

BACKGROUND

- Hereditary invasive lobular carcinomas (ILC) are rare and are known to occur in the context of germline mutations in *CDH1*, or other genes (including *BRCA2* and *PALB2*).
- The clinical and histopathological features of hereditary ILCs unrelated to *CDH1* remain poorly described in the literature to date.

OBJECTIVES

To determine the **clinical and pathologic features of ILCs associated with non-CDH1 germline mutations** (compared with sporadic ILCs) in a single-center retrospective series.

METHODS

Characteristic	Patients		Characteristic	Patients		Characteristic	Patients	
	No.	%		No.	%		No.	%
Age (years)			Grade			Lymphovascular invasion		
<50	53	21.1%	1	7	2.8%	No	224	89.2%
50-64	104	41.4%	2	207	82.5%	Yes	27	10.8%
≥65	94	37.5%	3	37	14.7%	Tumor cellularity		
Histological subtype			Estrogen receptor			<50%	146	58.2%
Classic	170	67.7%	<10%	9	3.6%	≥50%	105	41.8%
Alveolar	4	1.6%	≥10%	242	96.4%	Tumor infiltrating lymphocytes		
Pleomorphic	10	4.0%	Progesterone receptor			<5%	182	72.5%
Solid	1	0.4%	<10%	63	25.1%	≥5%	69	27.5%
Mixed	66	26.3%	≥10%	188	74.9%	Metastatic relapse		
Tumor Size			Histomolecular class			No	212	84.5%
pT1a	2	0.8%	Luminal	234	93.2%	Yes	39	15.5%
pT1b	38	15.1%	HER2	8	3.2%	Death from breast cancer		
pT1c	114	45.4%	Triple negative	9	3.6%	No	230	91.6%
pT2	76	30.3%			Yes	21	8.4%	
pT3	21	8.4%			Survival			
Nodal status					Alive	212	84.5%	
pN0	175	69.7%			Deceased	39	15.5%	
pN1	51	20.3%						
pN2	18	7.2%						
pN3	7	2.8%						

Table 1. Clinico-pathological characteristics of the ILC retrospective series

A **retrospective series** of ILCs diagnosed in a context of constitutional genetic predisposition **unrelated to CDH1** was retrieved within Institut Curie's department of Genetics database. The selection criteria were patients with ILC and a **pathogenic or likely pathogenic** germline mutation in genes other than *CDH1*. Clinico-pathological data were collected from the electronic patient record and were **compared to sporadic ILCs** from our institute (N=251) (**table 1**)

RESULTS

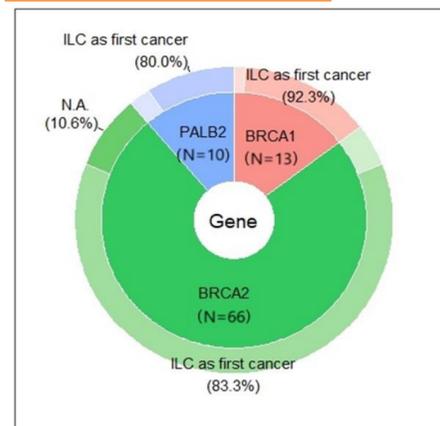


Figure 1. ILC is the first cancer diagnosed in almost all patients of our series with *BRCA1*, *BRCA2* or *PALB2* mutation

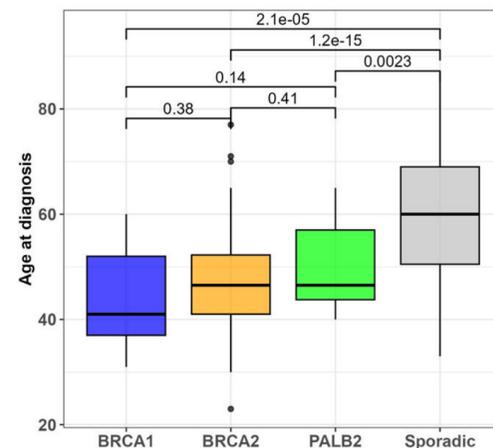


Figure 2. Age at ILC diagnosis for *BRCA1*, *BRCA2*, *PALB2* and control patients

- We identified 13 *BRCA1*, 66 *BRCA2*, 10 *PALB2* germline mutations in ILC patients with available clinico-pathological data.
- ILC was the first cancer diagnosed in almost all patients (12/13 [92%] for *BRCA1*, 55/59 [93%] for *BRCA2* and 8/10 [80%] for *PALB2*) (**Fig. 1**).
- Patients were index cases in 75% for *BRCA1*, 63.6% for *BRCA2* and 57.1% for *PALB2*.
- The mean age at diagnosis was 42.1, 45.9 and 49.3 years, respectively for patients with *BRCA1*, *BRCA2* and *PALB2* mutation (**Fig. 2**).

CONCLUSION

- ILCs associated with germline *BRCA1*, *BRCA2* or *PALB2* mutations occur at a **younger age** than sporadic ILCs
- Hereditary *BRCA2*- and *PALB2*-related ILCs exhibit histo-phenotypical features **comparable** to sporadic tumors
- BRCA1*-associated ILCs appear to be enriched for **grade 3** and **triple negative** phenotype suggesting that germline *BRCA1* mutations **impact** ILC phenotype although this gene has not yet been identified as a **predisposing factor for lobular carcinoma**

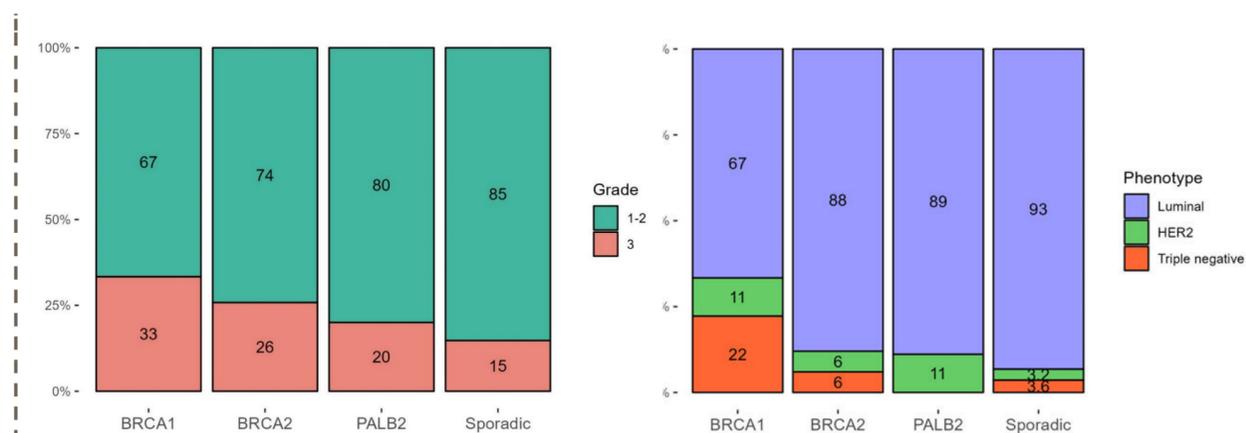


Figure 3. Grade and phenotype of ILC according to germline mutation status

- The occurrence of bilateral disease at diagnosis was not common (0/9 [0%] for *BRCA1*, 6/57 [10.5%] for *BRCA2*, and 1/8 [12.5%] for *PALB2*).
- In *BRCA1*-mutated patients, ILCs were enriched in grade 3 (4/12 [33,3%]) ($p = 0.06$) and non-luminal phenotype (3/9 [33.3%]) ($p=0.05$). The prevalence of HER2-positive status was found to be slightly higher among patients with *BRCA1* and *PALB2* mutations (1/9 [11.1%] and 1/9 [11.1%], respectively) in comparison to those with a *BRCA2* mutation (3/50 [6%]) (**Fig. 3**).

REREFENCES

Corso G, Marino E, Zanzottera C, Oliveira C, Bernard L, Macis D, Figueiredo J, Pereira J, Carneiro P, Massari G, Barberis M, De Scalzi AM, Taormina SV, Sajjadi E, Sangalli C, Gandini S, D'Ecclesiis O, Trovato CM, Rotili A, Pesapane F, Nicosia L, La Vecchia C, Galimberti V, Guerini-Rocco E, Bonanni B, Veronesi P. *CDH1* Genotype Exploration in Women With Hereditary Lobular Breast Cancer Phenotype. *JAMA Netw Open*. 2024 Apr 1;7(4):e247862. doi: 10.1001/jamanetworkopen.2024.7862.

CONTACT

Dr L DJERROUDI
R. BRAHIMAJ
Prof. A VINCENT-SALOMON

lounes.djerroudi@curie.fr
rigleta.brahimaj@curie.fr
anne.salomon@curie.fr