295	c.1223C>T	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F543	c.1224G>A	Synonymous	Synonymous	BS2_Supporting; BS3	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F679	c.1224G>A	Synonymous	Synonymous	BS2_Supporting; BS3	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F680	c.1224G>A	Synonymous	Synonymous	BS2_Supporting; BS3	LBV/BV	no criteria	no criteria	2 GC, 1<50	no criteria	Familial history of cancer	GC+BC	France
F681	c.1224G>A	Synonymous	Synonymous	BS2_Supporting; BS3	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	France
F682	c.1224G>A	Synonymous	Synonymous	BS2_Supporting; BS3	LBV/BV	no criteria	no criteria	DGC	no criteria	Personal history of cancer	GC-only	Italy

F669	c.1239C>T	Synonymous	Synonymous	BS1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F296	c.1241C>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F297	c.1241C>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F298	c.1241C>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F299	c.1241C>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F300	c.1250A>G	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F301	c.1250A>G	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F302	c.1250A>G	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F100	c.1264C>T	Nonsense	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Belgium
F687	c.1272C>T	Synonymous	Synonymous	BS1; BS2_Supporting	LBV/BV	2	4	DGC	4	Personal history of cancer	GC-only	Italy
F688	c.1272C>T	Synonymous	Synonymous	BS1; BS2_Supporting	LBV/BV	no criteria	4	DGC	4	Personal history of cancer	GC-only	Italy
F544	c.1272C>T	Synonymous	Synonymous	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F683	c.1272C>T	Synonymous	Synonymous	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F684	c.1272C>T	Synonymous	Synonymous	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F685	c.1272C>T	Synonymous	Synonymous	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F686	c.1272C>T	Synonymous	Synonymous	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F693	c.1272C>T	Synonymous	Synonymous	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F695	c.1272C>T	Synonymous	Synonymous	BS1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F694	c.1272C>T	Synonymous	Synonymous	BS1; BS2_Supporting	LBV/BV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F303	c.1273G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F304	c.1273G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France

F305	c.1273G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France
F306	c.1273G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F307	c.1297G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F308	c.1297G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F309	c.1297G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	France
F310	c.1301G>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	History of GC+BC, 1 LBC regardless of age	Familial history of cancer	GC+BC	France
F101	c.1320+1G>A	Splice-site	Coding truncating	PVS1_Strong; PM2	VUS	no criteria	no criteria	DGC	no criteria	Personal history of cancer	GC-only	Germany
F675	c.1320+35C>T	Intronic SNVs	Non-coding	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F676	c.1320+43C>G	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F545	c.1321-140T>C	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium
F705	c.1321-140T>C	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F706	c.1321-140T>C	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F707	c.1321-140T>C	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F708	c.1321-140T>C	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F546	c.1321-88C>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F709	c.1321-88C>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F715	c.1321-88C>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F547	c.1321-65A>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F716	c.1321-65A>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F717	c.1321-65A>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium

F718	c.1321-65A>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F689	c.1321-49A>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F690	c.1321-37T>C	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F691	c.1321-36C>T	Intronic SNVs	Non-coding	BA1; PS4_Supporting	LBV/BV	2	4	DGC	4	Personal history of cancer	GC-only	Italy
F102	c.(1320+1_1321-1)_(1711+1_1712-1)del [EX10_11del]	Large deletion	Coding truncating	PVS1; PS4_ Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	France
F103	c.(1320+1_1321-1)_(1711+1_1712-1)del [EX10_11del]	Large deletion	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	no criteria	no criteria	HBOC	History of GC+BC, 1 LBC regardless of age	Familial history of cancer	GC+BC	Belgium
F104	c.(1320+1_1321-1)_(1711+1_1712-1)del [EX10_11del]	Large deletion	Coding truncating	PVS1; PS4_ Supporting; PM2	PV/LPV	3	2	no criteria	2	Personal history of cancer	BC-only	Belgium
F105	c.(1320+1_1321-1)_(1711+1_1712-1)del [EX10_11del]	Large deletion	Coding truncating	PVS1; PS4_ Supporting; PM2	PV/LPV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	Belgium
F311	c.1325T>C	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F312	c.1332T>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F313	c.1360G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F314	c.1360G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F315	c.1360G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F316	c.1360G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Slovenia
F317	c.1370C>T	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F318	c.1385T>C	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F692	c.1392C>T	Synonymous	Synonymous	BP7	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	Other cancer	Spain
F106	c.1401del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	Spain
F107	c.1404del	Frameshift	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F108	c.1404del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands

F465	c.1409C>T	Missense	Coding non-truncating	BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F466	c.1409C>T	Missense	Coding non-truncating	BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F467	c.1409C>T	Missense	Coding non-truncating	BS2; BP2_Strong	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F110	c.1416dup	Frameshift	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	France
F109	c.1416dup	Frameshift	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	3	2	HBOC	2	Personal history of cancer	GC+BC	Germany
F319	c.1417G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F320	c.1417G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F321	c.1417G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F322	c.1421C>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F323	c.1426G>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F324	c.1465C>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F325	c.1466C>T	Missense	Coding non-truncating	PS4_Supporting; PM2	VUS	2	4	DGC	4	Personal history of cancer	GC-only	Germany
F111	c.1466_1467insC	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F112	c.1476_1477del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F326	c.1477G>C	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F327	c.1477G>C	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F113	c.1488_1494del	Frameshift	Coding truncating	PVS1; PS4_ Supporting; PM2	PV/LPV	no criteria	no criteria	HBOC	History of GC+BC, 1 LBC regardless of age	Familial history of cancer	GC+BC	France
F696	c.1488C>T	Synonymous	Synonymous	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F328	c.1493A>C	Missense	Coding non-truncating	PM2; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Slovenia
F329	c.1493A>C	Missense	Coding non-truncating	PM2; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Slovenia

F330	c.1493A>C	Missense	Coding non-truncating	PM2; BS2	LBV/BV	no criteria	no criteria	HBOC	Isolated LBC <55	Familial history of cancer	BC-only	Slovenia
F331	c.1493A>C	Missense	Coding non-truncating	PM2; BS2	LBV/BV	no criteria	no criteria	2 GC, 1<50	no criteria	Familial history of cancer	GC+BC	France
F332	c.1496T>C	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F333	c.1501G>A	Missense	Coding non-truncating	PS4_Supporting	VUS	2	4	DGC	4	Personal history of cancer	GC-only	Belgium
F334	c.1509G>C	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Unknown	-	Belgium
F697	c.1512A>G	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F335	c.1519T>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	France
F336	c.1526C>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	France
F337	c.1565C>T	Missense	Coding non-truncating	PS4_Supporting; PM2	VUS	1	1	DGC	1	Familial history of cancer	GC-only	Belgium
F116	c.1565+1G>A	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F114	c.1565+1G>T	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	GC+BC	Sweden
F115	c.1565+1G>A	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	Germany
F117	c.1565+1G>T	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy
F121	c.1565+1G>A	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	no criteria	no criteria	no criteria	History of GC+BC, 1 LBC regardless of age	Familial history of cancer	GC+BC	Slovenia
F122	c.1565+1G>A	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	Germany
F123	c.1565+1G>A	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy
F118	c.1565+1G>T	Splice-site	Coding truncating	PVS1_STRONG; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F120	c.1565+1G>A	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Portugal
F119	c.1565+1G>T	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F128	c.1565+2dup	Splice-site	Coding truncating	PS4; PM2; PP1_Moderate; PP3_Moderate	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands

F129	c.1565+2dup	Splice-site	Coding truncating	PS4; PM2; PP1_Moderate; PP3_Moderate	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F124	c.1565+2dup	Splice-site	Coding truncating	PS4; PM2; PP1_Moderate; PP3_Moderate	PV/LPV	no criteria	4	DGC	4	Personal history of cancer	GC-only	Germany
F126	c.1565+2dup	Splice-site	Coding truncating	PS4; PM2; PP1_Moderate; PP3_Moderate	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F125	c.1565+2dup	Splice-site	Coding truncating	PS4; PM2; PP1_Moderate; PP3_Moderate	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F127	c.1565+2dup	Splice-site	Coding truncating	PS4; PM2; PP1_Moderate; PP3_Moderate	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F698	c.1565+13A>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F699	c.1566-38T>G	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F700	c.1566-38T>G	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F130	c.(1565+1_1566-1)_(1711+1_1712-1)del [Ex11del]	Large deletion	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	France
F131	c.(1565+1_1566-1)_(2164+1_2165-1)del [EX11_13del]	Large deletion	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F338	c.1571G>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F701	c.1572G>C	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F132	c.1577G>A	Nonsense	Coding truncating	PVS1; PS4_Moderate; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	Spain
F133	c.1595G>A	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	no criteria	4	DGC	4	Personal history of cancer	GC-only	France
F135	c.1612del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F134	c.1612del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F339	c.1624A>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F136	c.1651G>T	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	Germany
F137	c.1679C>G	Splice-site	Coding truncating	PS3; PS4; PM2; PP1_Strong; PP3	PV/LPV	3	2	HBOC	2	Familial history of cancer	GC+BC	Germany
F139	c.1679C>G	Splice-site	Coding truncating	PS3; PS4; PM2; PP1_Strong; PP3	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Spain
F140	c.1679C>G	Splice-site	Coding truncating	PS3; PS4; PM2; PP1_Strong; PP3	PV/LPV	3	2	HBOC	2	Familial history of cancer	GC+BC	Germany

F138	c.1679C>G	Splice-site	Coding truncating	PS3; PS4; PM2; PP1_Strong; PP3	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F702	c.1680G>C	Synonymous	Synonymous	BA1; PS4_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F703	c.1680G>A	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F340	c.1687G>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	France
F341	c.1702A>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Italy
F704	c.1711+6G>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F722	c.1711+47G>A	Intronic SNVs	Non-coding	BA1; BS2_Supporting	LBV/BV	2	4	DGC	4	Personal history of cancer	GC-only	Italy
F548	c.1711+47G>A	Intronic SNVs	Non-coding	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F719	c.1711+47G>A	Intronic SNVs	Non-coding	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F720	c.1711+47G>A	Intronic SNVs	Non-coding	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F721	c.1711+47G>A	Intronic SNVs	Non-coding	BA1; BS2_Supporting	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F710	c.1712-184A>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F711	c.1712-168G>C	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F712	c.1712-161G>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F713	c.1712-151G>T	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F714	c.1712-151G>T	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F560	c.1712-128C>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F723	c.1712-128C>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F724	c.1712-128C>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F725	c.1712-128C>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F730	c.1712-128C>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	GC-only	Belgium

F731	c.1712-128C>T	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F561	c.1712-127G>A	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F732	c.1712-127G>A	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F734	c.1712-127G>A	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F735	c.1712-127G>A	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F736	c.1712-127G>A	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F737	c.1712-127G>A	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F738	c.1712-127G>A	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F739	c.1712-127G>A	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F726	c.1712-103A>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F727	c.1712-54dup	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F728	c.1712-52G>C	Intronic SNVs	Non-coding	BA1; BP2	LBV/BV	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F729	c.1712-52G>C	Intronic SNVs	Non-coding	BA1; BP2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F562	c.1712-37T>G	Intronic SNVs	Non-coding	BS1; BS2_Supporting; PM2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F740	c.1712-37T>G	Intronic SNVs	Non-coding	BS1; BS2_Supporting; PM2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F741	c.1712-37T>G	Intronic SNVs	Non-coding	BS1; BS2_Supporting; PM2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F733	c.1712-8T>C	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F753	c.1744C>T	Synonymous	Synonymous	BS2_Supporting; BP2; BP4; BP7	LBV/BV	1	1	HBOC	1	Familial history of cancer	GC+BC	The Netherlands
F563	c.1744C>T	Synonymous	Synonymous	BS2_Supporting; BP2; BP4; BP7	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F742	c.1744C>T	Synonymous	Synonymous	BS2_Supporting; BP2; BP4; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F743	c.1744C>T	Synonymous	Synonymous	BS2_Supporting; BP2; BP4; BP7	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium

F744	c.1744C>T	Synonymous	Synonymous	BS2_Supporting; BP2; BP4; BP7	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F748	c.1744C>T	Synonymous	Synonymous	BS2_Supporting; BP2; BP4; BP7	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F749	c.1744C>T	Synonymous	Synonymous	BS2_Supporting; BP2; BP4; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F750	c.1744C>T	Synonymous	Synonymous	BS2_Supporting; BP2; BP4; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F751	c.1744C>T	Synonymous	Synonymous	BS2_Supporting; BP2; BP4; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F752	c.1744C>T	Synonymous	Synonymous	BS2_Supporting; BP2; BP4; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F754	c.1744C>T	Synonymous	Synonymous	BS2_Supporting; BP2; BP4; BP7	LBV/BV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F141	c.1746dup	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F142	c.1748T>G	Missense	Coding non-truncating	PS4_Supporting; PM2	VUS	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F342	c.1753C>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F745	c.1767T>C	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F746	c.1773C>T	Synonymous	Synonymous	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F747	c.1773C>T	Synonymous	Synonymous	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F481	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	2	4	DGC	4	Personal history of cancer	GC-only	Germany
F482	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	2	4	DGC	4	Personal history of cancer	GC-only	The Netherlands
F483	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	4	DGC	4	Familial history of cancer	GC+BC	The Netherlands
F468	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	Belgium
F469	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F470	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	Other cancer	Spain
F471	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Italy
F472	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Italy

F473	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F474	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F475	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F476	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F477	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F478	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F479	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F480	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F484	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	2 GC, 1<50	no criteria	Familial history of cancer	GC-only	The Netherlands
F485	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Germany
F486	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	2 GC, 1<50	no criteria	Familial history of cancer	GC-only	Portugal
F487	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F489	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F490	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F491	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F492	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F493	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F494	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F495	c.1774G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	Other cancer	Spain
F143	c.1786G>T	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F147	c.1792C>T	Nonsense	Coding truncating	PVS1; PS2; PS4; PM2; PP1_Strong	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	UK

F145	c.1792C>T	Nonsense	Coding truncating	PVS1; PS2; PS4; PM2; PP1_Strong	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	Germany
F144	c.1792C>T	Nonsense	Coding truncating	PVS1; PS2; PS4; PM2; PP1_Strong	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F146	c.1792C>T	Nonsense	Coding truncating	PVS1; PS2; PS4; PM2; PP1_Strong	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F343	c.1793G>A	Missense	Coding non-truncating	-	VUS	no criteria	8	HBOC	8	Familial history of cancer	BC-only	France
F148	c.1795del	Frameshift	Coding truncating	PVS1; PM2	PV/LPV	no criteria	no criteria	HBOC	Isolated LBC <55	Familial history of cancer	BC-only	Italy
F344	c.1825C>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France
F755	c.1842C>T	Synonymous	Synonymous	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France
F345	c.1844T>C	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F488	c.1849G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	GC-only	Portugal
F346	c.1865A>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F347	c.1876T>G	Missense	Coding non-truncating	PM2; BP2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F756	c.1888C>G	Synonymous	Synonymous	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F564	c.1896C>T	Synonymous	Synonymous	BA1; BP2_Strong	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F762	c.1896C>T	Synonymous	Synonymous	BA1; BP2_Strong	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F763	c.1896C>T	Synonymous	Synonymous	BA1; BP2_Strong	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F764	c.1896C>T	Synonymous	Synonymous	BA1; BP2_STRONG	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F153	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	Portugal
F157	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	Portugal
F154	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	Portugal
F151	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	Portugal
F149	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	Italy

F156	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	Portugal
F150	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	3	2	HBOC	2	Familial history of cancer	GC+BC	Portugal
F152	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	Portugal
F155	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	Portugal
F158	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	France
F159	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	1	1	HBOC	1	Familial history of cancer	GC+BC	France
F160	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	no criteria	no criteria	HBOC	History of GC+BC, 1 LBC regardless of age	Familial history of cancer	GC+BC	Belgium
F161	c.1901C>T	Splice-site	Coding truncating	PVS1_Strong; PS3; PS4; PM2	PV/LPV	3	2	HBOC	2	Familial history of cancer	GC+BC	France
F348	c.1906G>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Italy
F162	c.1906_1907insA	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	Spain
F757	c.1917C>T	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F758	c.1929C>T	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F759	c.1937-111C>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F760	c.1937-37C>G	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F761	c.1937-29T>C	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F565	c.1937-25C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F765	c.1937-25C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F766	c.1937-25C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F767	c.1937-25C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F777	c.1937-25C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium

F778	c.1937-25C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F779	c.1937-25C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F780	c.1937-25C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F781	c.1937-25C>A	Intronic SNVs	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F163	c.1965del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy
F349	c.2017C>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F350	c.2026G>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	2 BC, 1 LBC	Familial history of cancer	BC-only	Belgium
F351	c.2026G>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F352	c.2026G>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F164	c.2031del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	no criteria	4	DGC	4	Familial history of cancer	GC+BC	France
F353	c.2033T>C	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Germany
F354	c.2053G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	2 BC, 1 LBC	Familial history of cancer	BC-only	Belgium
F165	c.2062del	Frameshift	Coding truncating	PVS1; PM2	PV/LPV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	UK
F166	c.2064_2065del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	The Netherlands
F768	c.2079C>T	Synonymous	Synonymous	PS4_Moderate	VUS	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F355	c.2080G>A	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F356	c.2080G>A	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F357	c.2080G>A	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F769	c.2091G>A	Synonymous	Synonymous	PS4_Supporting	VUS	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F167	c.2095C>T	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Spain
F358	c.2098C>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium

F359	c.2104G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F360	c.2104G>A	Missense	Coding non-truncating	BA1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France
F168	c.2114del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy
F169	c.2116C>T	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	Germany
F361	c.2122C>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F770	c.2136G>T	Synonymous	Synonymous	-	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	GC-only	Slovenia
F170	c.2164+2T>A	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F171	c.2164+2T>A	Splice-site	Coding truncating	PVS1_Strong; PS4_Moderate; PM2	PV/LPV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	UK
F172	c.2164+3_2164+6del	Splice-site &	Coding truncating &	PS4_Supporting; PM2	VUS	2	4	DGC	4	Personal history of cancer	GC-only	Spain
F771	c.2165-111G>C	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F772	c.2165-111G>C	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F773	c.2165-59C>T	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F173	c.2165-1G>T	Splice-site	Coding truncating	PVS1_Strong; PM2	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	GC-only	Slovenia
F362	c.2194C>T	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	Belgium
F363	c.2194C>T	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France
F178	c.2195G>A	Splice-site	Coding truncating	PS3; PS4; PM2; PP3	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F174	c.2195G>A	Splice-site	Coding truncating	PS3; PS4; PM2; PP3	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Spain
F179	c.2195G>A	Splice-site	Coding truncating	PS3; PS4; PM2; PP3	PV/LPV	no criteria	4	DGC	4	Personal history of cancer	GC-only	The Netherlands
F176	c.2195G>A	Splice-site	Coding truncating	PS3; PS4; PM2; PP3	PV/LPV	no criteria	no criteria	2 GC, 1<50	History of GC+BC, 1 LBC regardless of age	Familial history of cancer	GC+BC	France
F175	c.2195G>A	Splice-site	Coding truncating	PS3; PS4; PM2; PP3	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	Spain

F177	c.2195G>A	Splice-site	Coding truncating	PS3; PS4; PM2; PP3	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Spain
F364	c.2204C>T	Missense	Coding non-truncating	PS4_Supporting	VUS	2	4	DGC	4	Personal history of cancer	GC-only	Spain
F365	c.2204C>T	Missense	Coding non-truncating	PS4_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F366	c.2204C>T	Missense	Coding non-truncating	PS4_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F774	c.2205G>A	Synonymous	Synonymous	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F180	c.2220del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	UK
F367	c.2248G>A	Missense	Coding non-truncating	PS4_Supporting; PM2	VUS	2	4	DGC	4	Personal history of cancer	GC-only	UK
F368	c.2266G>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F181	c.2275G>T	Nonsense	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	no criteria	no criteria	HBOC	Isolated LBC <55	Personal history of cancer	BC-only	Belgium
F775	c.2280C>T	Synonymous	Synonymous	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F369	c.2281G>A	Missense	Coding non-truncating	PS4_Moderate; BS2_Supporting	VUS	1	1	HBOC	1	Familial history of cancer	GC+BC	France
F776	c.2286A>G	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France
F370	c.2292C>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	UK
F566	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F782	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F783	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F784	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F785	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F786	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F787	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F788	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy

F789	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F790	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F791	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F792	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Spain
F801	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F802	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	GC-only	Italy
F803	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F804	c.2292C>T	Synonymous	Synonymous	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F793	c.2295+45C>T	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F794	c.2295+46G>A	Intronic SNVs	Non-coding	PS4_Moderate	VUS	2	4	DGC	4	Personal history of cancer	GC-only	Italy
F795	c.2296-60C>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	personal history of cancer	BC-only	Belgium
F796	c.2296-42C>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F797	c.2296-41T>C	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F798	c.2296-14T>C	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F182	c.2315T>A	Missense	Coding non-truncating	PS4_Supporting; PM2	VUS	2	4	DGC	4	Personal history of cancer	GC-only	Italy
F371	c.2317C>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F799	c.2322G>A	Synonymous	Synonymous	PS4_Supporting; PM2	VUS	1	1	DGC	1	Familial history of cancer	GC-only	Germany
F372	c.2329G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F373	c.2329G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F374	c.2329G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F375	c.2329G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium

F376	c.2329G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F377	c.2332G>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F378	c.2332G>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F379	c.2336G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F380	c.2336G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F381	c.2336G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F382	c.2336G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F383	c.2336G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F384	c.2336G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F388	c.2343A>T	Missense	Coding non-truncating	BS2	LBV/BV	1	1	HBOC	1	Familial history of cancer	GC+BC	UK
F385	c.2343A>T	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	GC-only	France
F386	c.2343A>T	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Germany
F387	c.2343A>T	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F389	c.2371C>T	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F390	c.2371C>T	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F183	c.2386del	Frameshift	Coding truncating	PVS1; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	France
F391	c.2386C>T	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F392	c.2387G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F393	c.2387G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F394	c.2387G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F395	c.2387G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Slovenia

F396	c.2387G>A	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Slovenia
F397	c.2398C>T	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F398	c.2398C>T	Missense	Coding non-truncating	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F399	c.2399G>A	Missense	Coding non-truncating	BS2; BP2_Strong	LBV/BV	no criteria	no criteria	2 GC, 1<50	no criteria	Familial history of cancer	GC-only	The Netherlands
F800	c.2412C>T	Synonymous	Synonymous	BP7	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F496	c.2413G>A	Missense	Coding non-truncating	BA1; BS2_ Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F497	c.2413G>A	Missense	Coding non-truncating	BA1; BS2_ Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F498	c.2413G>A	Missense	Coding non-truncating	BA1; BS2_ Supporting	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F499	c.2413G>A	Missense	Coding non-truncating	BA1; BS2_ Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F500	c.2413G>A	Missense	Coding non-truncating	BA1; BS2_ Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F501	c.2413G>A	Missense	Coding non-truncating	BA1; BS2_ Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F502	c.2413G>A	Missense	Coding non-truncating	BA1; BS2_ Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F503	c.2413G>A	Missense	Coding non-truncating	BA1; BS2_ Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F504	c.2413G>A	Missense	Coding non-truncating	BA1; BS2_ Supporting	LBV/BV	no criteria	no criteria	HBOC	History of GC+BC, 1 LBC regardless of age	Familial history of cancer	GC+BC	France
F505	c.2413G>A	Missense	Coding non-truncating	BA1; BS2_ Supporting	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F400	c.2439+3A>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France
F808	c.2439+10C>T	Intronic SNVs	Non-coding	BS1	LBV/BV	no criteria	no criteria	DGC	no criteria	Personal history of cancer	GC-only	Italy
F567	c.2439+10C>T	Intronic SNVs	Non-coding	BS1	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F805	c.2439+10C>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F807	c.2439+10C>T	Intronic SNVs	Non-coding	BS1	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy

F806	c.2439+45C>G	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F568	c.2439+53G>A	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F812	c.2439+53G>A	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F813	c.2439+53G>A	Intronic SNVs	Non-coding	PM2; BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F184	g.67424298-67425126del [EX16del828bp]	Large deletion	Coding truncating	PVS1_Strong; PS4_Supporting; PM2	PV/LPV	2	4	DGC	4	Personal history of cancer	GC-only	UK
F809	c.2440-143G>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F810	c.2440-118G>A	Intronic SNVs	Non-coding	PM2	VUS	no criteria	no criteria	no criteria	no criteria	No familial/personal cancer history	-	Portugal
F811	c.2440-52A>G	Intronic SNVs	Non-coding	-	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F831	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	2	4	DGC	4	Personal history of cancer	GC-only	Italy
F825	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	2	4	DGC	4	Personal history of cancer	GC-only	Germany
F832	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	1	1	DGC	1	Familial history of cancer	GC-only	The Netherlands
F569	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F814	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F815	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F816	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F817	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F818	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F819	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F820	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F821	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Italy
F822	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy

F823	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F824	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Unknown	-	Italy
F826	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F827	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Spain
F828	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F829	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F830	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F833	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	GC-only	The Netherlands
F834	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	The Netherlands
F846	c.2440-6C>G	Intronic SNVs	Non-coding	BS1; BS2; BS3; BP4	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F516	c.2440-6_2440-4delCTT	Intronic deletion	Non-coding	BP4	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F185	g.(?_68833290)_(68835537_?)del [EX16del]	Large deletion	Coding truncating	PVS1_Strong; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	UK
F835	c.2451G>A	Synonymous	Synonymous	BS2; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F401	c.2474C>T	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F402	c.2474C>T	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Slovenia
F403	c.2474C>T	Missense	Coding non-truncating	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Slovenia
F404	c.2494G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Italy
F405	c.2494G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F406	c.2494G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F407	c.2494G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F408	c.2494G>A	Missense	Coding non-truncating	BS1; BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France

F409	c.2512A>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Germany
F410	c.2512A>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Germany
F411	c.2512A>G	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Germany
F412	c.2515G>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	France
F413	c.2520del	Frameshift	Coding truncating	PVS1_Moderate; PS4_Supporting; PM2	PV/LPV	1	1	DGC	1	Familial history of cancer	GC-only	Italy
F836	c.2520C>T	Synonymous	Synonymous	BS1; BP4; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	Other cancer	Spain
F414	c.2521G>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F837	c.2544G>C	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F415	c.2558C>T	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F416	c.2558C>T	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Spain
F417	c.2578G>A	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Portugal
F838	c.2589C>T	Synonymous	Synonymous	BP7	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F418	c.2602C>T	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F839	c.2628C>T	Synonymous	Synonymous	PM2; BP7	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F840	c.2634C>T	Synonymous	Synonymous	BA1; BP2_Strong	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F841	c.2634C>T	Synonymous	Synonymous	BA1; BP2_Strong	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Belgium
F419	c.2635G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F420	c.2635G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F421	c.2635G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F422	c.2635G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F423	c.2635G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium

F424	c.2635G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F425	c.2635G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F426	c.2635G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F427	c.2635G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F428	c.2635G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	France
F429	c.2635G>A	Missense	Coding non-truncating	BS2	LBV/BV	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	GC+BC	Belgium
F842	c.2637C>T	Synonymous	Synonymous	BS2_Supporting; BP7	LBV/BV	no criteria	no criteria	no criteria	no criteria	Unknown	-	Belgium
F843	c.2637C>T	Synonymous	Synonymous	BS2_Supporting; BP7	LBV/BV	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	France
F844	c.2640G>A	Synonymous	Synonymous	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F517	c.2644G>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Spain
F518	c.2644G>A	Missense	Coding non-truncating	-	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Spain
F430	c.2646C>G	Missense	Coding non-truncating	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F845	c.*7C>G	3'-UTR SNV	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F570	c.*8G>A	3'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F847	c.*8G>A	3'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F848	c.*8G>A	3'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F849	c.*8G>A	3'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F850	c.*8G>A	3'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F851	c.*8G>A	3'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	Other cancer	Belgium
F852	c.*8G>A	3'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	France
F853	c.*8G>A	3'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	BC-only	Belgium

F519	c.*16C>T	3'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Italy
F520	c.*16C>T	3'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Italy
F521	c.*16C>T	3'-UTR SNV	Non-coding	BS2_Supporting	VUS	no criteria	no criteria	HBOC	no criteria	Personal history of cancer	BC-only	Belgium
F522	c.*29C>A	3'-UTR SNV	Non-coding	-	VUS	no criteria	no criteria	no criteria	no criteria	Familial history of cancer	Other cancer	Belgium
F523	c.*55G>A	3'-UTR SNV	Non-coding	PM2	VUS	no criteria	no criteria	HBOC	no criteria	Familial history of cancer	BC-only	Belgium
F186	c.(163+1_164-1)_(387+1_388-1)del [EX3del]/ c.586G>T (cis)	Large deletion	Coding truncating	PVS1; PS4; PM2 / PVS1; PS4_Supporting; PM2; BP2	PV/LPV	no criteria	3	HBOC	3	Familial history of cancer	GC+BC	France
F506	c.532-18C>T/c.1774G>A	Missense	Coding non-truncating	BA1; BS2/BA1	LBV/BV	no criteria	4	DGC	4	Personal history of cancer	GC-only	Italy
F431	c.1406C>T/c.2590G>A	Missense	Coding non-truncating	PM2/BS2_Supporting	VUS	no criteria	no criteria	no criteria	no criteria	Personal history of cancer	BC-only	Spain
F432	c.1774G>A/c.2439+5_2439+8delGTAA	Splice-site	Coding truncating	PS4_Supporting; PM2; PP3	PV/LPV	1	1	DGC	1	Familial history of cancer	GC+BC	The Netherlands

UTR - Untranslated region; PV/LPV – Pathogenic/likely pathogenic variants; VUS – Variant of unknown significance; LB/BV - Likely benign/benign variants; NA – Not applicable; HDGC – Hereditary diffuse gastric cancer; DGC – Difusse gastric cancer; HBOC – Hereditary breast and ovarian cancer; BC – Breast cancer; GC – Gastric cancer; ins – Insertion. & – Predicted to affect splicing and be truncating based on *in silico* tools only

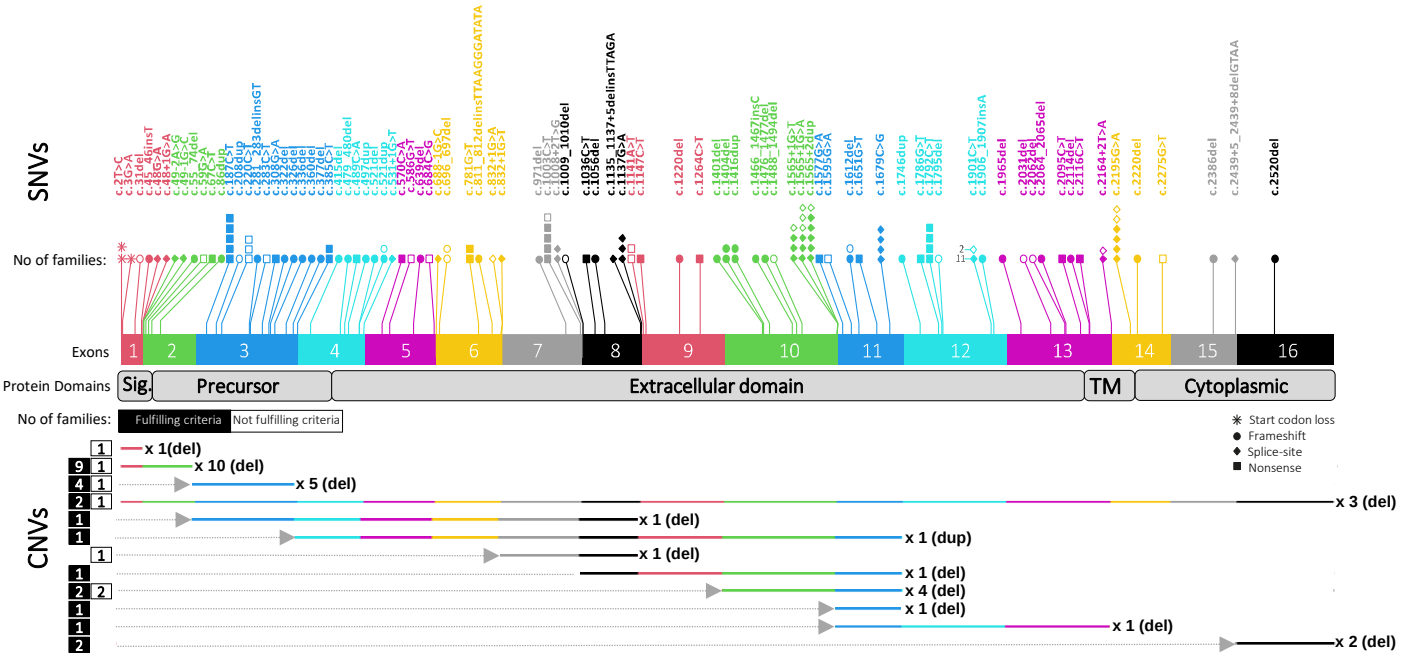
Variant group	% of families (n)	Molecular type	% of families (n)	Clinical classification		
				PV/LPV % (n)	VUS % (n)	LBV/BV % (n)
Coding truncating	22% (184)	Large del	4% (30)	100% (30)	0% (0)	0% (0)
		Start loss	0·4% (3)	100% (3)	0% (0)	0% (0)
		Nonsense	5% (40)	100% (40)	0% (0)	0% (0)
		Frameshift	5% (46)	100% (46)	0% (0)	0% (0)
		Splice-site	7% (63)	89% (56)	11% (7)	0% (0)
		Large dup	0·2% (2)	50% (1)	50% (1)	0% (0)
Coding non-truncating	37% (320)	Missense	37% (316)	0% (0)	53% (169)	47% (147)
		In-frame insertion	0·4% (3)	0% (0)	100% (3)	0% (0)
		In-frame exon skipping	0·1% (1)	0% (0)	100% (1)	0% (0)
Non-coding (regulatory)	27% (227)	Intronic del	0·5% (4)	0% (0)	100% (4)	0% (0)
		5′-UTR SNV	0·9% (8)	0% (0)	75% (6)	25% (2)
		3′-UTR SNV	2% (14)	0% (0)	100% (14)	0% (0)
		Intronic SNV	24% (201)	0% (0)	53% (106)	47% (95)
Synonymous	14% (123)	Synonymous	14% (123)	0% (0)	33% (40)	67% (83)
Total	**854**	**Total**	**854**	**176**	**351**	**327**

Molecular and clinical classification of *CDH1* germline variants in the cohort. Absolut number and frequency (%) in families of each variant group and molecular type were calculated based on the total number of families. Clinical classification frequencies (%) were calculated using the total number of families per molecular type. PV/LPV – Pathogenic/likely pathogenic variants; VUS – Variants of unknown significance; LBV/BV – likely benign/benign variants; dup – Duplications; del – Deletions; SNV – Single nucleotide variants

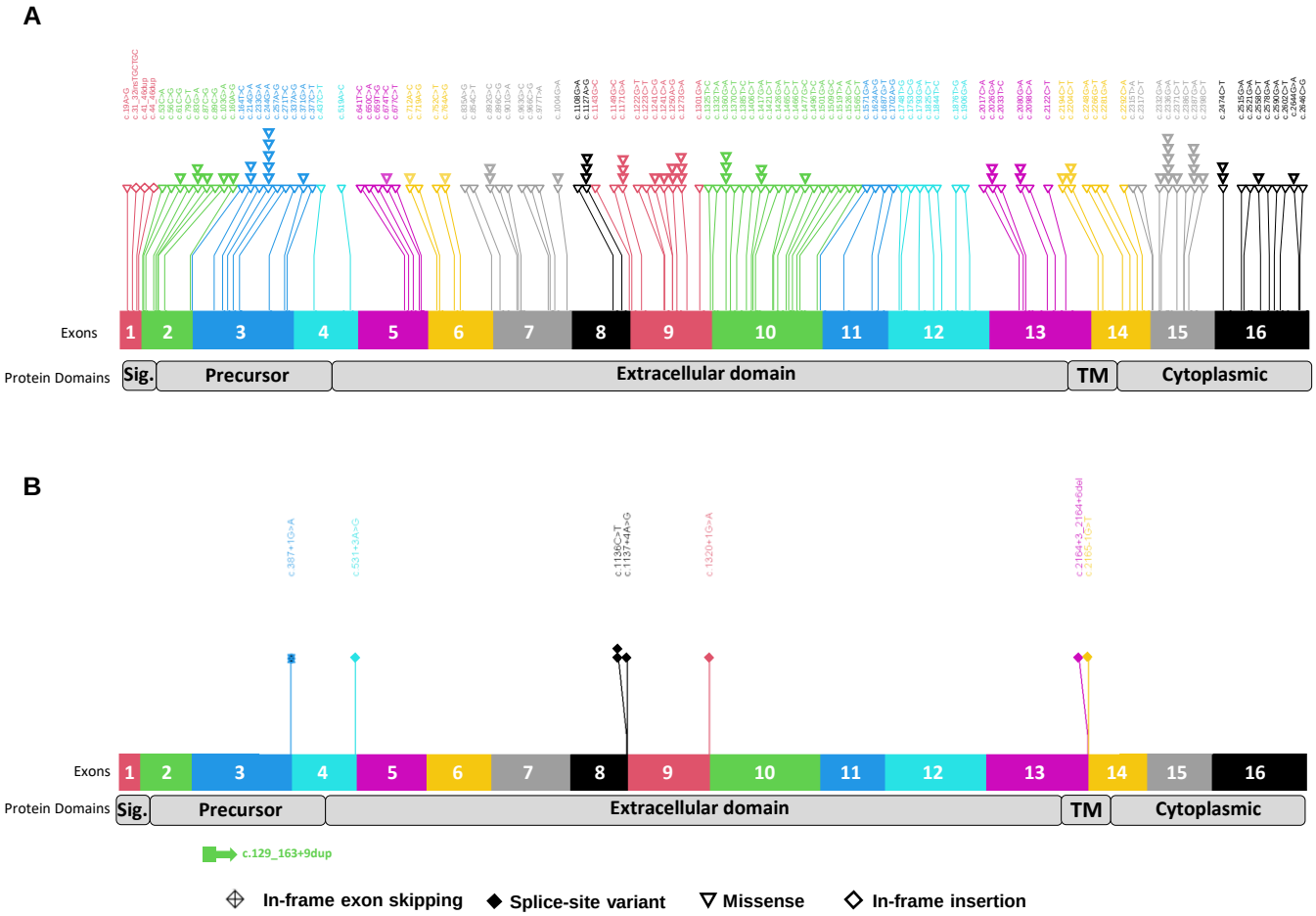
Description of families carrying two different *CDH1* germline variants, the classification of each and the final classification for analysis.

Family number	Variant 1 (*CDH1*)	Variant 1 group/ predicted consequence	Variant 1 ACMG/AMP *CDH1* classification	Variant 2 (*CDH1*)	Variant 2 group/ predicted consequence	Variant 2 ACMG/AMP *CDH1* classification	Final classification for analysis
432	c.2439+5_2439+8delGTAA	Truncating	PV/LPV	c.1774G>A	Missense	LBV/BV	PV/LPV
186	Ex3del	Truncating	PV/LPV	c.586G>T (*cis*)	Truncating	PV/LPV	PV/LPV
431	c.1406C>T	Missense	VUS	c.2590G>A	Missense	VUS	VUS
506	c.532-18C>T	Regulatory	LBV/BV	c.1774G>A	Missense	LBV/BV	LBV/BV

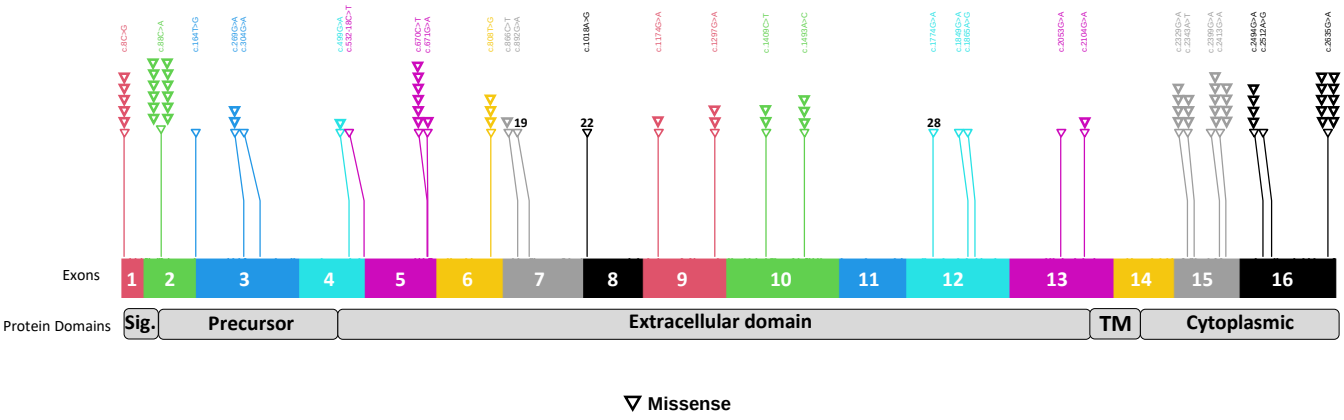
PV/LPV – pathogenic/likely pathogenic variants; VUS – variant of unknown significance; LB/BV - likely benign/benign variants



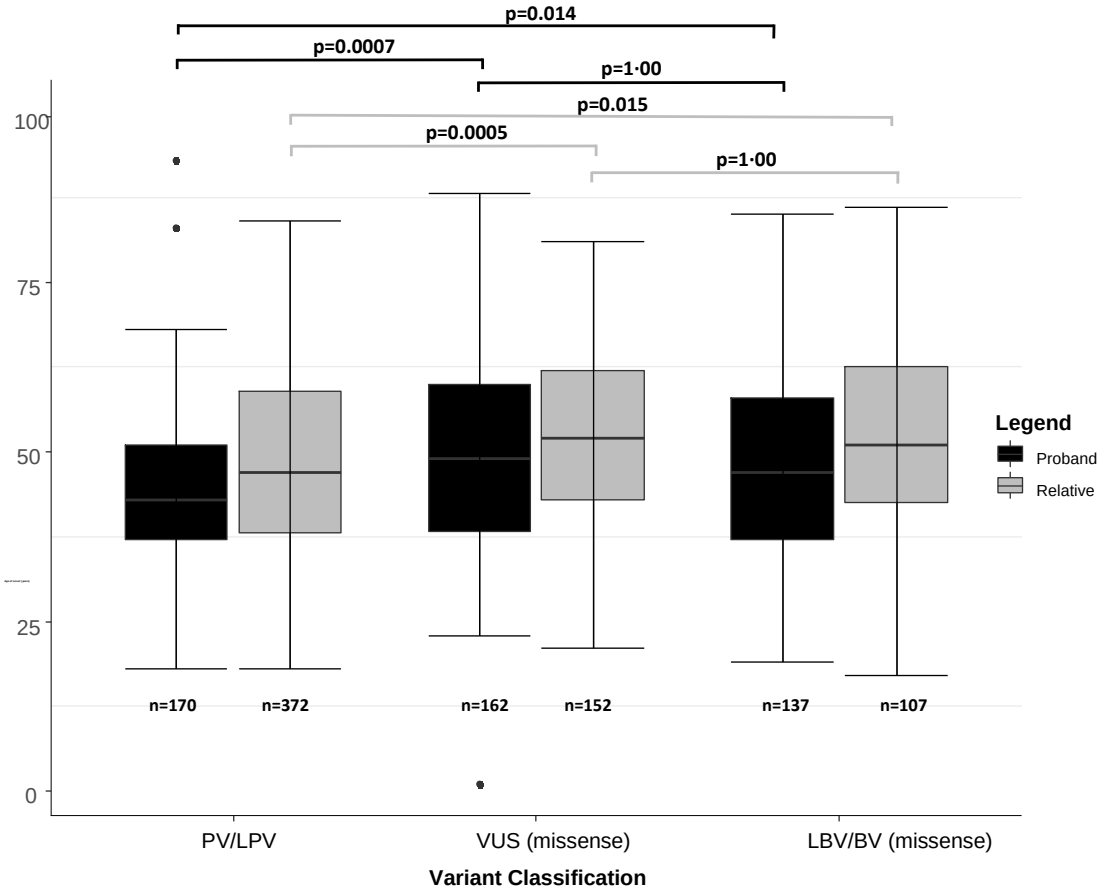
CDH1* gene model representing PV/LPV SNVs and CNVs in families fulfilling and lacking 2015 HDGC criteria.** 87 different SNVs: ***vertical pile of symbols - total number of families carrying each variant, ***symbol shape*** - variant molecular type. 13 different CNVs: type of structural alteration, extension across *CDH1 locus* and frequency in families is represented on the right. ***Families fulfilling 2015 HDGC criteria***: full colored or black symbols; ***Families lacking criteria:*** white or unfilled symbols. PV/LPV – Pathogenic/likely pathogenic variants; del – Deletion; dup – Duplication; SNVs – Single nucleotide variants; No. – Number; CNVs – Copy number variants; TM – Transmembrane domain; Sig. – Signaling domain



***CDH1* gene model representing genomic location and number of families of:** (A) **VUS – Missense (n=109) + in-frame insertion variants (n=3)** (B) **VUS - Splice-site variants (n=7).** Each symbol represents one family independently of fulfillment of criteria. VUS – variants of unknown significance



***CDH1* gene model representing genomic location and number of families of LBV/BV - Missense variants (n=29)**. Each symbol represents one family independently of criteria fulfillment. VUS – variants of unknown significance; LBV/BV – likely benign/benign variants



Comparison of the age of onset distribution of probands and relatives for different types of variants. The age was compared between groups using a kruskall wallis and the depicted significance is the adjusted p-value corrected with the Bonferroni method. Age of onset was missing for 232 phenotypes.

Supporting data for figure 1B. Distribution of the families fulfilling the 2015 HDGC clinical criteria[3] by the different classes of variants.

			VARIANT						
	Total (n=854)		PV/LPV (n=176)		Missense VUS (n=351)		Missense LBV/BV (n=327)		
	n	%	n	%	n	%	n	%	P-value
Fulfilling criteria[3]	182	21·3	136	77·3	20	5·7	26	8·0	**<0·0001**

The criteria fulfillment was compared using a chi-square test.

PV/LPV- Pathogenic Variant/Likely Pathogenic Variant; VUS- Variant of Unknown Significance; LBV/BV- Likely Benign Variant/Benign Variant

Distribution of families in families fulfilling 2015 HDGC criteria[3] families and lacking 2015 HDGC criteria[3] in accordance with the variant group and the molecular type of the variant carried by each proband.

Families fulfilling 2015 HDGC criteria (N=182)							
Clinical classification	**Number of families**	**%**	**Variant group**	**Number of families**	**%**	**Molecular type**	**Number of families**
PV/LPV	136	75%	Coding truncating	136	100%	Frameshift	35
						Large deletion	23
						Large duplication	1
						Nonsense	29
						Splice-site	45
						Start codon loss	3
VUS	20	11%	Coding truncating	2	10%	Large duplication	1
						Splice-site	1
			Coding non-truncating	14	70%	Missense	14
			Non-coding (Regulatory)	1	5%	Intronic SNV	1
			Synonymous	3	15%	Synonymous	3
LBV/BV	26	14%	Coding non-truncating	8	31%	Missense	8
			Non-coding (Regulatory)	12	46%	5'-UTR SNV	1
						Intronic SNV	11
			Synonymous	6	23%	Synonymous	6
Total	**182**	**100%**		**182**	**-**		**182**

Families not fulfilling 2015 HDGC criteria (N=672)							
Clinical classification	**Number of families**	**%**	**Variant group**	**Number of families**	**%**	**Molecular type**	**Number of families**
PV/LPV	40	6%	Coding truncating	40	100%	Frameshift	11
						Large deletion	7
						Nonsense	11
						Splice-site	11
VUS	331	49%	Coding truncating	6	2%	Splice-site	6
			Coding non-truncating	159	48%	Missense	155
						In-frame insertion	3
						In-frame exon skipping	1
			Non-coding (Regulatory)	129	39%	5'-UTR SNV	6
						3'-UTR SNV	14
						Intronic deletion	4
						Intronic SNV	105
			Synonymous	37	11%	Synonymous	37
LBV/BV	301	45%	Coding non-truncating	139	46%	Missense	139
			Non-coding (Regulatory)	85	28%	5'-UTR SNV	1
						Intronic SNV	84
			Synonymous	77	26%	Synonymous	77
Total	**672**	**100%**		**672**	**-**		**672**

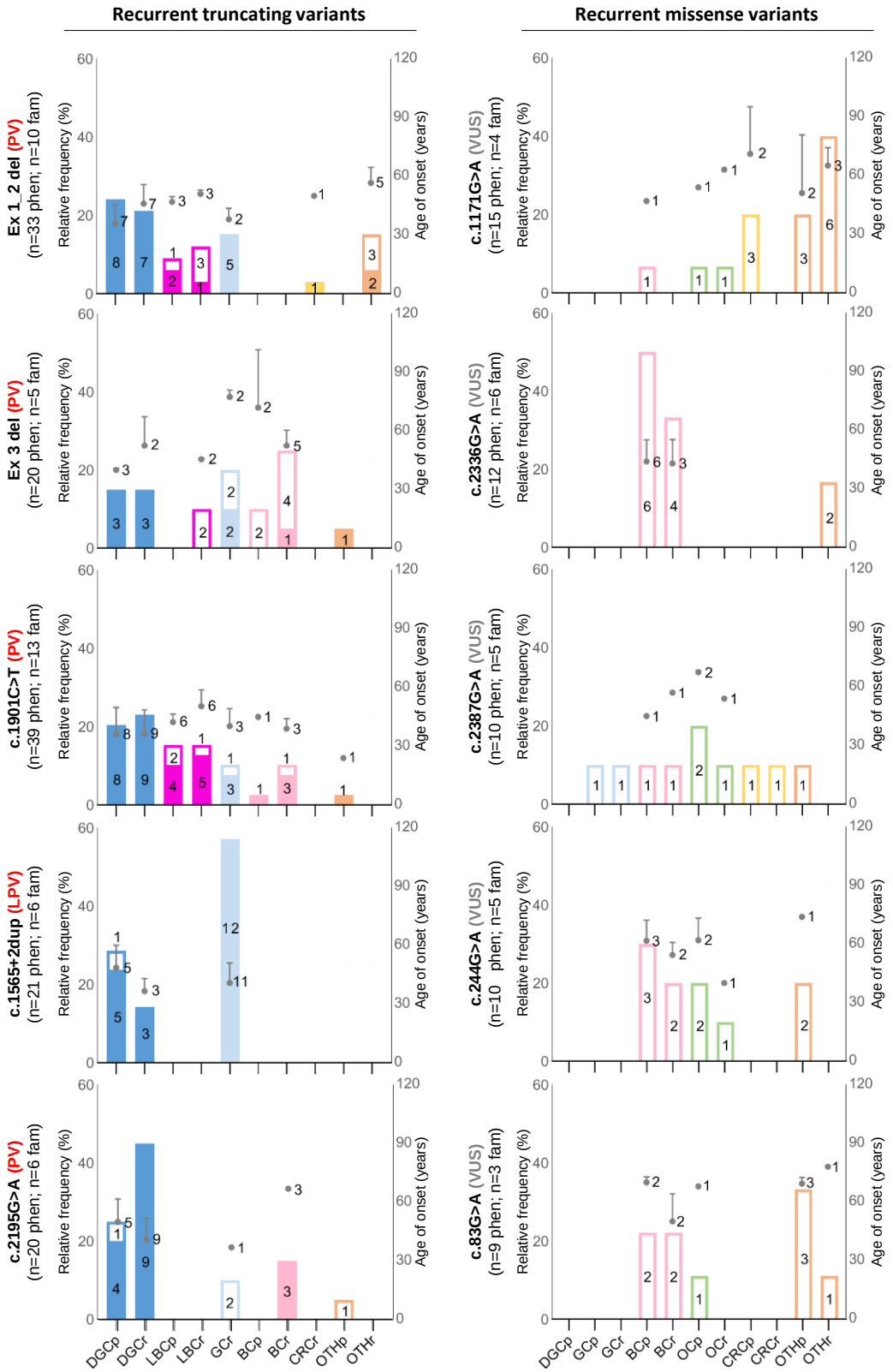
PV/LPV – Pathogenic/likely pathogenic variants; VUS – Variants of unknown significance; LBV/BV – Likely benign/benign variants; SNV – Single nucleotide variants; UTR – Untranslated region

Supporting data for figure 2. Details on phenotypes distribution and age of onset for families carrying pathogenic/likely pathogenic variants (PV/LPV) and variants of unknown significance (VUS) molecularly classified as missense.

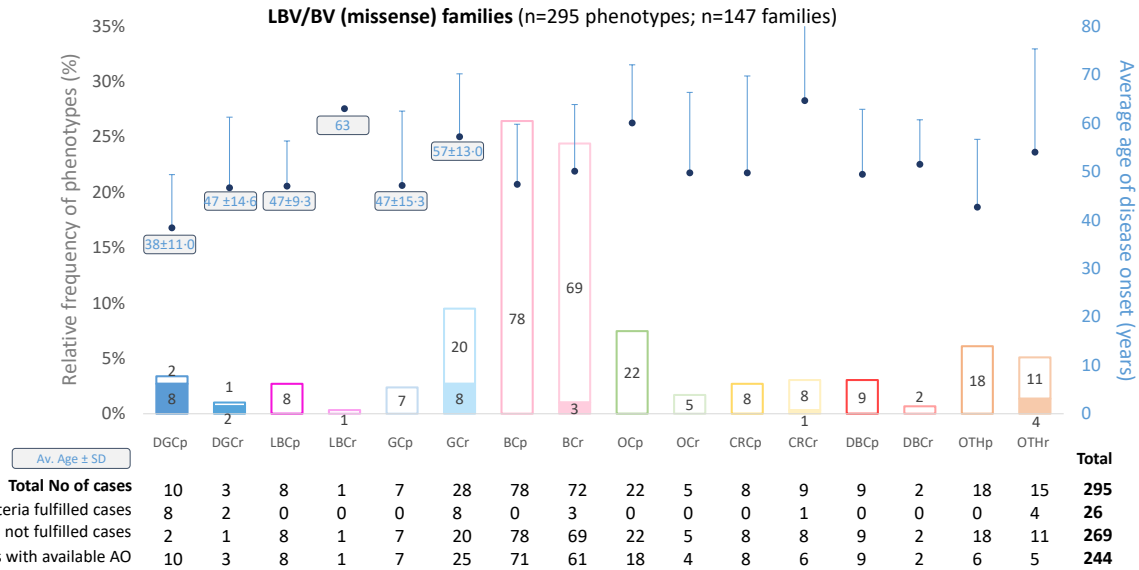
PV/LPV (all truncating)	**DGCp**	**DGCr**	**LBCp**	**LBCr**	**GCp**	**GCr**	**BCp**	**BCr**	**OCp**	**OCr**	**CRCp**	**CRCr**	**DBCp**	**DBCr**	**OTHERp**	**OTHERr**	**Total**
Total number of cases	122	116	36	31	3	151	10	80	2	3	0	12	3	2	16	44	631
Criteria fulfilled	114	114	17	15	2	132	3	47	1	1	0	8	0	1	11	26	492
Criteria not-fulfilled	8	2	19	16	1	19	7	33	1	2	0	4	3	1	5	18	1123
Cases with age of onset available	114	110	33	29	3	122	9	67	2	1	0	10	3	2	6	31	542
Average age of onset	42·06	41·91	46·76	50·76	40·67	47·18	53·00	53·43	54·00	50·00	-	66·10	55·67	47·00	38·67	55·35	
±SD	12·16	12·46	7·75	9·22	3·51	14·98	15·70	12·54	8·49	-	-	12·67	11·50	5·66	15·67	15·97	

VUS (missense)	**DGCp**	**DGCr**	**LBCp**	**LBCr**	**GCp**	**GCr**	**BCp**	**BCr**	**OCp**	**OCr**	**CRCp**	**CRCr**	**DBCp**	**DBCr**	**OTHERp**	**OTHERr**	**Total**
Total number of cases	15	13	5	0	2	19	101	118	24	10	11	14	7	0	33	34	406
Criteria fulfilled	14	13	0	0	0	5	0	1	0	0	0	2	0	0	0	5	40
Criteria not-fulfilled	1	0	5	0	2	14	101	117	24	10	11	12	7	0	33	29	366
Cases with age of onset available	15	13	5	0	1	15	93	101	19	5	7	2	5	0	17	16	314
Average age of onset	44·93	42·92	50·20	-	34·00	55·67	46·94	52·86	62·84	53·80	53·57	49·50	36·80	-	54·59	61·06	
±SD	12·23	14·03	5·02	-	-	17·29	11·52	11·57	12·43	9·44	20·29	17·68	13·68	-	22·42	14·59	

DGC- Diffuse Gastric Cancer; LBC- Lobular Breast Cancer; GC- Gastric Cancer; BC- Breast Cancer; OC- Ovarian Cancer; CRC- Colorectal Cancer; DBC- Ductal Breast Cancer; SD- Standard Deviation; p- Probands; r- Relatives; PV/LPV – Pathogenic/likely pathogenic variants; VUS – Variants of unknown significance



Distribution of phenotypes and respective age of onset of families with recurrent *CDH1* variants according to the type of the variant. Full colour represents fulfillment of criteria[3]; number close to the dots for the average age of onset represents number of cases to calculate average age of onset. Phen – phenotype; Fam – family; DGC - diffuse gastric cancer; LBC – lobular breast cancer; GC – gastric cancer; BC – breast cancer; OC – ovarian cancer; CRC – colorectal cancer; DBC – ductal breast cancer; OTH – other phenotypes; p – proband; r – relative; P/LPV - pathogenic/likely pathogenic variants; VUS - variants of unknown significance



LBV/BV (missense)	DGCp	DGCr	LBCp	LBCr	GCp	GCr	BCp	BCr	OCp	OCr	CRCp	CRCr	DBCp	DBCr	OTHERp	OTHERr	Total
Total number of cases	10	3	8	1	7	28	78	72	22	5	8	9	9	2	18	15	295
Criteria fulfilled	8	2	0	0	0	8	0	3	0	0	0	1	0	0	0	4	26
Criteria not-fulfilled	2	1	8	1	7	20	78	69	22	5	8	8	9	2	18	11	269
Cases with age of onset available	10	3	8	1	7	25	71	61	18	4	8	6	9	2	6	5	244
Average age of onset	38·40	46·67	47·00	63·00	47·14	57·20	47·37	50·08	60·06	49·75	49·75	64·67	49·44	51·50	42·67	54·00	
±SD	10·96	14·57	9·30	-	15·35	12·97	12·41	13·74	11·98	16·58	20·00	17·45	13·41	9·19	13·98	21·32	

Distribution of phenotypes and cancer average age of onset, in probands carrying LBV/BV molecularly classified as missense and their relatives. Relative frequency (%) of phenotypes, phenotype distribution, number of cases and average age of onset in probands (p) and relatives (r). Left Y-axis: Relative frequency over the total number of phenotypes (%). Full-colored bars: probands/relatives from families fulfilling 2015 HDGC criteria. Right Y-axis: average age of onset ± SD with values for HDGC-associated phenotypes only. p – Probands; r – Relatives; LBV/BV – Likely benign/benign variants; DGC – Diffuse gastric cancer; GC – Gastric cancer; LBC – Lobular breast cancer; BC – Breast cancer of unknown histotype; DBC – ductal breast cancer; OC – Ovarian cancer; CRC – Colorectal cancer; OTHER – Other phenotypes No. – Number; Av. Age – Average age of onset; AO – Age of onset; ±SD – ± Standard deviation. Probands may present more than one phenotype.

Supporting data for figure 2A and 2B. Distribution of the sample with breast cancer (n=309) fulfilling 2015 HDGC clinical criteria[3] and carrying PV/LPV and missense-VUS.

	Total (n=309)		VARIANT: PV/LPV (n=90)		VARIANT: Missense VUS (n=219)		Odds ratio of fulfilling 2015 HDGC criteria[3] with BC if carrier of a missense-VUS		
	n	%	n	%	n	%	Odds ratio	95%CI	p-value
BC & fulfilling criteria (2015)[3]	51	16·5	50	55·6	1	0·5	0·004	0·00-0·03	**<0·0001**

The criteria fulfillment was compared using a chi-square test.

PV/LPV- Pathogenic/Likely Pathogenic Variant; VUS - Variant of Unknown Significance; BC - Breast cancer (of unknown histotype); 95%CI: 95% Confidence Interval;

Supporting data for figure 2A and Supplementary appendix (p 57). Distribution of the sample with breast cancer (n=309) fulfilling the 2015 HDGC clinical criteria by the PV/LPV and missense-LBV/BV classes.

	Total (n=240)		VARIANT: PV/LPV (n=90)		VARIANT: Missense LBV/BV (n=150)		Odds ratio of fulfilling 2015 HDGC criteria[3] with BC if carrier of an missense-LBV/BV		
	n	%	n	%	n	%	Odds ratio	95%CI	p-value
BC fulfilling criteria (2015)[3]	53	22·1	50	55·5	3	2·0	0·02	0·005-0·05	**<0·0001**

The criteria fulfillment was compared using a chi-square test.

PV/LPV- Pathogenic Variant/Likely Pathogenic Variant; LBV/BV- Likely Benign/Benign Variant; BC - Breast cancer (of unknown histotype); 95%CI: 95% Confidence Interval;

Supporting data for figure 2A and 2B. Distribution of PV/LPV and missense VUS associated phenotypes. The HDGC-related phenotypes are highlighted in grey.

			VARIANT						
	Total (n=1037)		PV/LPV (n=631)		Missense VUS (n=406)		Odds ratio of presenting a cancer phenotype if carrying missense VUS		
	n	%	n	%	n	%	Odds ratio	95%CI	p-value
Mean age (SD), years[a]	48·5 (14·0)	-	46·9 (13·8)	-	51·3 (14·0)	-			**<0·0001**
HDGC-associated phenotypes[b]	513	49·5	459	72·7	54	13·3	0·06	0·04-0·08	**<0·0001**
BC	309	29·8	90	14·3	219	53·9	7·04	5·23-9·47	**<0·0001**
CRC	37	3·6	12	1·9	25	6·2	3·38	1·68-6·82	**<0·0001**
OC	39	3·8	5	0·8	34	8·4	11·4	4·44-29·5	**<0·0001**
DBC	12	1·2	5	0·8	7	1·7	2·19	0·69-6·97	0·17
DGC	266	25·7	238	37·7	28	6·9	0·12	0·08-0·18	**<0·0001**
GC	175	16·9	154	24·4	21	5·2	0·17	0·10-0·27	**<0·0001**
LBC	72	6·9	67	10·6	5	1·2	0·10	0·04-0·26	**<0·0001**
Other	127	12·2	60	9·5	67	16·5	1·88	1·29-2·73	**0·0008**

[a]181 missing information; [b]HDGC-associated phenotypes combines DGC, GC and LBC phenotypes. Age was compared using an independent sample Student's t-test while all the other variables were compared using a chi-square test.

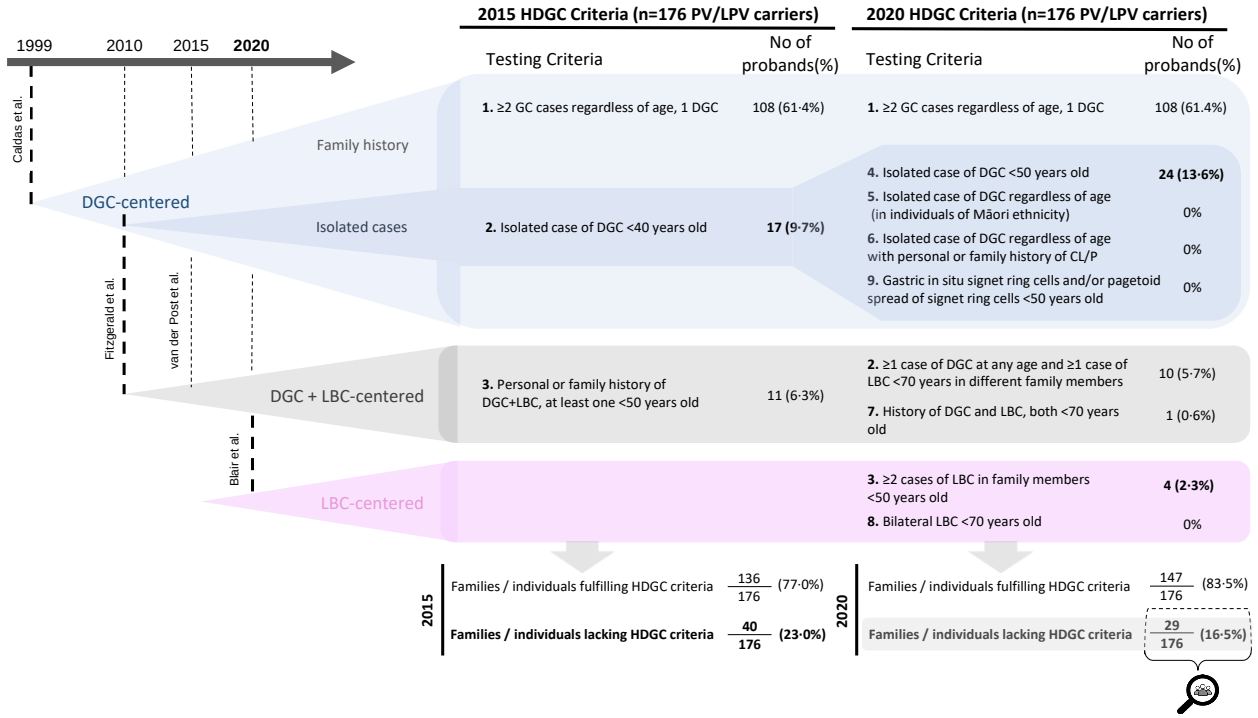
PV/LPV- Pathogenic Variant/Likely Pathogenic Variant; VUS- Variant of Unknown Significance; SD- Standard deviation; HDGC- Hereditary Diffuse Gastric Cancer; BC- Breast Cancer; CRC- Colorectal Cancer; OC- Ovarian Cancer; DBC- Ductal Breast Cancer; DGC- Diffuse Gastric Cancer; GC- Gastric Cancer; LBC- Lobular Breast Cancer; 95%CI: 95% Confidence Interval;

Supporting data for figure 2C. Univariate and multivariable logistic regression analysis in 856 phenotypes with available age of disease onset: PV/LPV *vs.* missense VUS. The HDGC-related phenotypes are highlighted in grey.

	PV/LPV *vs.* Missense VUS					
	Univariable			**Multivariable**		
	OR	**CI 95%**	**p-value**	**OR**	**CI 95%**	**p-value**
Age (Older *vs.* younger)	1·02	1·01-1·03	**<0·0001**	1·00	0·99-1·01	0·97
Phenotypes (Yes *vs.* No)						
BC	0·14	0·11-0·19	**<0·0001**	0·39	0·11-1·39	0·15
CRC	0·29	0·15-0·56	**0·0006**	1·11	0·24-5·19	0·90
OC	0·09	0·03-0·23	**<0·0001**	0·12	0·02-0·71	**0·019**
DBC*	0·46	0·14-1·44	0·18	-	-	-
DGC	8·18	5·39-12·4	**<0·0001**	8·00	2·18-29·4	**0·0017**
GC	0·17	0·11-0·27	**<0·0001**	7·81	2·03-30·0	**0·0027**
LBC	9·53	3·81-23·9	**<0·0001**	12·4	2·66-57·7	**0·0014**
Other	0·53	0·37-0·77	**0·0009**	1·12	0·29-4·24	0·87

*Phenotype not considered in the multivariable model due to being non-significant in the univariable model.

PV/LPV- Pathogenic Variant/Likely Pathogenic Variant; VUS- Variant of Unknown Significance; BC- Breast Cancer; CRC- Colorectal Cancer; OC- Ovarian Cancer; DBC- Ductal Breast Cancer; DGC- Diffuse Gastric Cancer; GC- Gastric Cancer; LBC- Lobular Breast Cancer; OR- Odds ratio



HDGC criteria along time, PV/LPV pick-up rate, *CDH1* variant frequency associated with disease setting: Evolution of HDGC genetic testing criteria and *CDH1* pick-up rate according to 2015 and 2020 HDGC criteria. HDGC – Hereditary diffuse gastric cancer; DGC – Diffuse gastric cancer; LBC – Lobular breast cancer; CL/P – Clef lip/palate; GC – Gastric cancer; BC – Breast cancer; PV/LPV – Pathogenic/likely pathogenic variants.

Phenotypical distribution for families lacking 2020 HDGC criteria[4] and proposed LBC-centred criteria and their proportion among PV/LPV carriers.

Family_ID	Nucelotide Change (HGVS) (NM_004360.4; LRG_301)	Molecular classification	Variant group/Predicted consequence	ACMG/AMP *CDH1* classification for analysis	2020 HDGC Criteria	Family history	LBC-centred criteria	No. of cases	% among families lacking 2020 HDGC criteria (n=29)	% among families with LPV/PV (n=176)
F001	EX_1del	Large deletion	Truncating	PV/LPV	no criteria	2 BC (1 LBC>50)	2 BC, 1 LBC	7	24%	4%
F040	c.220C>T	Nonsense	Truncating	PV/LPV	no criteria	2 LBC (1<50)				
F066	c.684C>G	Nonsense	Truncating	PV/LPV	no criteria	5 BC (1 LBC)				
F069	c.696_697del	Frameshift	Truncating	PV/LPV	no criteria	2 LBC (1<50)				
F115	c.1565+1G>A	Splice-site	Truncating	PV/LPV	no criteria	2 BC (1 LBC<50)				
F122	c.1565+1G>A	Splice-site	Truncating	PV/LPV	no criteria	4 BC (2 LBC (1<50))				
F152	c.1901C>T	Splice-site	Truncating	PV/LPV	no criteria	2 LBC (1<50)				
F103	EX10_11del	Large deletion	Truncating	PV/LPV	no criteria	2 GC (1<50), 3 BC (1 LBC)	History of GC+BC, 1 LBC regardless of age	7	24%	4%
F176	c.2195G>A	Splice-site	Truncating	PV/LPV	no criteria	2 GC (1<50), 1 LBC				
F073	c.832+1G>A	Splice-site	Truncating	PV/LPV	no criteria	3 BC (1 LBC<50), 1 GC<50, 1 CRC<50				
F097	c.1141A>T	Nonsense	Truncating	PV/LPV	no criteria	1 GC<50, 3 LBC (1<50)				
F113	c.1488_1494del	Frameshift	Truncating	PV/LPV	no criteria	1 GC<50, 4 BC (2 LBC (1<50))				
F121	c.1565+1G>A	Splice-site	Truncating	PV/LPV	no criteria	1 GC<50, 2 BC (1 LBC>50)				
F160	c.1901C>T	Splice-site	Truncating	PV/LPV	no criteria	1 GC<50, 2 BC (1 LBC<50)				
F075	EX7_8del	Large deletion	Truncating	PV/LPV	no criteria	1 LBC<50	Isolated LBC <55	4	14%	2·3%
F087	c.1009_1010del	Frameshift	Truncating	PV/LPV	no criteria	1 LBC>50				
F148	c.1795del	Frameshift	Truncating	PV/LPV	no criteria	1 LBC<50				
F181	c.2275G>T	Nonsense	Truncating	PV/LPV	no criteria	1 LBC<50				
F014	EX1_16del	Large deletion	Truncating	PV/LPV	no criteria	1 DBC>50; 1 BC>60; 1 other	No specific criteria met	11	38%	6%
F039	c.208dup	Frameshift	Truncating	PV/LPV	no criteria	1 GC<50; 1 CRC >70; 3 other				
F041	c.220C>T	Nonsense	Truncating	PV/LPV	no criteria	1DGC>50				
F044	c.283C>T	Nonsense	Truncating	PV/LPV	no criteria	1 BC>50; 1 BC<50; 2 other				
F061	c.521dup	Frameshift	Truncating	PV/LPV	no criteria	No family history				
F082	c.1003C>T	Nonsense	Truncating	PV/LPV	no criteria	1 OC>50				
F105	EX10_11del	Large deletion	Truncating	PV/LPV	no criteria	6 BC>50; 2 GC				
F114	c.1565+1G>T	Splice-site	Truncating	PV/LPV	no criteria	GC <50; 1 BC; 3 other				
F134	c.1612del	Frameshift	Truncating	PV/LPV	no criteria	BC				
F165	c.2062del	Frameshift	Truncating	PV/LPV	no criteria	2 DBC, 1<50 and 1 DGC>50; 1 BC>50				
F171	c.2164+2T>A	Splice-site	Truncating	PV/LPV	no criteria	1 DGC, 1 BC>50, 2 CRC 1>50, 1 OC				

PV/LPV - pathogenic/likely pathogenic variants; GC – gastric cancer; DGC – diffuse gastric cancer; BC – breast cancer; LBC – lobular breast cancer; HDGC – hereditary diffuse gastric cancer

Supporting data of Figure 4. Details on phenotypes distribution and age of onset for GC-only, GC+BC and BC-only families.

GC-only	DGCp	DGCr	LBCp	LBCr	GCp	GCr	BCp	BCr	OCp	OCr	CRCp	CRCr	DBCp	DBCr	OTHERp	OTHERr	Total
Total number of cases	84	72	0	0	0	74	0	0	0	1	0	4	0	0	7	13	255
2015 HDGC criteria fulfilled	79	72	NA	NA	0	73	NA	NA	0	1	0	3	NA	NA	6	10	244
2020 HDGC criteria contribution	4	0	NA	NA	0	0	NA	NA	0	0	0	0	NA	NA	0	0	4
LBC-centred contribution	NA	NA	NA	NA	0	0	NA	NA	0	0	0	0	NA	NA	0	0	0
No criteria fulfilled	1	0	NA	NA	0	1	NA	NA	0	0	0	1	NA	NA	1	3	7
Cases with age of onset available	80	67	0	0	0	57	0	0	0	1	0	3	0	0	2	8	218
Average age of onset	41·40	40·27	-	-	-	45·46	-	-	-	50·00	-	74·00	-	-	31·00	62·50	
±SD	12·17	11·02	-	-	-	13·87	-	-	-	-	-	9·54	-	-	8·49	12·38	

GC+BC	DGCp	DGCr	LBCp	LBCr	GCp	GCr	BCp	BCr	OCp	OCr	CRCp	CRCr	DBCp	DBCr	OTHERp	OTHERr	Total
Total number of cases	38	44	24	24	3	77	9	69	1	1	0	8	2	2	6	23	331
2015 HDGC criteria fulfilled	35	42	16	15	2	59	3	47	1	0	0	5	0	1	5	16	247
2020 HDGC criteria contribution	2	1	1	6	0	7	4	8	0	0	0	0	0	0	1	1	31
LBC-centred contribution	0	0	7	3	0	9	1	6	0	0	0	1	1	0	0	1	29
No criteria fulfilled	1	1	0	0	1	2	1	8	0	1	0	2	1	1	0	5	24
Cases with age of onset available	34	43	22	22	3	65	9	59	1	0	0	7	2	2	4	15	288
Average age of onset	43·59	44·47	47·41	49·73	40·67	48·69	53·00	54·17	48·00	-	-	62·71	55·50	47·00	42·50	50·73	
±SD	12·17	14·17	7·18	8·91	3·51	15·85	15·70	12·86	-	-	-	12·88	16·26	5·66	18·06	17·34	

BC-only	DGCp	DGCr	LBCp	LBCr	GCp	GCr	BCp	BCr	OCp	OCr	CRCp	CRCr	DBCp	DBCr	OTHERp	OTHERr	Total
Total number of cases	0	0	12	7	0	0	1	11	0	1	0	0	1	0	2	8	43
2015 HDGC criteria fulfilled	NA	NA	1	0	NA	NA	0	0	0	0	0	0	0	0	0	0	1
2020 HDGC criteria contribution	NA	NA	1	3	NA	NA	0	0	0	0	0	0	0	0	0	3	7
LBC-centred contribution	NA	NA	10	4	NA	NA	0	8	0	1	0	0	0	0	1	2	26
No criteria fulfilled	NA	NA	0	0	NA	NA	1	3	0	0	0	0	1	0	1	3	9
Cases with age of onset available	0	0	11	7	0	0	0	8	0	0	0	0	1	0	0	8	35
Average age of onset	-	-	45·45	54·00	-	-	-	48·00	-	-	-	-	56·00	-	-	56·88	
±SD	-	-	9·02	10·13	-	-	-	8·67	-	-	-	-	-	-	-	15·21	

DGC- Diffuse Gastric Cancer; LBC- Lobular Breast Cancer; GC- Gastric Cancer; BC- Breast Cancer; OC- Ovarian Cancer; CRC- Colorectal Cancer; DBC- Ductal Breast Cancer; NA – Not applicable; SD- Standard Deviation; p- Probands; r- Relatives

Distribution of families presenting isolated/family history of GC only, BC only, GC+BC, other cancers or no personal or family history of cancer in PV/LPV carriers. Families GC-only: 91 (Fulfilling 2020 HDGC criteria=89); families BC-only: 16 (Fulfilling 2020 HDGC criteria=2); Families GC+BC: 67 (Fulfilling 2020 HDGC criteria=56); total number of families: 176.

Family_ID	Nucelotide Change (HGVS) (NM_004360.4; LRG_301)	Molecular classification	Variant group/Predicted consequence	ACMG/AMP *CDH1* classification for analysis	GC and/or BC history	Number of families	2015 HDGC Criteria	2020 HDGC Criteria	Variants herein identified exclusively in BC-only families but previously reported in GC-families - PMID ref
F001	EX_1del	Large deletion	Truncating	PV/LPV	Exclusively_BC only	1	No criteria	No criteria	Not found
F003	EX1_2del	Large deletion	Truncating	PV/LPV	BC only	1	Criteria 4	Criteria 3	
F002; F004; F006; F007; F008; F009; F011	EX1_2del	Large deletion	Truncating	PV/LPV	GC only	7	6 x criteria 1; 1 x criteria 2	6 x criteria 1; 1 x criteria 4	
F05; F010	EX1_2del	Large deletion	Truncating	PV/LPV	GC+BC	2	Criteria 1; criteria 3	Criteria 1; criteria 7	
F012	EX1_16del	Large deletion	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F013	EX1_16del	Large deletion	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F014	EX1_16del	Large deletion	Truncating	PV/LPV	BC only	1	No criteria	No criteria	
F015	c.2T>C	Start codon loss	Truncating	PV/LPV	GC only	1	Criteria 2	Criteria 4	
F016	c.2T>C	Start codon loss	Truncating	PV/LPV	GC+BC	1	Criteria 3	Criteria 2	
F017	c.3G>A	Start codon loss	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F018	c.31del	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 4	Criteria 3	
F019	c.45_46insT	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F021	c.48+1G>A	Splice-site	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F022	c.49-2A>G	Splice-site	Truncating	PV/LPV	GC only	1	Criteria 2	Criteria 4	
F024	c.55_74del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 2	Criteria 4	
F025	c.59G>A	Nonsense	Truncating	PV/LPV	GC only	1	No criteria	Criteria 4	
F026	c.67C>T	Nonsense	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F027	c.86dup	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	

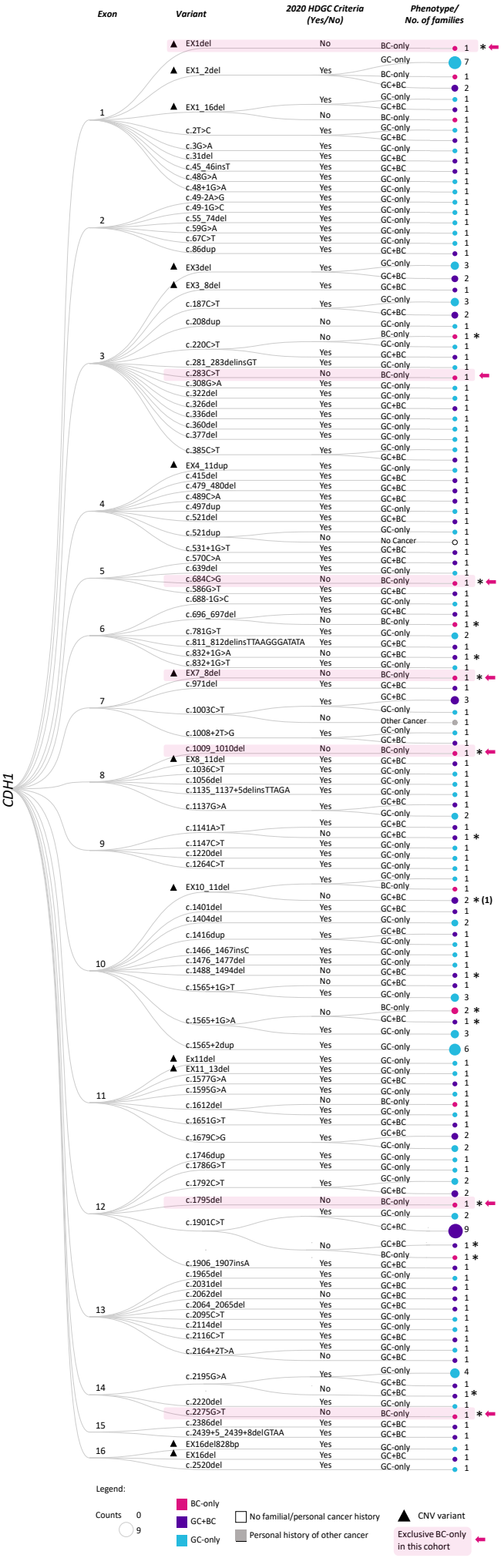
F029; F031; F032	EX3del	Large deletion	Truncating	PV/LPV	GC only	3	Criteria 2; 2 x criteria 1	Criteria 4; 2 x criteria 1	
F030; F186	EX3del	Large deletion	Truncating	PV/LPV	GC+BC	2	Criteria 1; criteria 4	Criteria 1; criteria 3	
F033	EX3_8del	Large deletion	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F034; F035; F036	c.187C>T	Nonsense	Truncating	PV/LPV	GC only	3	Criteria 2; 2 x criteria 1	Criteria 4; 2 x criteria 1	
F037; F038	c.187C>T	Nonsense	Truncating	PV/LPV	GC+BC	2	2 x criteria 1	2 x criteria 1	
F039	c.208dup	Frameshift	Truncating	PV/LPV	GC only	1	No criteria	No criteria	
F041	c.220C>T	Nonsense	Truncating	PV/LPV	GC only	1	No criteria	No criteria	
F042	c.220C>T	Nonsense	Truncating	PV/LPV	GC+BC	1	No criteria	Criteria 4	
F040	c.220C>T	Nonsense	Truncating	PV/LPV	BC only	1	No criteria	No criteria	
F043	c.281_283delinsGT	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F044	c.283C>T	Nonsense	Truncating	PV/LPV	Exclusively_BC only	1	No criteria	No criteria	11434599
F045	c.308G>A	Nonsense	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F046	c.322del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F047	c.326del	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F048	c.336del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F049	c.360del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F050	c.377del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 2	Criteria 4	
F051	c.385C>T	Nonsense	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F052	c.385C>T	Nonsense	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F054	EX4_11dup	Large duplication	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F055	c.415del	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F056	c.479_480del	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 3	Criteria 2	
F057	c.489C>A	Nonsense	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F058	c.497dup	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 2	Criteria 4	
F059	c.521del	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 3	Criteria 2	
F060	c.521dup	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F063	c.570C>A	Nonsense	Truncating	PV/LPV	GC+BC	1	Criteria 3	Criteria 2	
F064	c.639del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F066	c.684C>G	Nonsense	Truncating	PV/LPV	Exclusively_BC only	1	No criteria	No criteria	Not found
F067	c.688-1G>C	Splice-site	Truncating	PV/LPV	GC only	1	Criteria 2	Criteria 4	
F068	c.696_697del	Frameshift	Truncating	PV/LPV	GC+BC	1	No criteria	Criteria 4	
F069	c.696_697del	Frameshift	Truncating	PV/LPV	BC only	1	No criteria	No criteria	
F070; F071	c.781G>T	Nonsense	Truncating	PV/LPV	GC only	2	2 x criteria 1	2 x criteria 1	

F072	c.811_812delinsTTAAGGGATATA	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F073	c.832+1G>A	Splice-site	Truncating	PV/LPV	GC+BC	1	No criteria	No criteria	
F074	c.832+1G>T	Splice-site	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F075	EX7_8del	Large deletion	Truncating	PV/LPV	Exclusively_BC only	1	No criteria	No criteria	Not found
F078	c.971del	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F080; F081; F084	c.1003C>T	Nonsense	Truncating	PV/LPV	GC+BC	3	3 x criteria 1	3 x criteria 1	
F083	c.1003C>T	Nonsense	Truncating	PV/LPV	GC only	1	Criteria 2	Criteria 4	
F085	c.1008+2T>G	Splice-site	Truncating	PV/LPV	GC only	1	Criteria 2	Criteria 4	
F086	c.1008+2T>G	Splice-site	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F087	c.1009_1010del	Frameshift	Truncating	PV/LPV	Exclusively_BC only	1	No criteria	No criteria	ClinGen entry
F088	EX8_11del	Large deletion	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F089	c.1036C>T	Nonsense	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F090	c.1056del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F092	c.1135_1137+5delinsTTAGA	Splice-site	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F093	c.1137G>A	Splice-site	Truncating	PV/LPV	GC+BC	1	Criteria 2	Criteria 4	
F94; F95	c.1137G>A	Splice-site	Truncating	PV/LPV	GC only	2	2 x criteria 1	2 x criteria 1	
F096; F097	c.1141A>T	Nonsense	Truncating	PV/LPV	GC+BC	2	Criteria 4; no criteria	Criteria 3; no criteria	
F098	c.1147C>T	Nonsense	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F099	c.1220del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F100	c.1264C>T	Nonsense	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F102	EX10_11del	Large deletion	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F103; F105	EX10_11del	Large deletion	Truncating	PV/LPV	GC+BC	2	2 x no criteria	2 x no criteria	
F104	EX10_11del	Large deletion	Truncating	PV/LPV	BC only	1	Criteria 3	Criteria 2	
F106	c.1401del	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F107; F108	c.1404del	Frameshift	Truncating	PV/LPV	GC only	2	2 x criteria 1	2 x criteria 1	
F109	c.1416dup	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 3	Criteria 2	
F110	c.1416dup	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 2	Criteria 4	
F111	c.1466_1467insC	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F112	c.1476_1477del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F113	c.1488_1494del	Frameshift	Truncating	PV/LPV	GC+BC	1	No criteria	No criteria	
F114	c.1565+1G>T	Splice-site	Truncating	PV/LPV	GC+BC	1	No criteria	No criteria	
F117; F118; F119	c.1565+1G>T	Splice-site	Truncating	PV/LPV	GC only	3	3 x criteria 1	3 x criteria 1	

F116; F120; F123	c.1565+1G>A	Splice-site	Truncating	PV/LPV	GC only	3	3 x criteria 1	3 x criteria 1	
F121	c.1565+1G>A	Splice-site	Truncating	PV/LPV	GC+BC	1	No criteria	No criteria	
F115; F122	c.1565+1G>A	Splice-site	Truncating	PV/LPV	BC only	2	2 x no criteria	2 x no criteria	
F124; F125; F126; F127; F128; F129	c.1565+2dup	Splice-site	Truncating	PV/LPV	GC only	6	No criteria; 5 x criteria 1	Criteria 4; 5 x criteria 1	
F130	Ex11del	Large deletion	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F131	EX11_13del	Large deletion	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F132	c.1577G>A	Nonsense	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F133	c.1595G>A	Nonsense	Truncating	PV/LPV	GC only	1	No criteria	Criteria 4	
F135	c.1612del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F134	c.1612del	Frameshift	Truncating	PV/LPV	BC only	1	No criteria	No criteria	
F136	c.1651G>T	Nonsense	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F137; F140	c.1679C>G	Splice-site	Truncating	PV/LPV	GC+BC	2	2 x criteria 3	2 x criteria 2	
F138; F139	c.1679C>G	Splice-site	Truncating	PV/LPV	GC only	2	2 x criteria 1	2 x criteria 1	
F141	c.1746dup	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F143	c.1786G>T	Nonsense	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F144; F146	c.1792C>T	Nonsense	Truncating	PV/LPV	GC only	2	2 x criteria 1	2 x criteria 1	
F145; F147	c.1792C>T	Nonsense	Truncating	PV/LPV	GC+BC	2	2 x criteria 1	2 x criteria 1	
F148	c.1795del	Frameshift	Truncating	PV/LPV	Exclusively_BC only	1	No criteria	No criteria	Not found
F150; F151; F153; F155; F156; F157; F158; F159; F160; F161	c.1901C>T	Splice-site	Truncating	PV/LPV	GC+BC	10	Criteria 3; 7 x criteria 1; no criteria; criteria 3	Criteria 2; 7 x criteria 1; no criteria; criteria 2	
F149; F154	c.1901C>T	Splice-site	Truncating	PV/LPV	GC only	2	2 x criteria 2	2 x criteria 4	
F152	c.1901C>T	Splice-site	Truncating	PV/LPV	BC only	1	No criteria	No criteria	
F162	c.1906_1907insA	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F163	c.1965del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F164	c.2031del	Frameshift	Truncating	PV/LPV	GC+BC	1	No criteria	Criteria 4	

F165	c.2062del	Frameshift	Truncating	PV/LPV	GC+BC	1	No criteria	No criteria	
F166	c.2064_2065del	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F167	c.2095C>T	Nonsense	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F168	c.2114del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F169	c.2116C>T	Nonsense	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F174; F177; F178; F179	c.2195G>A	Splice-site	Truncating	PV/LPV	GC only	4	3 x criteria 1; no criteria	3 x criteria 1; criteria 4	
F175; F176	c.2195G>A	Splice-site	Truncating	PV/LPV	GC+BC	2	Criteria 1; no criteria	Criteria 1; no criteria	
F180	c.2220del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F181	c.2275G>T	Nonsense	Truncating	PV/LPV	Exclusively_BC only	1	No criteria	No criteria	20471195
F183	c.2386del	Frameshift	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F432	c.2439+5_2439+8delGTAA	Splice-site	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F184	EX16del828bp	Large deletion	Truncating	PV/LPV	GC only	1	Criteria 2	Criteria 4	
F185	EX16del	Large deletion	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F413	c.2520del	Frameshift	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F020	c.48G>A	Splice-site	Truncating	PV/LPV	GC only	1	Criteria 2	Criteria 4	
F023	c.49-1G>C	Splice-site	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F171	c.2164+2T>A	Splice-site	Truncating	PV/LPV	GC+BC	1	No criteria	No criteria	
F170	c.2164+2T>A	Splice-site	Truncating	PV/LPV	GC only	1	Criteria 1	Criteria 1	
F062	c.531+1G>T	Splice-site	Truncating	PV/LPV	GC+BC	1	Criteria 1	Criteria 1	
F061	c.521dup	Frameshift	Truncating	PV/LPV	No personal/family history of cancer	1	No criteria	No criteria	
F082	c.1003C>T	Nonsense	Truncating	PV/LPV	Other cancer	1	No criteria	No criteria	

PV/LPV – pathogenic/likely pathogenic variants; GC – gastric cancer; BC – breast cancer; HDGC – hereditary diffuse gastric cancer



Representation of all PV/LPV variants found in families from GC-only, GC+BC and BC-only settings and with reference to clinical criteria. This scheme also pinpoints exclusive variants found in BC-only families and families resolved by LBC-centred criteria. PV/LPV found in the cohort are depicted by *CDH1* exon location, pink-shaded variants were exclusively found in BC-only families. *Represents families resolved by the herein proposed LBC-centred criteria. No. – Number; EX – Exon; del – Deletion; ins – insertion; dup – duplication. The size of the circular forms is proportional to the number of families found to carry a particular variant, and the color represents the GC-only, GC+BC and BC-only setting.

Positive predictive value, negative predictive value, specificity, sensitivity and Youden-index considering 2015 HDGC criteria,[3] 2020 HDGC criteria,[4] 2020 HDGC criteria + LBC-centred criteria (LBC-expanded criteria) and Yale criteria[5] using as molecular testing the ACMG/AMP *CDH1* guidelines for variants classification.[7]

Yale criteria[5]												
	Positive (PV/LPV)	**Negative (LBV/BV) + VUS**	**NPV**	95%CI	**PPV**	95%CI	**Sensitivity**	95%CI	**Specificity**	95%CI	**Youden**	95%CI
Criteria fulfilled	**168**	**449**	**0·97**	0·93-0·99	**0·27**	0·24-0·31	**0·95**	0·91-0·98	**0·34**	0·3-0·37	**0·29**	0·25-0·34
Criteria not fulfilled	**8**	**229**										
2015 HDGC criteria[3]												
	Positive (PV/LPV)	**Negative (LBV/BV) + VUS**	**NPV**	95%CI	**PPV**	95%CI	**Sensitivity**	95%CI	**Specificity**	95%CI	**Youden**	95%CI
Criteria fulfilled	136	46	**0·94**	0·92-0·96	**0·75**	**0·68-0·81**	**0·77**	**0·7-0·83**	**0·93**	**0·91-0·95**	**0·70**	0·64-0·77
Criteria not fulfilled	40	632										
2020 HDGC criteria[4]												
	Positive (PV/LPV)	**Negative (LBV/BV) + VUS**	**NPV**	95%CI	**PPV**	95%CI	**Sensitivity**	95%CI	**Specificity**	95%CI	**Youden**	95%CI
Criteria fulfilled	147	52	**0·96**	0·94-0·97	**0·74**	0·67-0·80	**0·84**	0·77-0·89	**0·92**	0·9-0·94	**0·76**	0·70-0·82
Criteria not fulfilled	29	626										
2020 HDGC criteria + LBC-centred criteria (LBC-expanded criteria)												
	Positive (PV/LPV)	**Negative (LBV/BV) + VUS**	**NPV**	95%CI	**PPV**	95%CI	**Sensitivity**	95%CI	**Specificity**	95%CI	**Youden**	95%CI
Criteria fulfilled	**165**	**65**	**0·98**	0·97-0·99	**0·72**	0·65-0·77	**0·94**	**0·89-0·97**	**0·90**	0·88-0·93	**0·84**	0·80-0·88
Criteria not fulfilled	**11**	**613**										

PPV - positive predictive value; NPV - negative predictive value; VUS – variants of unknown significance; PV/LPV – pathogenic/likely pathogenic variants; LBV/BV – likely benign/benign variants; HDGC – hereditary diffuse gastric cancer; CI – confidence interval

Supporting data for figure 5B. Results of the AUC difference between all sets of HDGC clinical criteria.

Criteria comparison	AUC Difference	95% CI	Z-score	p-value
LBC-expanded *vs.* 2020 HDGC criteria[4]	0·04	0·02-0·06	3·54	**0·0004**
LBC-expanded *vs.* 2015 HDGC criteria[3]	0.07	0·04-0·09	4·76	**<0·0001**
LBC-expanded *vs.* Yale criteria[5]	0·27	0·25-0·30	21·35	**<0·0001**
2020 *vs.* 2015 HDGC criteria[3]	0·03	0·01-0·05	2·88	**0·004**
2020 *vs.* Yale criteria[5]	0·23	0·20-0·26	14·57	**<0·0001**
2015 *vs.* Yale criteria[5]	0·21	0·17-0·24	11·57	**<0·0001**

The AUC differences between the different criteria were compared using a Z-test.

AUC – Area Under the Curve; 95%CI: 95% Confidence Interval; LBC-expanded - 2020 HDGC + Lobular Breast Cancer-expanded criteria; 2020 - 2020 HDGC criteria; 2015 - 2015 HDGC criteria; Yale – Yale criteria

Supporting data for figure 5C. Results of equivalence test comparing the LBC-expanded criteria with all the other sets.

	Cases (True positive detection)				Controls (True negative detection)			
	Difference	**95% CI**	**p-value**	**Conclusion (LBC; δ=0·12)**	**Difference**	**95% CI**	**p-value**	**Conclusion (LBC; δ=0·12)**
LBC-expanded criteria *vs.* Yale criteria[5]	-0·02	-0·06-0·03	0·48	Equivalence	0·57	0·52-0·61	**< 0·0001**	Superiority
LBC-expanded criteria *vs.* 2015 HDGC criteria[3]	0·17	0·09-0·24	**<0·0001**	Superiority	-0·03	-0·06-0·001	0·059	Equivalence
LBC-expanded criteria *vs.* 2020 HDGC criteria[4]	0·10	0·04-0·17	**0·0025**	Superiority	-0·02	-0·05-0·01	0·21	Equivalence

The true positive detection and true negative detection differences between the different criteria were compared using an equivalence test.

95%CI: 95% Confidence Interval; δ: Equivalence limit; LBC-expanded - 2020 HDGC + Lobular Breast Cancer-expanded criteria; Yale – Yale criteria; 2015 - 2015 HDGC criteria; 2020 - 2020 HDGC criteria

BC-only families carrying *CDH1* germline variants described to date in the literature and reports on families carrying the same variants but GC or other phenotypes.
*Identified in two families BC-only same publication; [a] Identified in two families BC-only;[8,9] [b] Also seen in a healthy patient without family history of BC/GC.

Publication with reference to HLBC	Original publication	Reported *CDH1* variant	HGVS *CDH1* variant	Identified in the current study	ACMG criteria	ACMG classification for analysis (2022)	Cancer history BC/GC/OTHER current study	Protein change	Number of families in the current study	Comments
Gamble et al., 2022;[9] Girardi et al., 2021[10]	Schrader et al., 2011[11]	c.8C>G	c.8C>G	YES	BS2	LBV/BV	BC only	p.Pro3Arg	6	Not relevant: Variant classified as LBV/BV (ACMG)
Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Petridis et al., 2014[14]	c.48 + 1G>A	c.48 + 1G>A	YES	PSV1_Strong, PS4_Moderate, PM2, PP1_Moderate	PV/LPV	GC only	-	1	Current study: 1 GC-only family
Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Schrader et al., 2011[11]	c.88C>A*	c.88C>A*	YES	BA1; BS2	LBV/BV	3 GC-only; 2GC+BC; 6 BC-only; 1 OTHER; 1 no cancer history	p.Pro30Thr	13	Not relevant: Variant classified as LBV/BV (ACMG)
Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Xie et al., 2011[15]	c.283C>T	c.283C>T	YES	PVS1, PS4_Moderate, PM2	PV/LPV	BC only	p.Gln95Ter	1	Reported in literature in GC-family (PMID 17545690)
Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Masciari et al., 2007[16]	c.517insA	c.517insA	NO	PVS1, PS4_Supporting, PM2	PV/LPV	NA	p.Lys173fs	0	Not found in current study nor literature

Gamble et al., 2022[9]	Gamble et al., 2022[9]	c.888C>A	c.888C>A	NO	PVS1, PS4_Supporting, PM2	PV/LPV	NA	p.Tyr296Ter	0	Not found in current study nor literature
Gamble et al., 2022[9]	Gamble et al., 2022;[9] Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.1147C>T[a]	c.1147C>T[a]	YES	PSV1, PS4_Supporting, PM2	PV/LPV	GC only	p.Gln383Ter	1	Current study: 1 GC-only family
Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Schrader et al., 2011[11]	c.1223C>T	c.1223C>T	YES	-	VUS	OTHER	p.Ala408Val	1	Current study: No GC or BC in the family (VUS)
Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Schrader et al., 2011[11]	c.1297G>A	c.1297G>A	YES	BS2	LBV/BV	BC only	p.Asp433Asn	3	Not relevant: Variant classified as LBV/BV (ACMG)
Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Petridis et al., 2014[14]	c.1465insC	c.1465insC	NO	PVS1, PS4_Moderate, PM2	PV/LPV	NA	p.Pro489fs	0	Reported in literature in GC-family (PMID 18825658)
Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Xie et al., 2011[15]	c.1582delC	c.1582del	NO	PVS1, PS4_Supporting, PM2	PV/LPV	NA	p.Asp528Fs	0	Not found in current study nor literature

Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12]	Stuebs et al., 2018[17]	c.1774G>A	c.1774G>A	YES	BA1	LBV/BV	5 GC-only; 2 GC+BC; 13 BC-only; 8 OTHER; 1 no cancer history	p.Ala592Thr	29	Not relevant: Variant classified as LBV/BV (ACMG)
Gamble et al., 2022;[9] Girardi et al., 2021[10]	Schrader et al., 2011[11]	c.1813A>G	c.1813A>G	NO	PM2	VUS	NA	p.Arg605Gly	0	Not found in current study nor literature (ClinVar SCV002140541.1)
Gamble et al., 2022[9]	Gamble et al., 2022[9]	c.1999del	c.1999del	NO	PVS1, PM2, PS4_Moderate	PV/LPV	NA	p.Leu667fs	0	Reported in literature in GC-family (PMID 31077828)
Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Benusiglio et al., 2013[18]	c.2164 + 2T>A	c.2164 + 2T>A	YES	PSV1_Strong; PS4_Moderate; PM2	PV/LPV	1 GC-only; 1 GC+BC	-	2	Current study: 2 GC-families
Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Petridis et al., 2014[14]	c.2398delC	c.2398del	NO	PVS1_Strong, PM2, PS4, PP1	PV/LPV	NA	p.Arg800fs	0	Reported in literature in GC-family (PMID 17545690)
Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Schrader et al., 2011[11]	c.2494G>A	c.2494G>A	YES	BS1; BS2	LBV/BV	1 GC+BC; 3 BC-only; 1 OTHER	p.Val832Met	5	Not relevant: Variant classified as LBV/BV (ACMG)
Gamble et al., 2022[9]	Stuebs et al., 2018[17]	c.2512A>G	c.2512A>G	YES	BS2	LBV/BV	OTHER+BC only	p.Ser838Gly	3	Not relevant: Variant classified as LBV/BV (ACMG)

Gamble et al., 2022;[9] Girardi et al., 2021;[10] Corso et al., 2018;[12] Corso et al., 2016[13]	Petridis et al., 2014[14]	c.1942G>T	c.1942G>T	NO	PVS1, PM2_Supporting, PM5_Supporting	PV/LPV	NA	p.Glu648Ter	0	Reported in literature in CRC-family (32175104); Not found in current study nor literature for GC
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.1137+1delG	c.1137+1del	NO	PVS1, PM2, PS4_Supporting	PV/LPV	NA	-	0	Not found in current study nor literature (ClinVar SCV000275921.4)
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.163+1_687del	c.(163+1_164-1)_(687+1_688-1) [EX3_EX6del]	NO	PVS1, PM2	PV/LPV	NA	-	0	Not found in current study nor literature
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.76G>T	c.76G>T	NO	PVS1, PM2_Supporting, PM5_Supporting	PV/LPV	NA	p.Glu26Ter	0	Not found in current study nor literature (ClinVar SCV000936635.3)
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.1137+2T>C	c.1137+2T>C	NO	PVS1_strong, PM2, PS4_Supporting	PV/LPV	NA	-	0	variants in the same splice-site reported in literature in GC-family: 10477433
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.1488_1494delCGAGGAC	c.1488_1494del	YES	PSV1; PS4_Supporting; PM2	PV/LPV	1 GC+BC	p.Glu497LeufsTer23	1	Current study: 1 GC+BC family
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.1636delG[b]	c.1636del[b]	NO	PVS1, PM2_Supporting, PM5_Supporting	PV/LPV	NA	p.Ala546fs	0	Not found in current study nor literature
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.529C>T	c.529C>T	NO	PVS1, PM2, PS4_Supporting	PV/LPV	NA	p.Gln177Ter	0	Not found in current study nor literature (ClinVar SCV001365465.1)
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.1008G>T	c.1008G>T	NO	PVS1_Moderate, PM2, PS3, PS4_Supporting	PV/LPV	NA	p.Glu336Asp	0	Reported in literature in GC-family (9537325)
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.124_126delCCCinsT[b]	c.124_126delinsT[b]	NO	PVS1, PM2, PS4_Supporting	PV/LPV	NA	p.Pro42fs	0	Reported in literature in GC-family (30745422)

NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.2164+1_2439del	c.(2164+1_2165-1)_(2439+1_2440-1)del [EX14_EX16del]	NO	PVS1, PM2, PS4_Supporting	PV/LPV	NA	-	0	Reported in literature in GC-family (19168852)
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.2506G>T	c.2506G>T	NO	PVS1_Strong, PM2, PS2	PV/LPV	NA	p.Glu836Ter	0	Not found in current study nor literature
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.2029dupC	c.2029dup	NO	PVS1, PM2_Supporting, PM5_Supporting	PV/LPV	NA	p.Gln677fs	0	Not found in current study nor literature
NA	Lerner et al., 2022;[5] Xicola et al., 2019[8]	c.202delT	c.202del	NO	PVS1, PM2_Supporting, PM5_Supporting	PV/LPV	NA	p.Tyr68fs	0	Not found in current study nor literature

GC – gastric cancer; BC – breast cancer; CRC – colorectal cancer; OTHER – no involvement of GC/BC in family history; PV/LPV – pathogenic/likely pathogenic variants; LBV/BV – likely benign/benign variants; NA – not applicable

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