
# *Carcinoma mammario: quando la donna è giovane*

## *Il rischio genetico e il rischio familiare*

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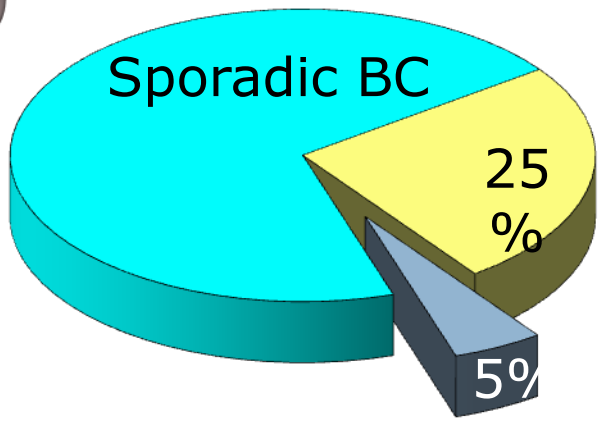
DI MODENA E REGGIO EMILIA

# How Much BC is Familial- Hereditary?

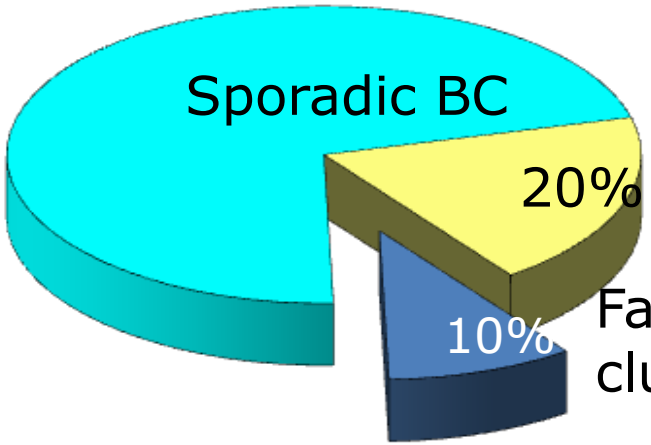
1980




Family clusters

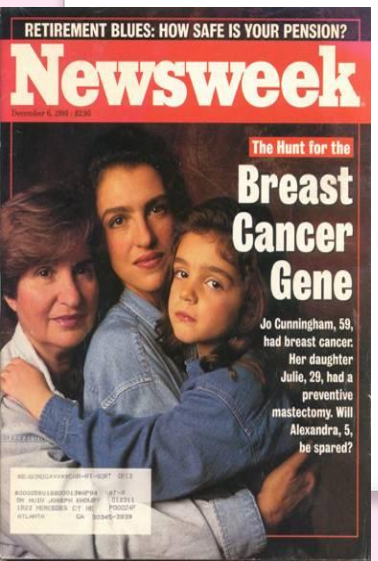
Hereditary

2015

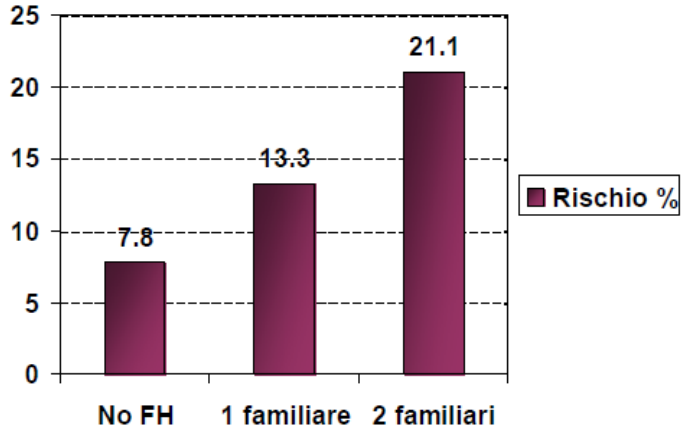



Family clusters

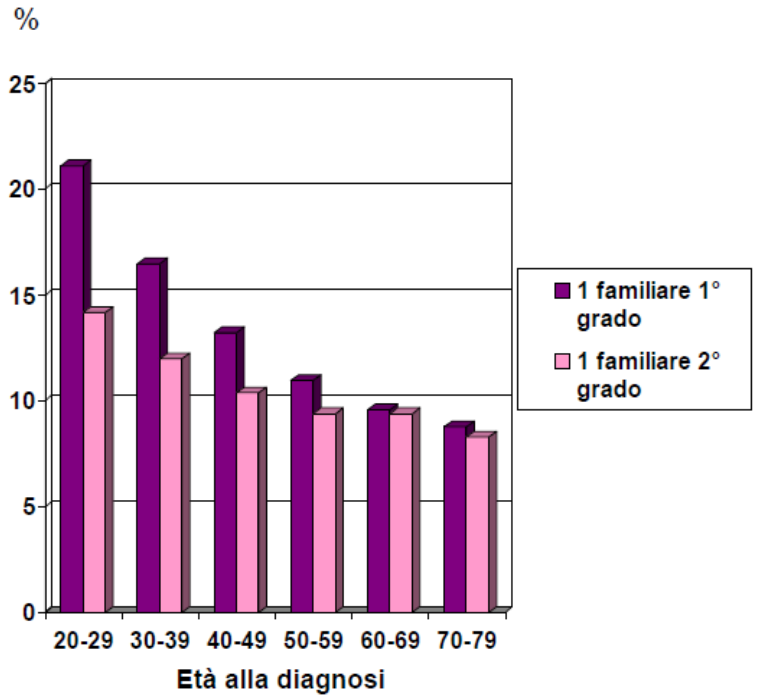
Hereditary



# Rischio familiare



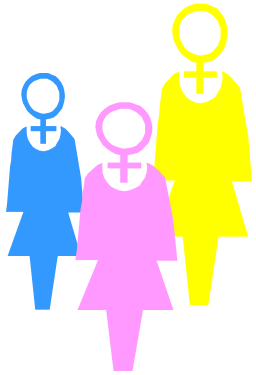

Collaborative Group on Hormonal Factors in Breast Cancer, 2001




Claus et al, Cancer, 1994

# *HBC according to Lynch*

**3 or more relatives with Breast Cancer…**



+

***Other factors suggesting hereditary susceptibility***

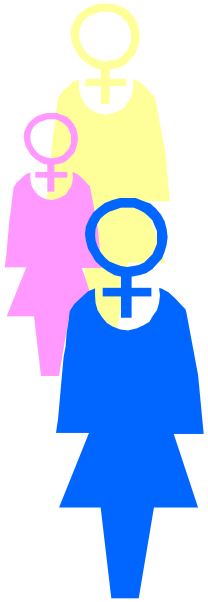
- Early onset BC
- Bilateral BC
- High frequency of extra-mammary neoplasms

=

**Hereditary Breast Cancer**

*Lynch et al., Breast Cancer Research and Treatment, 1990*

# *FBC according to Lynch*

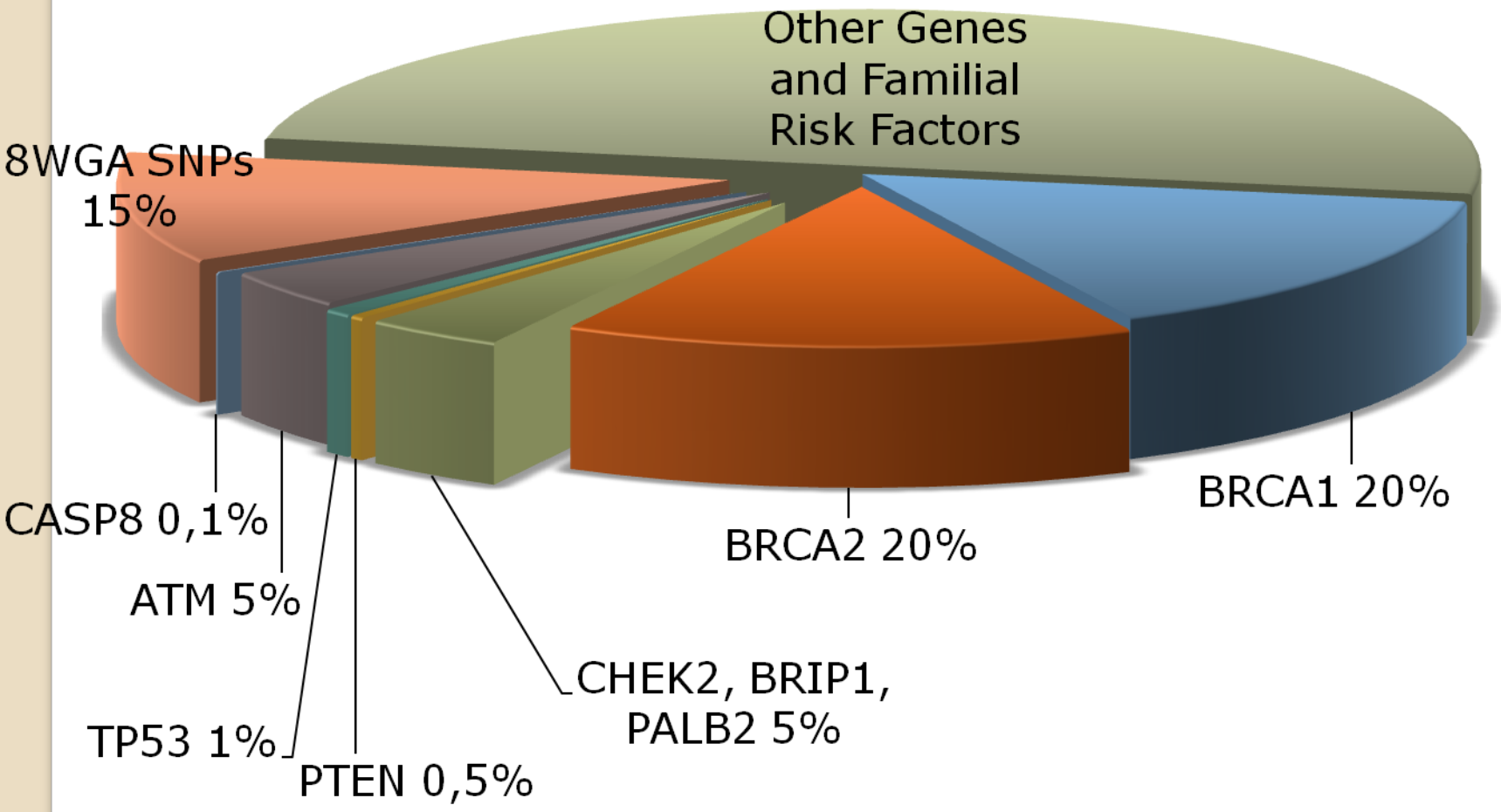


- Two or more relatives with Breast Cancer
- No other features suggesting inherited predisposition

**Familial Breast Cancer**

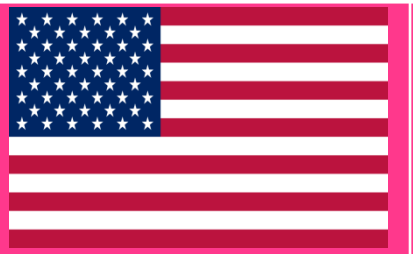
*Lynch et al., Breast Cancer Research and Treatment, 1990*

# *Spectrum of Mutations in in Families at High Risk of Breast Cancer*




**Modified by Offit, 2010**

# *Test genetico BRCA1/BRCA2 nelle donne giovani: quando proporlo ?*

| |  |  |  |
|---|---|---|---|
| | **Nice 2013** | **NCCN 2015** | **RER 2014** |
| **Limiti di età di insorgenza del BC nelle donne senza familiarità** | NESSUN LIMITE DI ETÀ MA DEVE AVERE UNA PROBABILITÀ DI MUTAZIONE GENETICA DI BRCA1+BRCA ≥ 10% | BC ≤ 45 ANNI SENZA FAMILIARITA'<br>TNBC ≤ 60 anni | BC ≤ 35 ANNI<br>(OPPURE ENTRO I 40 ANNI SE UN PARENTE DI PRIMO GRADO AFFETTO DA BC/OC)<br>BC ≤ 40 ANNI se TRIPLE NEG |

# Identification of HBC

## Indicator: age at onset

PERGAMON

European Journal of Cancer 36 (2000) 2083–2089

European Journal of Cancer

www.ejconline.com

# *BRCA1* mutations and clinicopathological features in a sample of Italian women with early-onset breast cancer

D. Turchetti [a], L. Cortesi [b], M. Federico [a,*], C. Bertoni [b], L. Mangone [a], Se. Ferrari [b], V. Silingardi [a]

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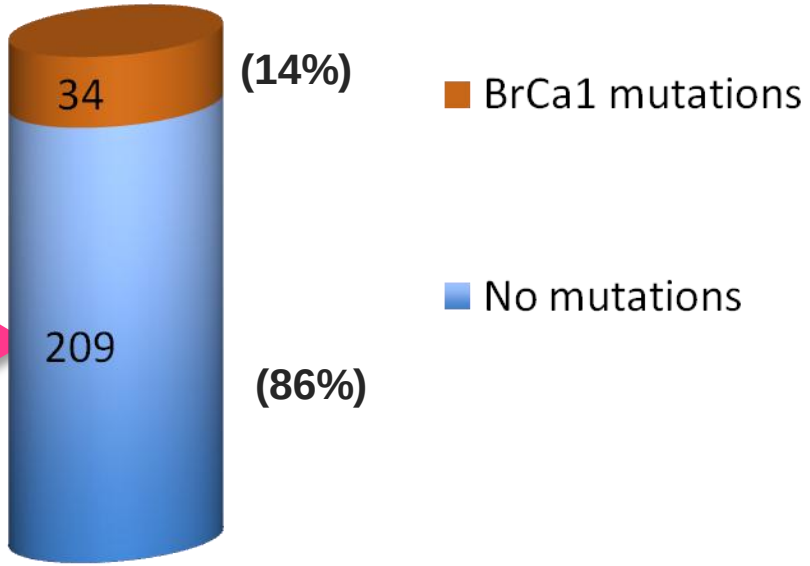
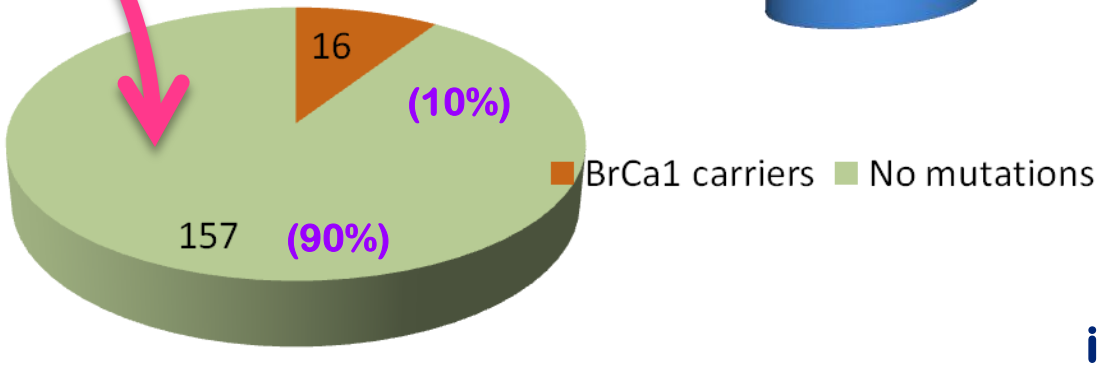
[b] *Dipartimento di Scienze Biomediche, Sezione di Chimica Biologica, Via Campi 287, 41100 Modena, Italy*

Received 6 March 2000; received in revised form 12 June 2000; accepted 21 July 2000

# *243 women*
# *BC at age ≤35 regardless family history*




**173**
**No BC and OC family history**




**BrCa1 testing in "Early Onset Breast Cancer" is appropriate independently by family history**

# *Medullary Carcinoma*

| Age at diagnosis (years) | Medullary Ca (n=22) Average 54.7 Range ( 33-80) N | % | General pop 61.9 % |
|---|---|---|---|
| <40 | 5 | 23 | 5 |
| 40-49 | 4 | 18 | 17 |
| ≥50 | 13 | 59 | 78 |

*Turchetti et al., in press*

# *Conclusions*

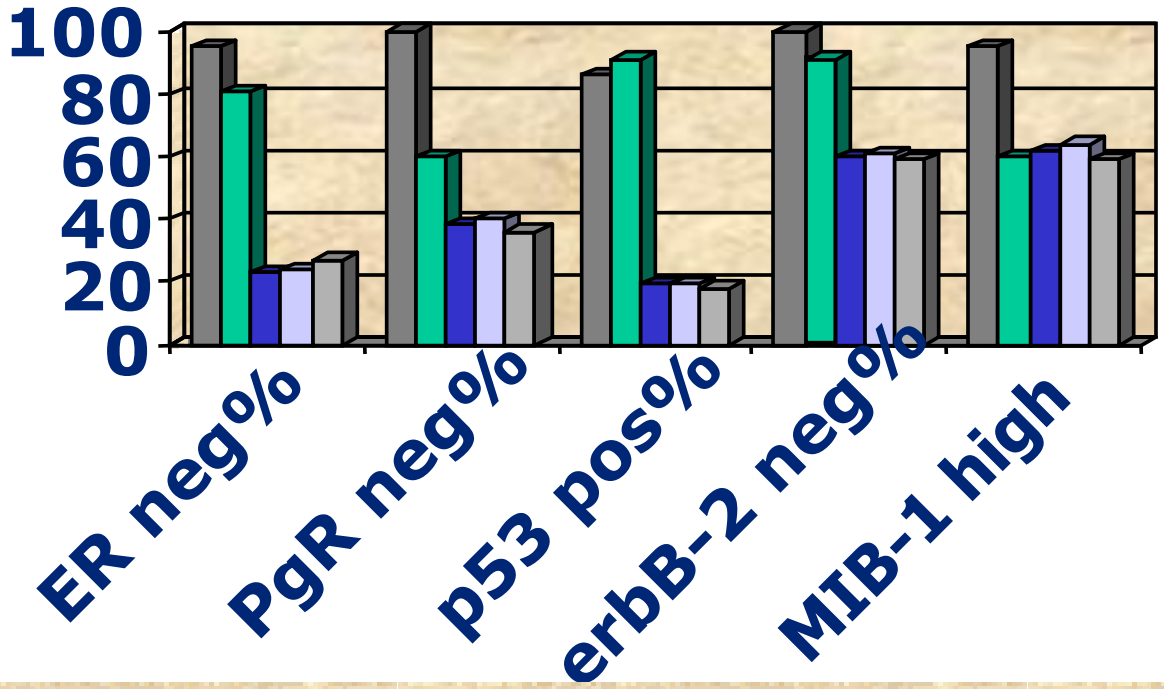
- Medullary BCs have an earlier median age of onset than other hystotypes
- MCs  are more likely BRCA1+ (30%)
- All BRCA1-MCs have a relative affected with BC and/or OC and are diagnosed at age less than 50 years
- MCs have the same histologic characteristics of BRCA1-related DCI (ER/PgR negative, high Mib-1, p53 overexpression, c-Erb negative)

**Table 1.** Clinicopathologic characteristics of patients with medullary breast carcinoma and invasive ductal carcinoma

| Characteristic | MBC (n=52) No. of cases (%) | IDC (n=5,716) No. of cases (%) | *p*-value | Characteristic | MBC (n=52) No. of cases (%) | IDC (n=5,716) No. of cases (%) | *p*-value |
|---|---|---|---|---|---|---|---|
| Mean age (yr)* | 44±9 | 48±10 | 0.005 | N stage | | | <0.001 |
| Menopause | | | 0.280 | N0 | 45 (86.5) | 3,341 (58.4) | |
| Yes | 13 (25.5) | 1,981 (35.1) | | N1 | 7 (13.5) | 1,560 (27.3) | |
| No | 38 (74.5) | 3,656 (64.9) | | N2 | 0 | 512 (9.0) | |
| FHx | | | 0.084 | N3 | 0 | 302 (5.3) | |
| Yes | 7 (13.5) | 412 (7.2) | | Stage | | | 0.027 |
| No | 45 (86.5) | 5,304 (92.8) | | I | 26 (50.0) | 2,240 (39.2) | |
| Surgery | | | 0.341 | IIa | 19 (36.5) | 1,815 (31.8) | |
| Mastectomy | 18 (34.6) | 2,352 (41.1) | | IIb | 7 (13.5) | 774 (13.5) | |
| BCS | 34 (65.4) | 3,364 (58.7) | | III | 0 | 887 (15.6) | |
| Tumor size (cm)* | 2.25±1.47 | 2.37±1.21 | 0.536 | ER | | | <0.001 |
| Mean no. of metastatic lymph node (range) | 0.2 (0-2) | 1.9 (0-49) | <0.001 | (+) | 7 (15.2) | 3,896 (69.0) | |
| | | | | (-) | 39 (84.8) | 1,754 (31.0) | |
| Multiplicity | | | 0.001 | PR | | | <0.001 |
| Yes | 0 | 956 (16.9) | | (+) | 4 (8.7) | 3,457 (61.2) | |
| No | 48 (100) | 4,716 (83.1) | | (-) | 42 (91.3) | 2,188 (38.8) | |
| LVI | | | <0.001 | HER2 | | | 0.293 |
| Yes | 0 | 1,579 (27.8) | | (+) | 15 (37.5) | 1,516 (28.9) | |
| No | 50 (100) | 4,094 (72.2) | | (-) | 25 (62.5) | 3,721 (71.1) | |

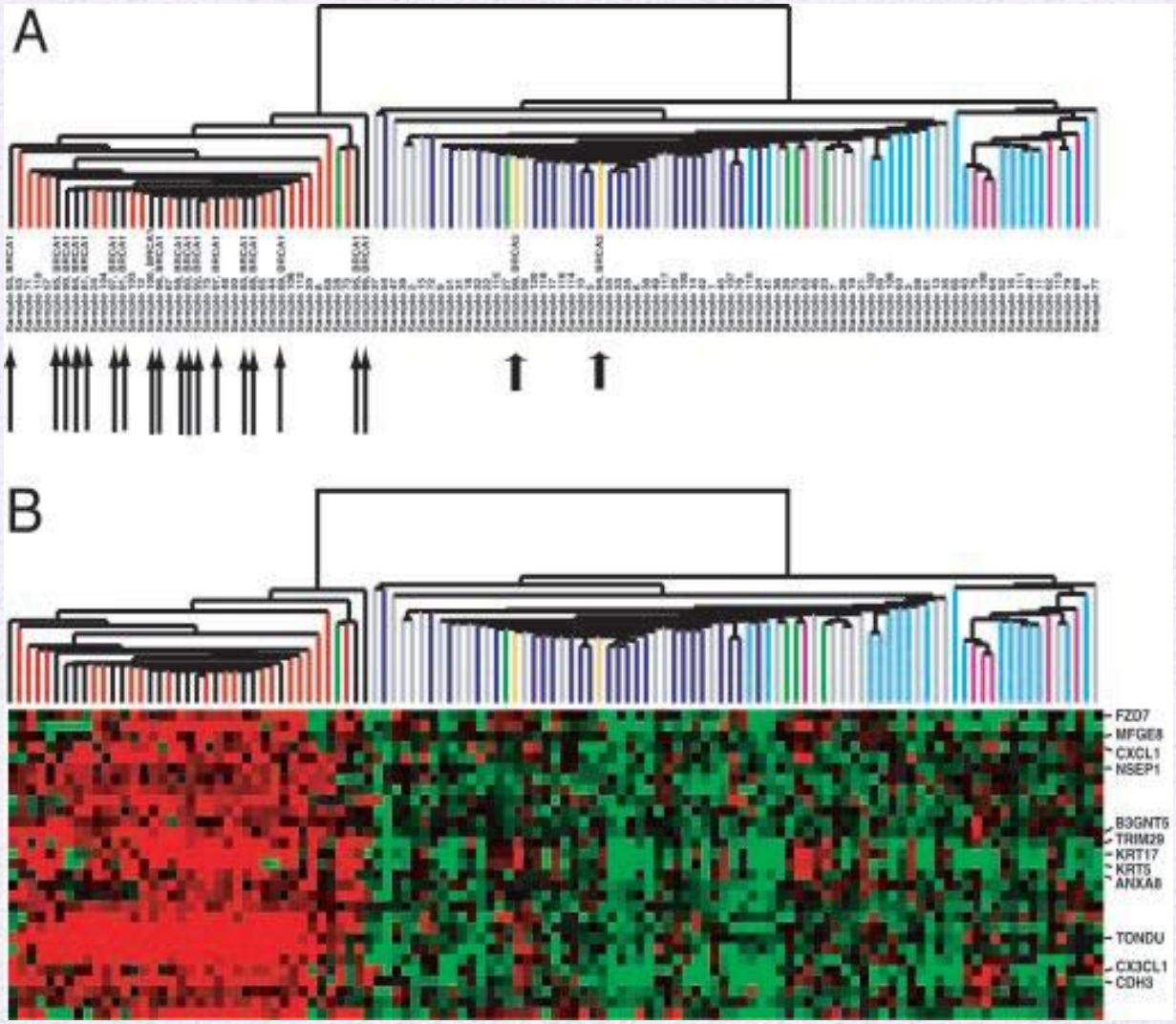
*Park et al., J Breast Cancer 2013*

# *Immunophenotype*




- Medullary (22)
- DCI BrCa1+ (11)
- Consecutive BCs (99)
- Consecutive DCI (84)
- DCI matched for age (22)

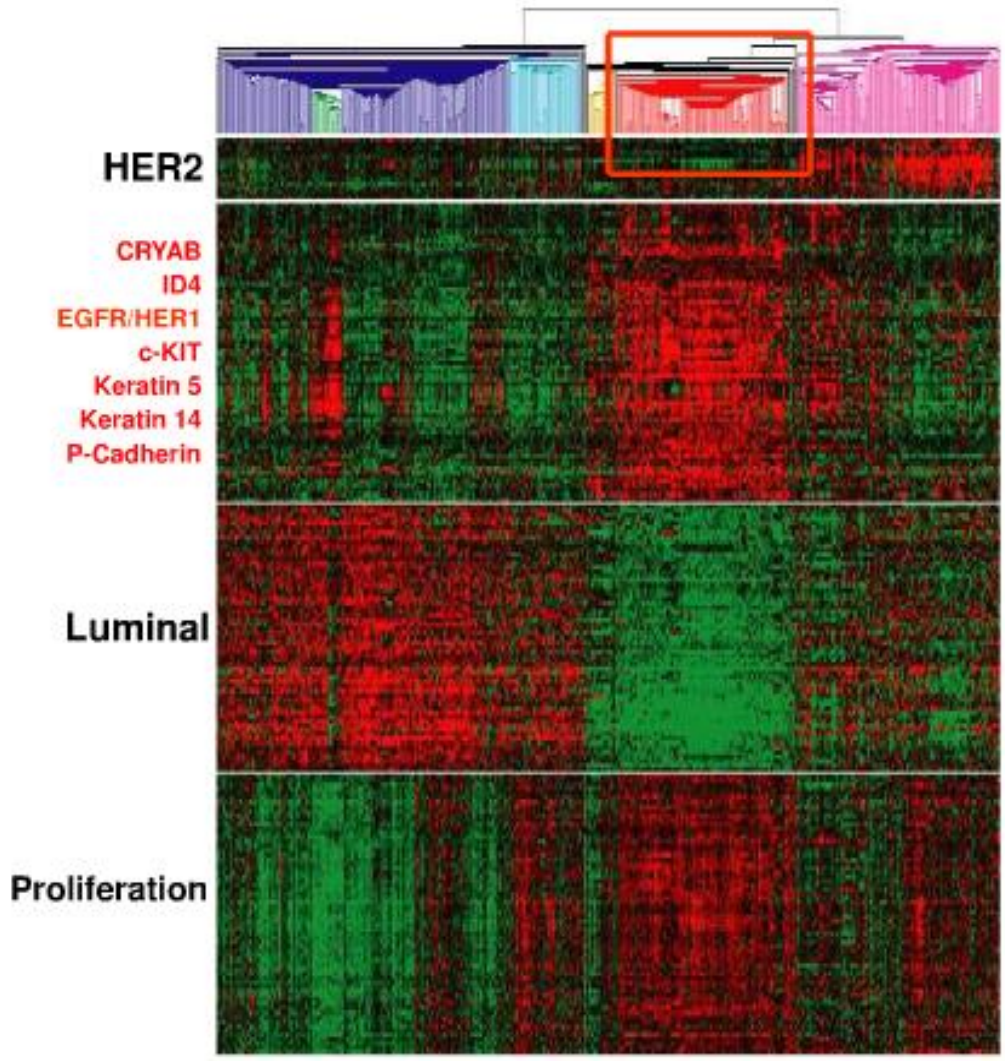
# *BRCA 1 mutation associated Breast tumors with basal like features*




All tumors from Patients carrying BRCA 1 mutations fell within the basal subgroup

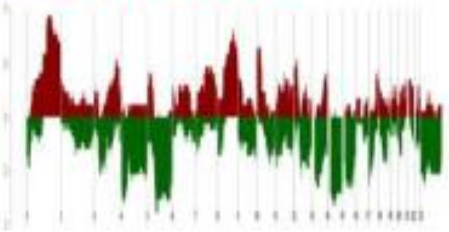
Two BRCA 2 tumors showed luminal A expression

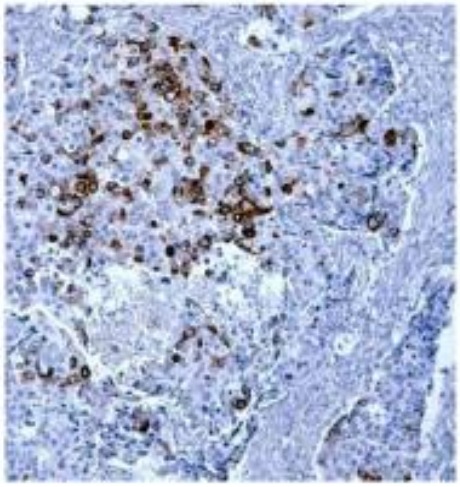
**Sorlie et al.Pnas.2003**



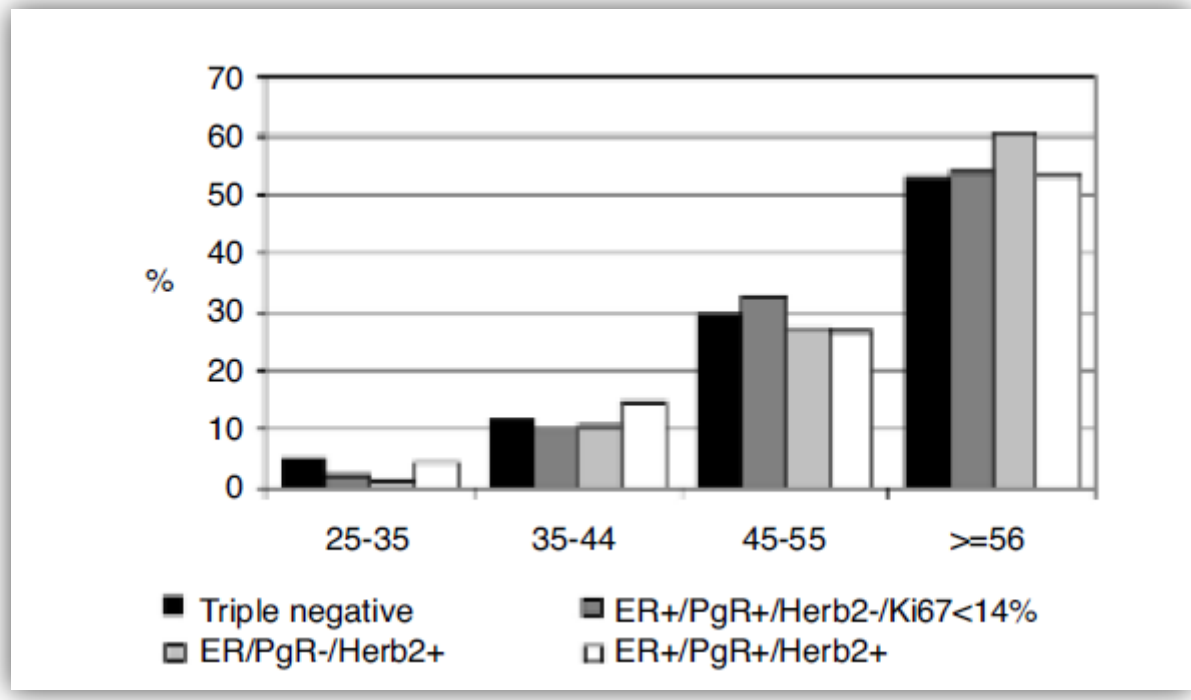

## Basal-like subtype

1. 10-25% of all tumors
2. ~75% of TN tumors
3. distinct cell type of origin or developmental stage of arrest
4. >50% TP53 mutated
5. highly proliferative (RB-loss)
6. BRCA1-associated
7. highly aneuploid





# Subtype Distribution by Age




*Cortesi et al., Tumori., 2012*

# *RISULTATO DEL TEST GENETICO*

## Informativo

**TRUE POSITIVE**:
sorveglianza intensificata
Chirurgia profiilattica
Chemioprevenzione

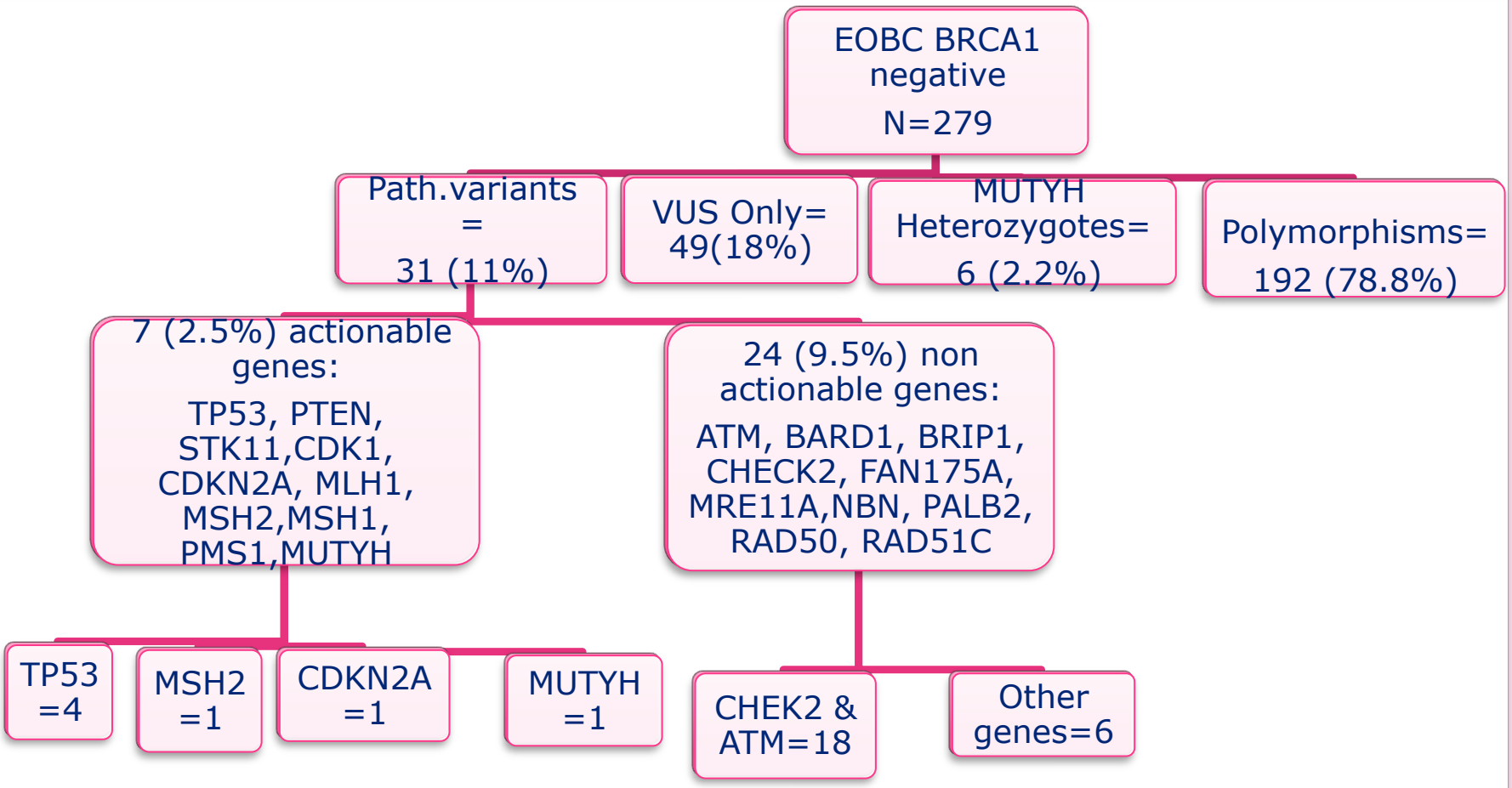
**TRUE NEGATIVE:**
FOLLOW UP STANDARD

## Non informativo

**IDENTIFICAZIONE DI UNCLASSIFIED VARIANT:**
Proposta di sorveglianza intensificata come da protocollo BRCA+

**NESSUNA MUTAZIONE IDENTIFICATA**
Gestione della sorveglianza per rischio alto

# *Prevalence of mutations in a panel of BRCA negative early onset breast cancer*




**Maxwell KN et al. Genetics in Medicine (2014)**

Breast Cancer Res Treat (2015) 149:547–554
DOI 10.1007/s10549-014-3260-8

BRIEF REPORT

# Mutation screening of *PALB2* in clinically ascertained families from the Breast Cancer Family Registry

Tú Nguyen-Dumont · Fleur Hammet · Maryam Mahmoodi · Helen Tsimiklis · Zhi L. Teo · Roger Li · Bernard J. Pope · Mary Beth Terry · Saundra S. Buys · Mary Daly · John L. Hopper · Ingrid Winship · David E. Goldgar · Daniel J. Park · Melissa C. Southey

- Loss-of-function mutations in PALB2 are associated with an increased risk of breast cancer
- 12/1240 probands had pathogenic mutations
- The majority of tumors were high histological grade, invasive ductal carcinomas.
- Young onset was apparent in most families, with **19 breast cancers under 50 years of age**, **including eight under the age of 40 years**.

# *Clinical History*

- Affected at 35 years of age by DIC in the right breast (GIII, ER=0, PgR=0, Ki67=65%,c-Erb=negative, pT4, N0, M0)
- At 39 years she was found to be affected by endometrial adenocarcinoma without myometrial infiltration (grading I), ovarian adenocarcinoma (grading I) and renal clear cell carcinoma
- Affected at 46 years of age by DIC in the left breast (GIII, ER=0, PgR=0, Ki67=80%, c-Erb=negative, pT4, N3, M1)
- Found to carry *BRCA1* and *hMLH1* mutations

Pedroni et al , Tech Coloproct 2014

# *Clinical History*

- Affected at 32, 36 and 40 years of age by DIC, luminal A breast cancer (GIII, ER=0, PgR=0, Ki67=65%,c-Erb=negative, pT4, N0, M0)
- At 39 years she was found to be affected by mucocutaneous  disorder was suggestive of Cowden Syndrome.
- PTEN genetic testing revealed the novel c.71A > T (p.Asp24Val) mutation

Pradella et al, BMC Cancer 2014

**Table 3.** Cumulative 5- and 10-Year Risk of Developing CBC After a First Primary Invasive Breast Cancer According to Mutation Carrier Status and Age at Diagnosis of First Breast Cancer

| Age at First Breast Cancer (years) | *BRCA1* Mutation Carrier | | *BRCA2* Mutation Carrier | | *BRCA1* or *BRCA2* Mutation Carrier | | Noncarriers | |
|---|---|---|---|---|---|---|---|---|
| | Cumulative Risk (%) | 95% CI | Cumulative Risk (%) | 95% CI | Cumulative Risk (%) | 95% CI | Cumulative Risk (%) | 95% CI |
| 5-Year risk for age group | | | | | | | | |
| 25-29 | 16.0 | 8.5 to 30.1 | 14.6 | 6.5 to 32.9 | 15.5 | 8.8 to 27.4 | 3.2 | 2.3 to 4.4 |
| 30-34 | 17.0 | 9.5 to 30.5 | 15.5 | 7.1 to 33.7 | 16.5 | 9.9 to 27.6 | 3.4 | 2.8 to 4.2 |
| 35-39 | 13.2 | 7.4 to 23.5 | 12.0 | 5.6 to 26.0 | 12.8 | 7.7 to 21.3 | 2.6 | 2.2 to 3.1 |
| 40-44 | 9.8 | 5.5 to 17.4 | 8.9 | 4.1 to 19.3 | 9.5 | 5.8 to 15.8 | 1.9 | 1.6 to 2.3 |
| 45-49 | 7.3 | 2.7 to 19.7 | 6.5 | 2.9 to 14.4 | 6.7 | 3.6 to 12.6 | 2.8 | 2.6 to 3.1 |
| 50-54 | 6.0 | 2.2 to 16.3 | 5.3 | 2.4 to 11.9 | 5.6 | 2.9 to 10.3 | 2.3 | 2.1 to 2.6 |
| All ages combined (25-54) | 10.9 | 6.7 to 17.5 | 8.3 | 4.8 to 14.2 | 9.7 | 8.4 to 11.2 | 2.5 | 2.3 to 2.7 |
| 10-Year risk for age group | | | | | | | | |
| 25-29 | 29.0 | 15.4 to 54.7 | 26.6 | 11.8 to 60.1 | 28.2 | 16.0 to 50.0 | 6.1 | 4.4 to 8.5 |
| 30-34 | 31.6 | 17.6 to 56.7 | 29.0 | 13.4 to 63.1 | 30.7 | 18.4 to 51.5 | 6.8 | 5.5 to 8.4 |
| 35-39 | 24.4 | 13.7 to 43.4 | 22.3 | 10.3 to 48.2 | 23.7 | 14.3 to 39.3 | 5.1 | 4.2 to 6.1 |
| 40-44 | 20.0 | 11.3 to 35.5 | 18.3 | 8.5 to 39.4 | 19.4 | 11.8 to 32.1 | 4.1 | 3.4 to 4.9 |
| 45-49 | 13.1 | 4.8 to 35.7 | 11.7 | 5.3 to 26.1 | 12.2 | 6.5 to 22.9 | 5.3 | 4.8 to 5.8 |
| 50-54 | 11.7 | 4.3 to 31.8 | 10.4 | 4.7 to 23.2 | 10.8 | 5.8 to 20.3 | 4.7 | 4.2 to 5.1 |
| All ages combined (25-54) | 20.5 | 12.7 to 33.0 | 15.9 | 9.2 to 27.2 | 18.4 | 16.0 to 21.3 | 4.9 | 4.5 to 5.4 |

NOTE. 5-Year and 10-year risks are calculated using the rate ratios for dichotomized age (< 45, ≥ 45).

*Malone KE et al, J Clin Oncol 2010*

# Conclusions BRCA carriers

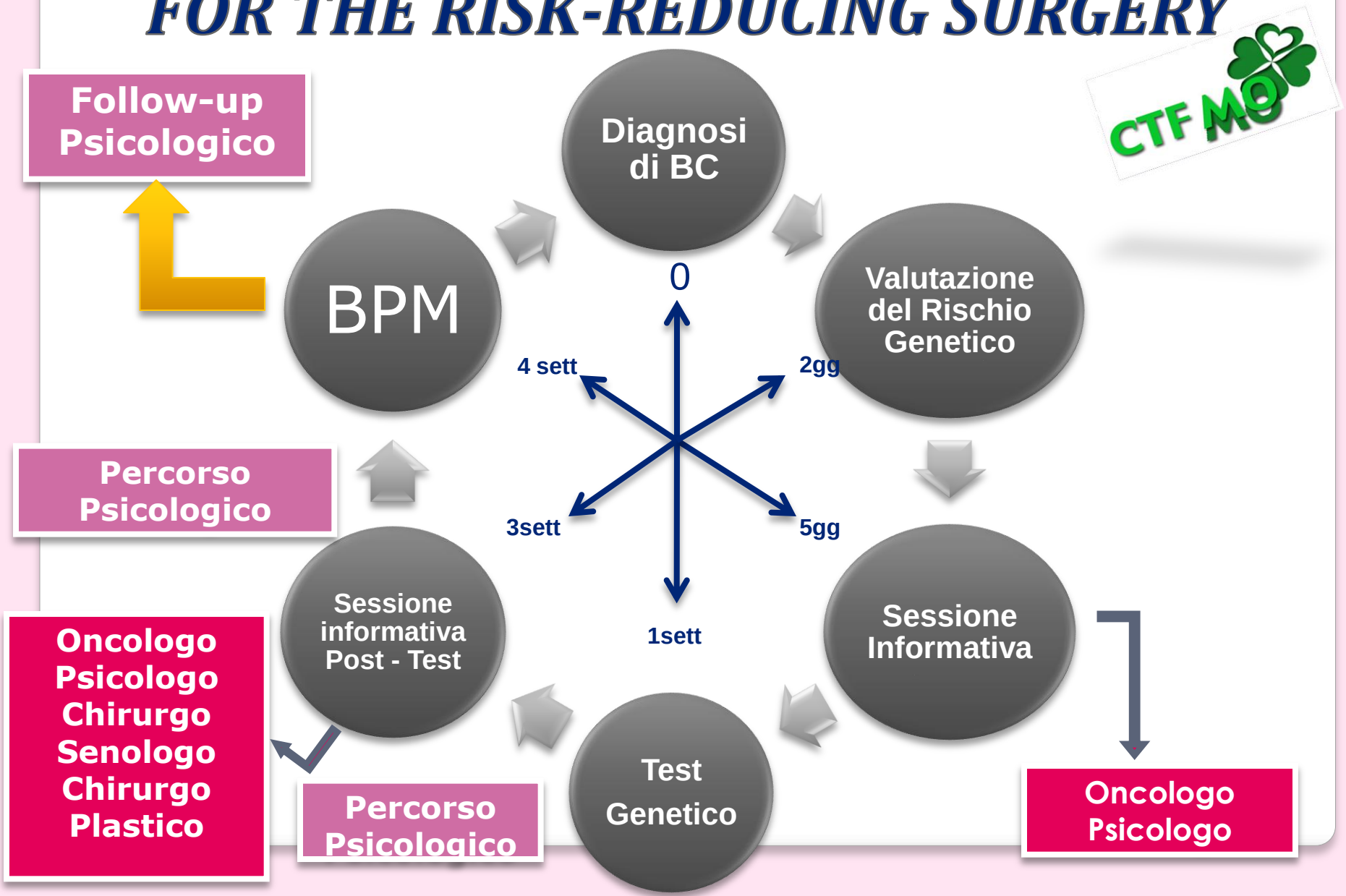
10-year cumulative risk for CBC

- Non-carriers: 6%
- BRCA1 carriers: 20%
- BRCA2 carriers: 11%

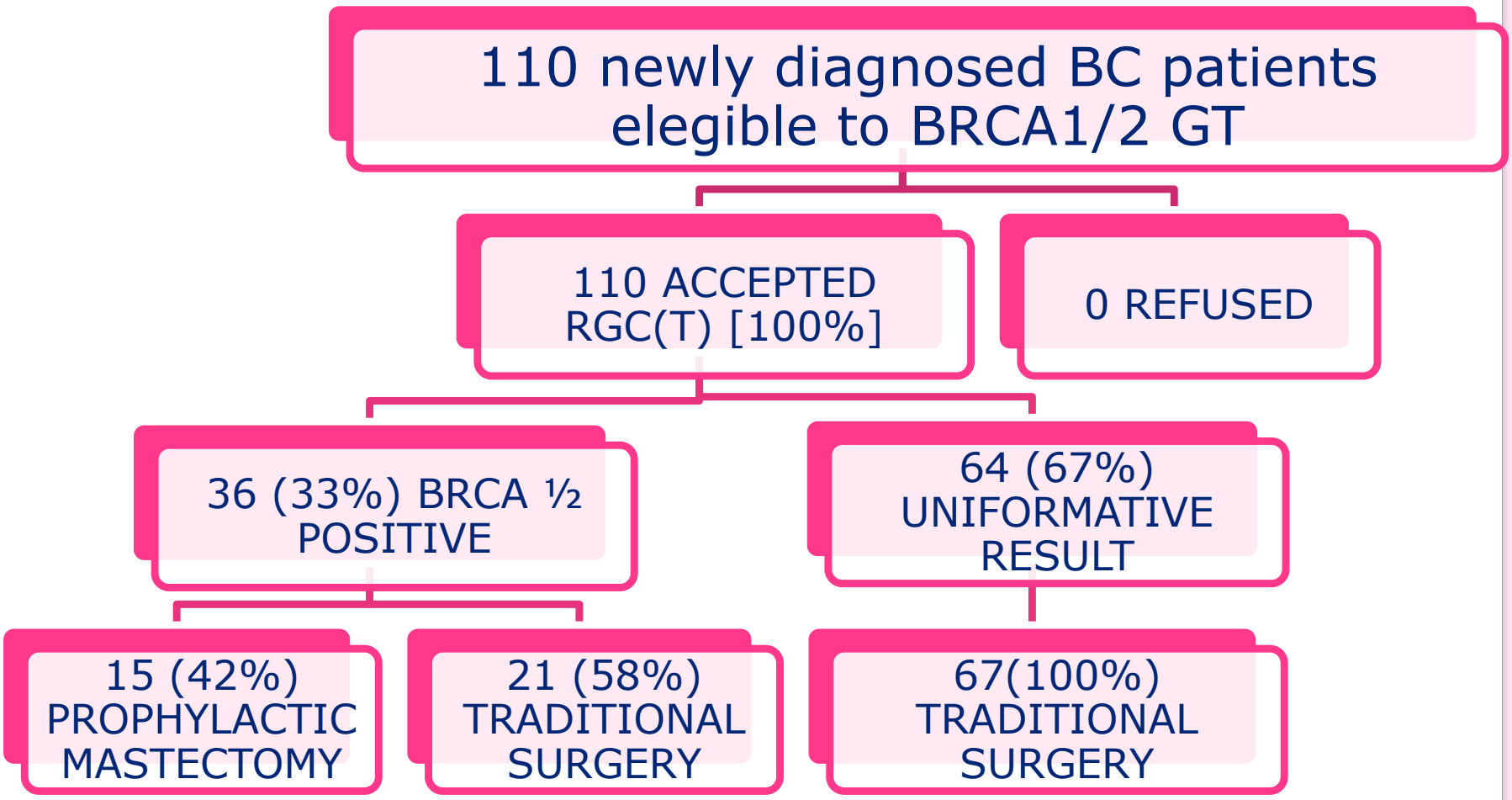
Subgroups of BRCA carriers:

| | | |
|---|---|---|
| **Low risk subgroup** | *Patients with a non-TN first BC diagnosed between ages 41-50* | 3.5 % |
| **Higher risk subgroups** | *Patients with a TN first BC diagnosed between ages 41-50* | 15 % |
| | *Patients with a first BC diagnosed under age 41* | 26 % |

# MULTIDISCIPLINARY CLINICAL PATHWAY FOR THE RISK-REDUCING SURGERY

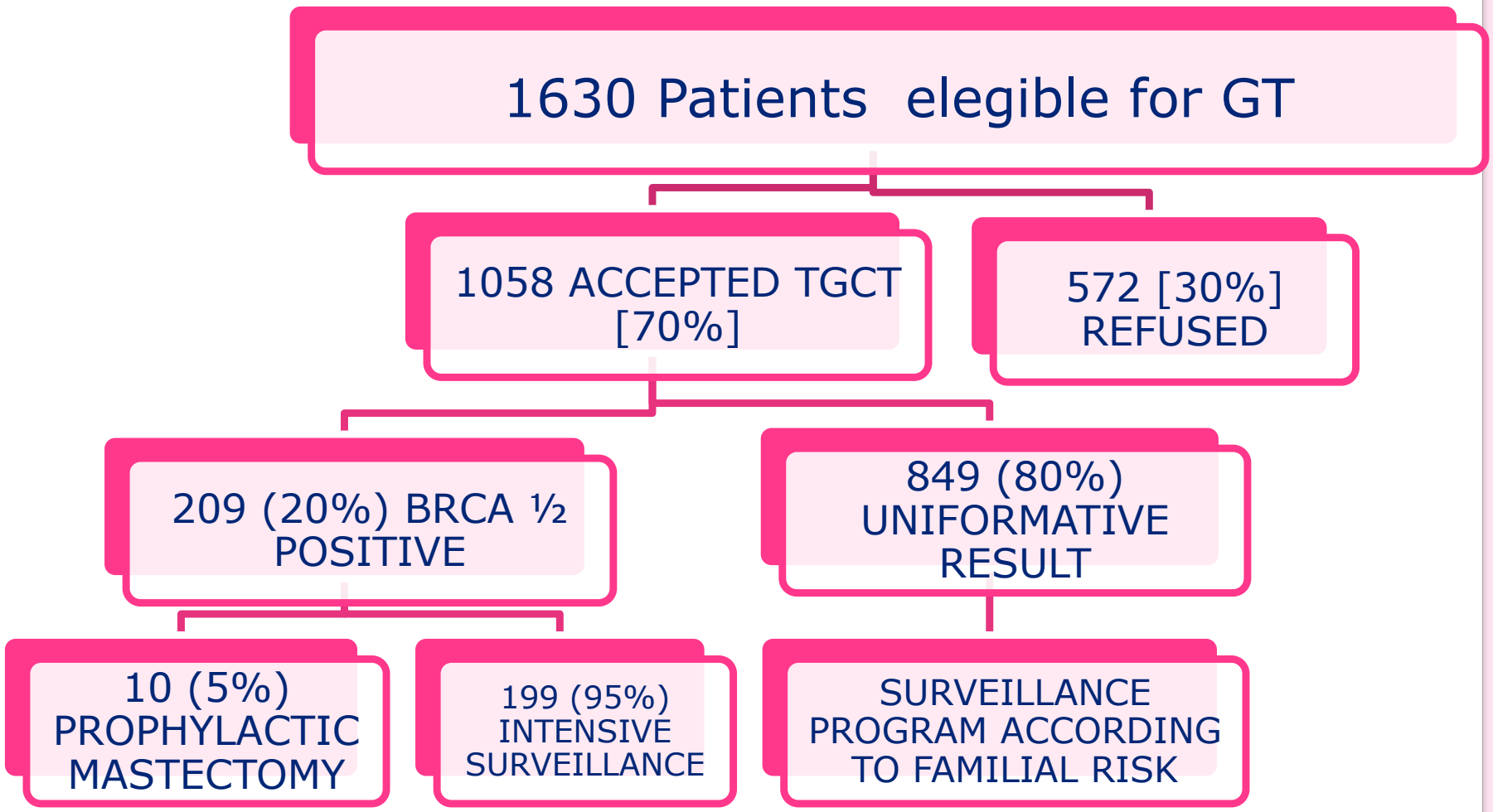


# Results of RGCT




*Cortesi et al, Annals of Oncology, 2014*

# Results of TGCT




*Cortesi et al, Annals of Oncology, 2014*

# *Characteristics of BC in affected and contralateral breast of patients that underwent RRM*

| | Affected Breast (N=25) | | Contralateral BC (N=6) (24%) | |
|---|---|---|---|---|
| | TGCT (10) | RGCT (15) | TGCT (2) | RGCT (4) |
| Histology | | | | |
| DIC | 7 (70%) | 13(87%) | 0 (0%) | 1(25%) |
| LIC | 1 (10%) | 0 (0%) | 0 (0%) | 0 (0%) |
| DCIS | 1 (10%) | 2 (13%) | 1 (50%) | 1 (25%) |
| DIN1a | 0 (0%) | 0 (0%) | 0 (0%) | 2 (50%) |
| DIN1b | 1 (10%) | 0 (0%) | 1 (50%) | 0 (0%) |
| Grading* | | | | |
| 1 | 0 (0%) | 0 (0%) | 0(0%) | 0 (0%) |
| 2 | 3 (37%) | 4 (40%) | 0 (0%) | 0 (0%) |
| 3 | 5 (63%) | 9 (60%) | 0 (0%) | 1(100%) |
| ER* | | | | |
| Positive | 3(37%) | 8 (53%) | 0(0%) | 0(0%) |
| Negative | 5 (63%) | 5 (47%) | 0(100%) | 1(100%) |
| PgR* | | | | |
| Positive | 2(25%) | 9 (69%) | 0(100%) | 0(100%) |
| Negative | 6 (75%) | 4 (31%) | 0 (0%) | 1(100%) |
| Ki67* | | | | |
| ≤ 14% | 3 (37%) | 3(23%) | 0 (0%) | 0(100%) |
| >14% | 5 (63%) | 10 (77% | 0 (100%) | 1(100%) |
| c-Erb* | | | | |
| Positive | 0 (0%) | 2 (15 %) | 0 (0%) | 0(0%) |
| Negative | 11 (15%) | 11(85%) | 0 (0%) | 1(0%) |
| BRCA1 | 6 (60%) | 5 (33%) | 0 (0%) | 1(25%) |
| BRCA2 | 4 (40%) | 10 (67%) | 2 (100%) | 3(75%) |
| T size* | | | | |
| T1 | 5 (63%) | 9(69%) | 0 (0%) | 1(100%) |
| T2 | 3 (37%) | 4(31%) | 0 (0%) | 0(0%) |
| Nodes* | | | | |
| N0 | 3 (37%) | 9(69%) | 0 (0%) | 0(0%) |
| N1 | 4(50%) | 3(23%) | 0(0%) | 1(100%) |
| N2 | 1(13%) | 1 (8%) | 0(0%) | 0(0%) |

*Cortesi et al, Annals of Oncology, 2014*

# *OCG-Rapid: descriptive features of patient with newly breast cancer diagnosis*

| | BRCA1/2 CARRIERS | PATIENTS WITH UNINFORMATIVE RESULTS |
|---|---|---|
| MEAN AGE<br>(MIN-MAX) | 38 ± 11<br>(24 – 51) | 38 ± 11<br>(18 – 81) |

# *Impatto psicologico della Mastectomia Profilattica: la nostra esperienza*

**Valutazione Psicologica a 12 mesi dall'intervento:**

Buon adattamento psicologico e soddisfazione per la scelta effettuata.
Significativa riduzione delle paure relative alla possibilità di sviluppare una futura neoplasia

Graduale ma non definitiva accettazione della nuova immagine corporea (che migliora significativamente dopo il posizionamento delle protesi definitive)
In alcune pazienti, permangono **comunque** delle problematiche relative alla sfera sessuale e una lieve insoddisfazione inerente al risultato estetico dell'intervento
Solo 1 paziente su 15 ha mostrato uno stato depressivo persistente successivamente all'intervento principalmente dovuto all'insoddisfazione relativa al risultato estetico.

Cancer Treatment Reviews 41 (2015) 187–196

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Complications of Treatment

# Diagnostic and therapeutic ionizing radiation and the risk of a first and second primary breast cancer, with special attention for *BRCA1* and *BRCA2* mutation carriers: A critical review of the literature

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# *Conclusions*

For screening purposes there seems sufficiently enough evidence to incorporate mammography in breast cancer screening programs for BRCA1/2 mutation carriers only after the age of **30 years.**

For those BRCA1/2 mutation carriers who developed breast cancer **above the age of 30 years** and opting for breast conserving therapy, there are no hard data regarding a possibly increased carcinogenic effect of adjuvant radiotherapy with respect to a second primary breast cancer, either ipsilateral or contralateral. However, a carcinogenic effect of adjuvant radiotherapy on the longterm in this population has certainly not been excluded.

Since low dose diagnostic radiation increases the risk of primary breast cancer in **very young BRCA1/2 mutation carriers (<30 years),** caution with regard to breast conserving surgery and radiotherapy seems warranted in this patient group.

# *Profili di rischio*

**Profilo 1 - Familiarità con rischio assimilabile alla popolazione generale:**

- 1 familiare di primo grado diagnosticato dopo i 40 anni
- 2 familiari di primo grado diagnosticati dopo i 60 anni
- senza alcuna delle condizioni che seguono

**Profilo 2 - Familiarità con rischio moderatamente più elevato rispetto alla popolazione generale:**

- 2 familiari di primo grado con diagnosi tra i 50-59 anni
- 2 familiari di secondo grado del ramo materno con diagnosi di cancro mammario a < 50 anni
- 1 familiare di primo o secondo grado con diagnosi di cancro mammario 50-59 anni + 1 familiare di primo o secondo grado con diagnosi di cancro ovarico ad ogni età
- senza alcuna delle condizioni che seguono.

DGR 220/2011

# *Profili di rischio*

**Profilo 3 - Familiarità con rischio molto elevato e relativi criteri per considerare l'invio alla consulenza genetica**
**Storia personale o familiare di:**

- Maschio con carcinoma mammario
- Donna con carcinoma mammario e carcinoma ovarico
- Donna con carcinoma mammario con le seguenti caratteristiche:
  < 36 anni, con o senza storia familiare
  < 50 anni con carcinoma bilaterale, con o senza storia familiare
  < 50 anni e 1 o più parenti di primo grado con:
- carcinoma mammario <50 anni
- carcinoma ovarico a qualsiasi età
- carcinoma mammario bilaterale
- carcinoma mammario maschile
- >50 anni solo se storia familiare di carcinoma mammario o ovarico in 2 o più parenti in primo grado tra loro (di cui uno in primo grado con lei)
- Donna con carcinoma ovarico e un parente di primo grado con:
  carcinoma mammario < 50 anni
  carcinoma ovarico a qualsiasi età
  carcinoma mammario bilaterale
  carcinoma mammario maschile
  storia familiare di carcinoma mammario o ovarico in >2 parenti di primo grado (di cui uno in primo grado con lei)
- Mutazione nota di BRCA1, BRCA2, P53

DGR 220/2011

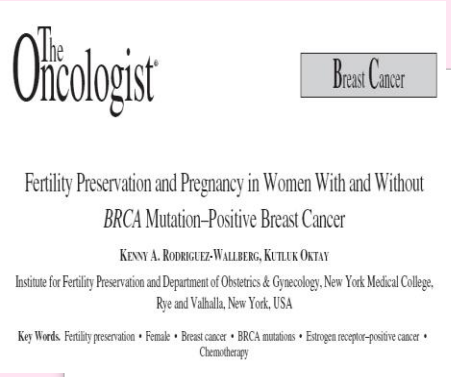
# Surveillance for risk categories

| RISK PROFILE | START | US | MX | MRI |
|---|---|---|---|---|
| Profile 1 | 45 yrs | If suspected mammogram image | 45 -50 yrs A<br>51 -74 yrs B<br>(Population Screening) | |
| Profile 2 | 25 yrs<br>(if familiar with EOBC)<br>36 yrs | ≥ 41yrs if high breast density or suspected mammogram image | 40 -50 yrs A<br>51 -74 yrs B<br>(Population Screening) | According to FONCAM guidelines |
| Profile 3<br>(without detected mutations) | 25 yrs | 25 – 60 yrs S | 35-69 yrs A<br>70-74 yrs B | According to FONCAM guidelines |
| Profile 3<br>(with detected mutations) | From the mutation detection | From the mutation detection-69 yrs S | 35-69 yrs A<br>70-74 yrs B | ≥ 25 yrs A |

A = annual; B = biennial; S = six-monthly; EOBC = Early Onset Breast Cancer

DGR 220/2011

# *Gestione dei fattori Riproduttivi nelle Pazienti Brca+*




# *SAFETY OF PREGNANCY BEFORE AND AFTER BREAST CANCER: DO BRCA MUTATIONS CONFER ADDITIONAL RISK?*

- No specific information on whether or not pregnancy is safe following a breast cancer diagnosis in women with *BRCA* mutations.
- **Parity and number of children appear to be protective against developing breast cancer in carriers of *BRCA1* and *BRCA2* mutations in most large studies.**
- However, results have been contradictory, particularly in women with ***BRCA2* mutations**, but also those with *BRCA1* mutations.
- **A case– control study in 1,380 matched pairs of women with *BRCA1* and *BRCA2* mutations did not find an adverse effect of fertility treatment on the risk for developing breast cancer, compared with controls (odds ratio, 1.21; 95% CI, 0.81–1.82).**

***The Oncologist*** 2012;17:1409–1417

# *AN INDIVIDUALIZED APPROACH TO CHOOSING THE APPROPRIATE FP PROCEDURE*

## VALUE OF EARLY REFERRAL FOR FP

There is some difference for women who carry *BRCA* mutations and for those with a family history of breast cancer in terms of referral patterns.

It appeared that women with a family history of breast cancer tended to be referred earlier.

The latter observation could be a result of the increased awareness of *BRCA* mutation carriers because other family members might have had similar experiences or possibly because a looming risk-reducing salpingo-oophorectomy (RRSO) made FP a more urgent issue

***The Oncologist*** 2012;17:1409–1417

# *OVARIAN RESERVE IN BRCA PATIENTS*

**Recent research suggested that *BRCA* mutation carriers may have a lower ovarian reserve**

**OVARIAN TISSUE CRYOPRESERVATION AND TRANSPLANTATION: RECENT PROGRESS AND THE ISSUES SPECIFIC TO *BRCA* CARRIERS**

An early oophorectomy can be performed to cryopreserve ovarian tissue from women with *BRCA* mutations before the risk for ovarian cancer increases with age, but the safety of transplanting this tissue back must be determined.

**PGD FOR *BRCA* MUTATION CARRIERS**

Women with *BRCA* mutations may elect to use preimplantation genetic diagnosis during in vitro fertilization to avoid transmitting the mutation

***The Oncologist*** 2012;17:1409–1417

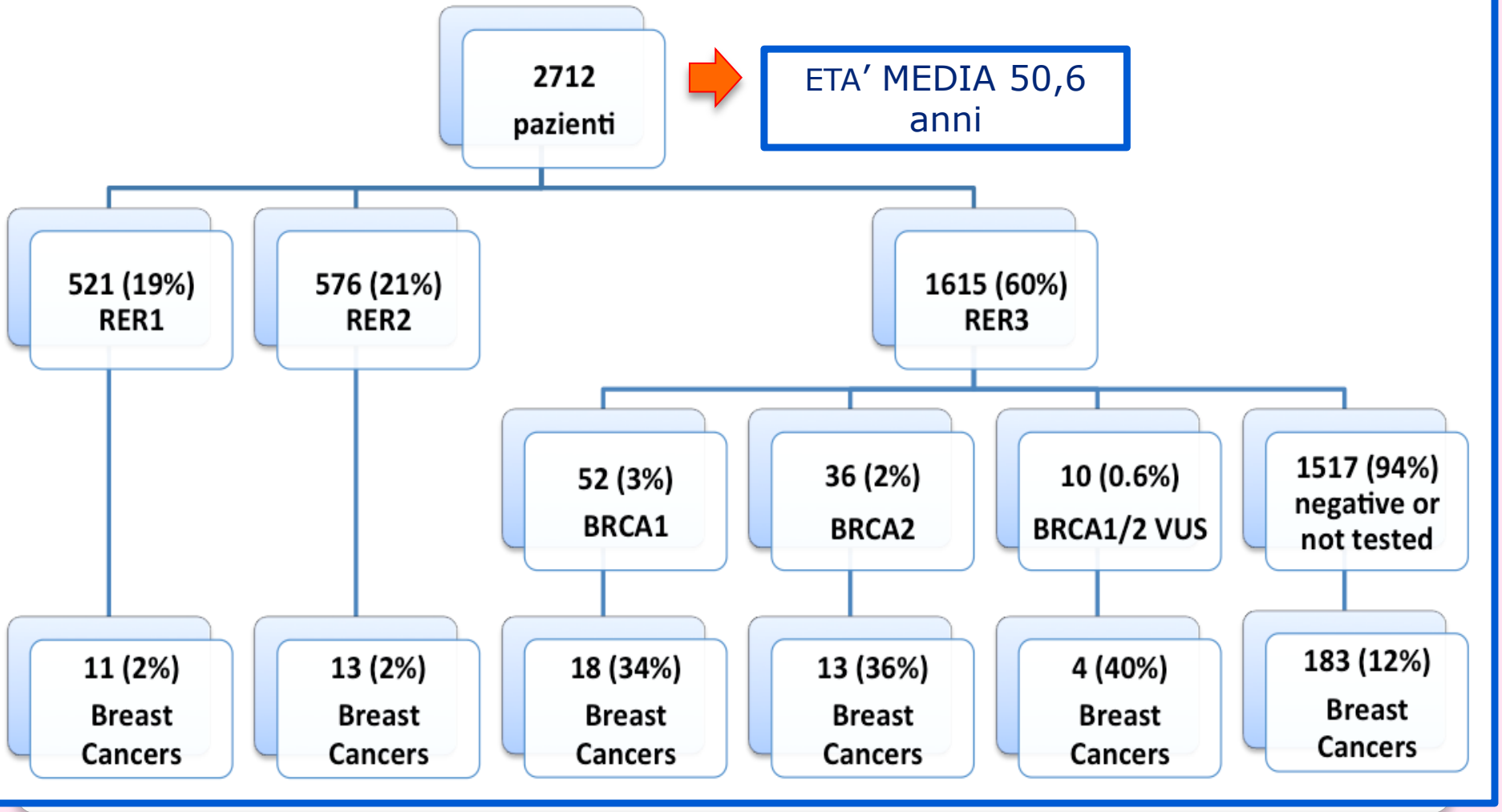
# *IMPATTO DEI FATTORI ENDOCRINO-RIPRODUTTIVI SUL RISCHIO DI TUMORE MAMMARIO IN DONNE A INCREMENTATO RISCHIO PER STORIA FAMILIARE*

# *OBIETTIVO DELLO STUDIO*

- Indagare l'impatto dei seguenti fattori legati alla vita endocrino/riproduttiva:
  - **numero di gravidanze a termine**
  - **età alla prima gravidanza**
  - **allattamento**
  - **età al menarca e alla menopausa**
  - **aborti**
  - **utilizzo di terapia contracettiva e ormonale sostitutiva**

- sul rischio della nostra popolazione di donne che sono già ad aumentato rischio per storia familiare e/o per mutazione genetica.

# *Pazienti che hanno effettuato i controlli periodici presso il CTF tra Maggio 2010 e Dicembre 2014 per le quali era stata compilata (anche solo parzialmente) la scheda anamnestica.*

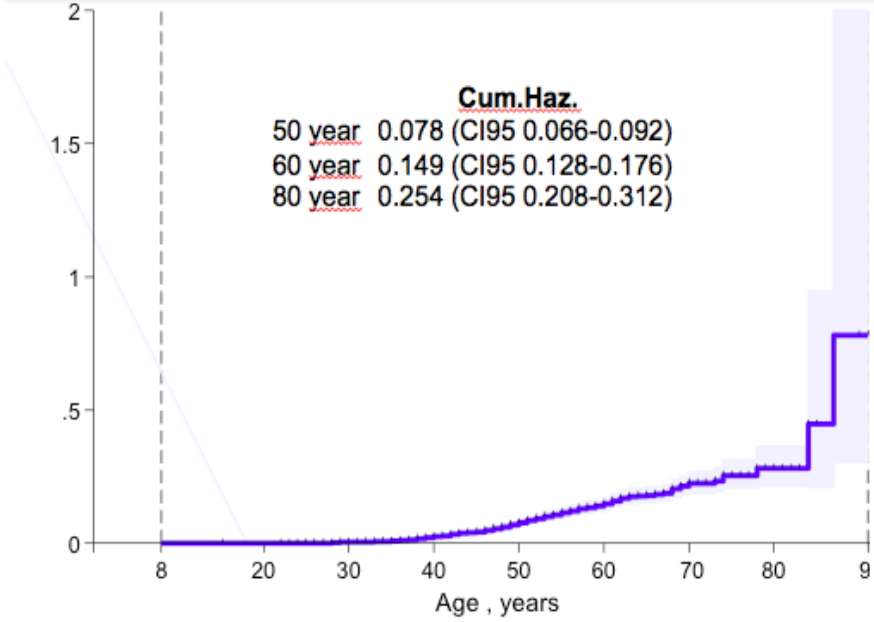


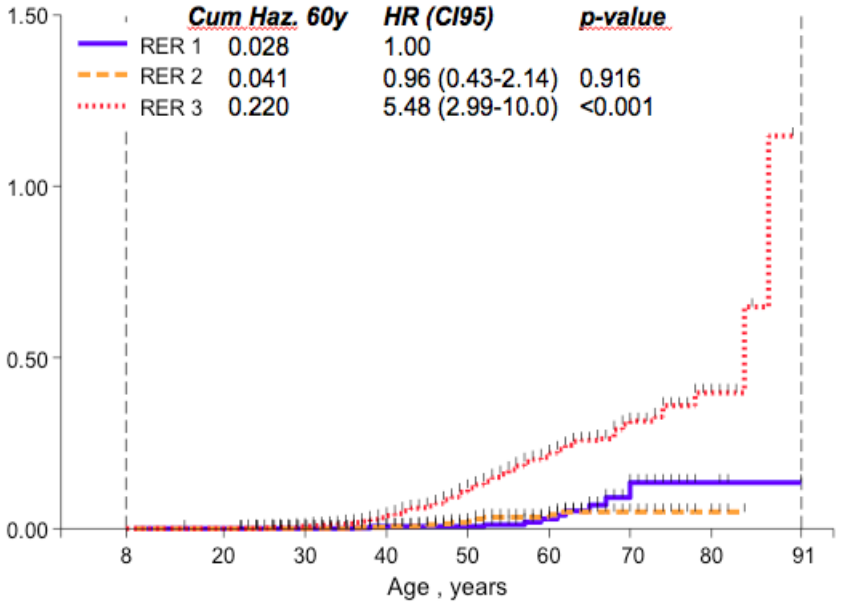
| Variabile | Status | n (%) | Non Noti (%) |
|---|---|---|---|
| **Gravidanze** | No | 295 (13.8%) | 589 (21.7%) |
| | Si | 1828 (86.1%) | |
| **Numero di Gravidanze** | 1 | 783 (42.8%) | - |
| | 2+ | 1045 (57.1%) | |
| **Età alla prima gravidanza** | > 30 anni | 401 (22.6%) | 61 (3.3% di 1828) |
| | ≤ 30 anni | 1366 (77.3%) | |
| **Allattamento** | No | 185 (20.1%) | 909 (49.7% di 1828) |
| | Yes | 734 (79.8%) | |
| **Mesi di allattamento** | ≤ 6 mesi | 272 (37.5%) | 9 (1.2% di 734) |
| | >6 ≤12 | 193 (26.6%) | |
| | > 12 mesi | 260 (35.8%) | |
| **Menarca** | ≤ 12 anni | 1358 (54.1%) | 205 (7.5%) |
| | > 12 anni | 1149 (45.8%) | |
| **Menopausa** | No | 975 (63.7%) | 1182 (43.5%) |
| | Si | 555 (36.2%) | |
| **Età alla Menopausa** | ≤ 50 anni | 208 (59.5%) | 206 (33.1% di 555) |
| | > 50 anni | 141 (40.4%) | |
| **HRT** | No | 328 (77.3%) | 131 (23.6% di 555) |
| | Si | 96 (22.6%) | |
| **Aborti** | No | 965 (72.5%) | 1381 (50.9%) |
| | Si | 366 (27.4%) | |
| **Terapia Contraccettiva** | No | 433 (30.7%) | 1306 (48.1%) |
| | ≤ 5 anni | 501 (35.6%) | |
| | >5 ≤10 | 310 (22%) | |
| | > 10 anni | 162 (11.5%) | |

# *PAZIENTI AFFETTE DA CARCINOMA MAMMARIO (n=242)*

| Variable | Status | n (%) | Missing, n (%) |
|---|---|---|---|
| **Mean age of diagnosis** | | **48 (SD 11)** | *5 (2,0)* |
| **Diagnosis** | Early (<35) | **20 (8,4)** | *5 (2,0)* |
| | Late (≥35) | **217 (91,5)** | |
| **Invasive** | No | **42 (20,0)** | *33 (13,6)* |
| | Yes | **167 (80,0)** | |
| *Invasive HR+* | No | **36 (21,6)** | *1 (0,5)* |
| | Yes | **130 (78,3)** | |
| **Second tumor** | No | **210 (88,9)** | *6 (2,4)* |
| | Yes | **26 (11,0)** | |
| **RER** | 1 | **11 (4,5)** | - |
| | 2 | **13 (5,3)** | |
| | 3 | **218 (90,0)** | |

# RISCHIO CUMULATIVO DI CARCINOMA MAMMARIO



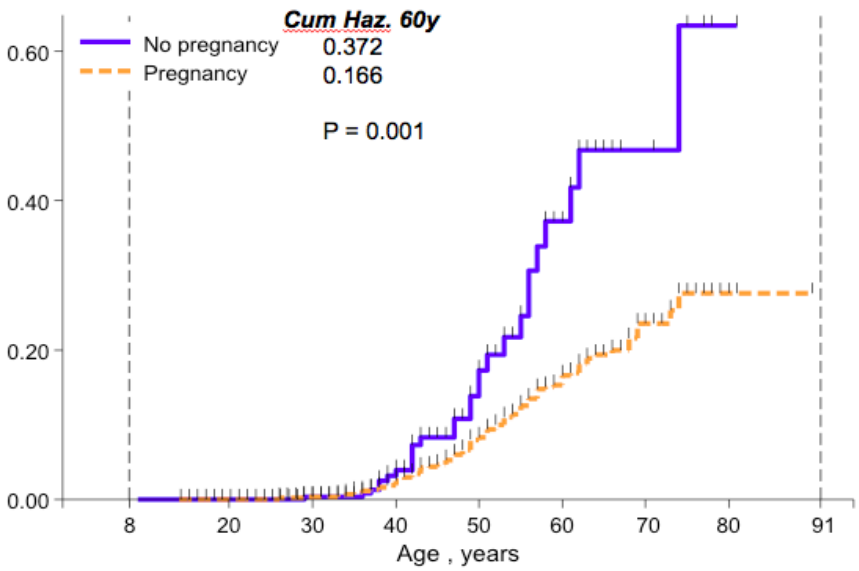

**POPOLAZIONE GENERALE**

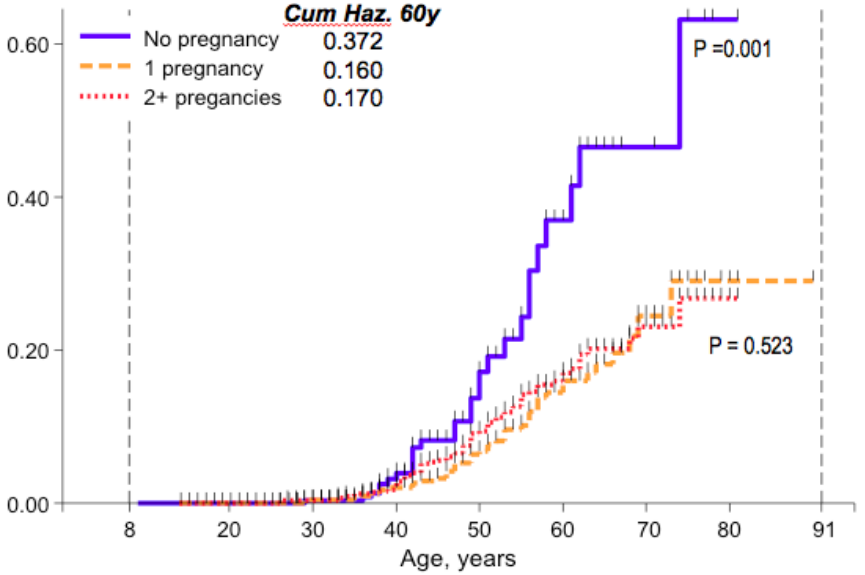
**SOTTO-POPOLAZIONI DI RISCHIO**

**IL RISCHIO CUMULATIVO NELLE PAZIENTI RER3 E' MAGGIORE RISPETTO ALLE ALTRE SOTTO-POPOLAZIONI**

# NUMERO DI GRAVIDANZE A TERMINE

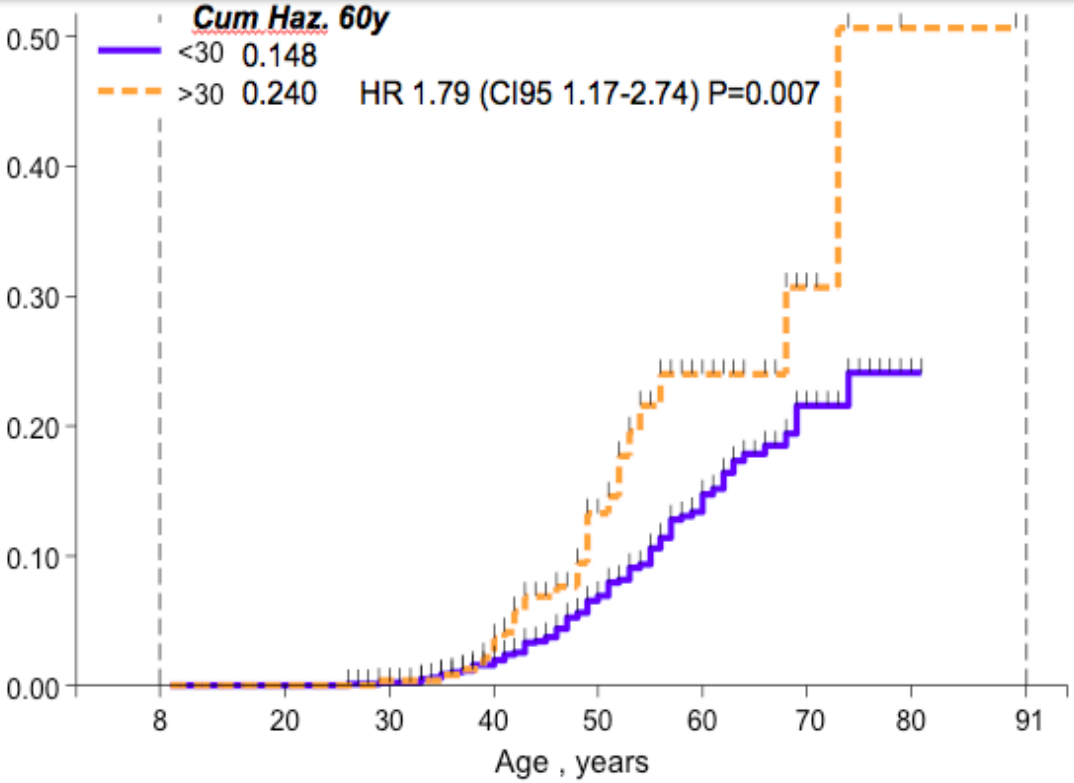
## RER3




**ALMENO 1 PARTO A TERMINE E' UN FATTORE PROTETTIVO PER IL TUMORE MAMMARIO**

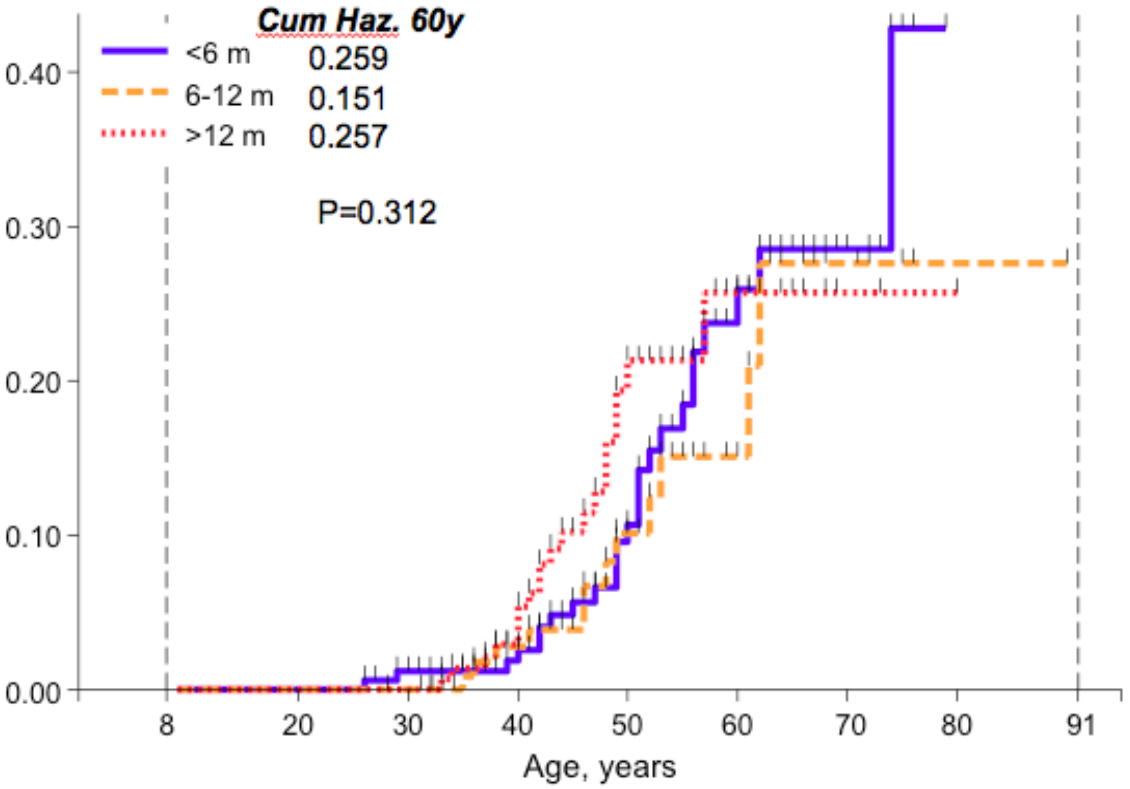
# ETA' ALLA PRIMA GRAVIDANZA A TERMINE




**RER3**

**UN'ETA' ALLA PRIMA GRAVIDANZA ≤30 ANNI**
**E' UN FATTORE PROTETTIVO PER IL TUMORE MAMMARIO**

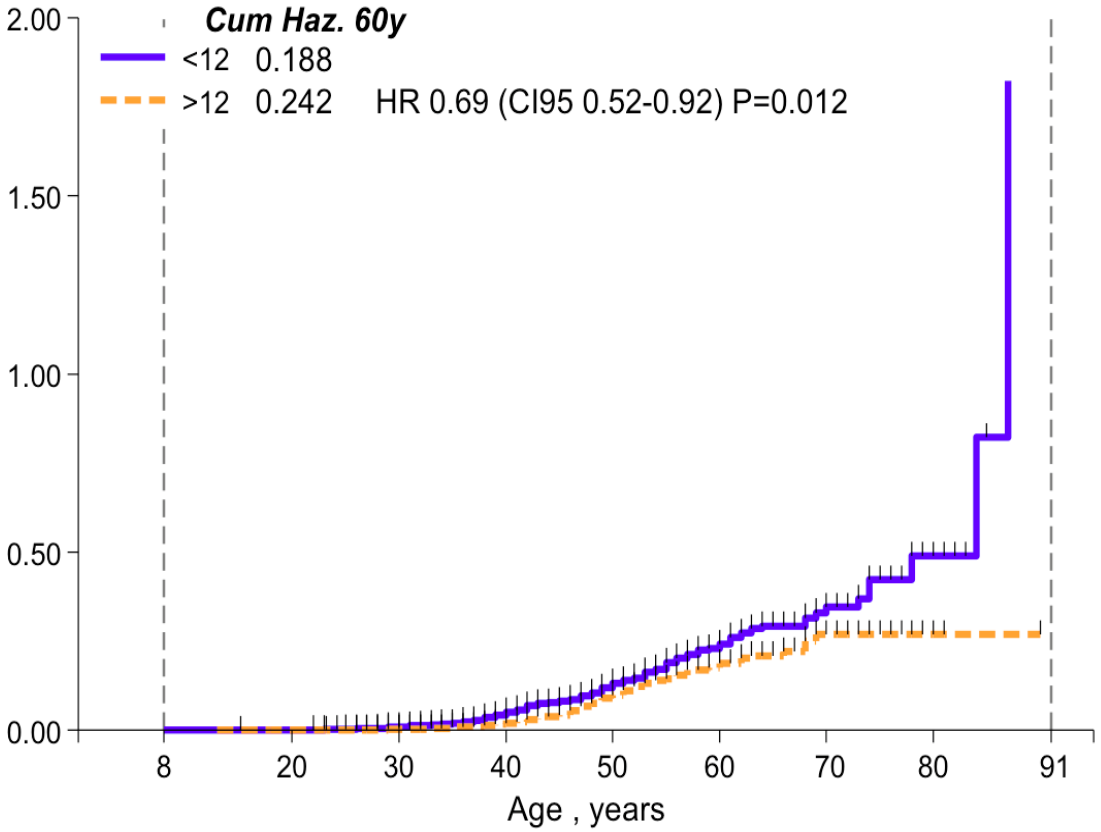
# ALLATTAMENTO




**RER3**

**LA DURATA COMPLESSIVA DI ALLATTAMENTO NON MODIFICA IL RISCHIO DI TUMORE MAMMARIO**

# *MENARCA*

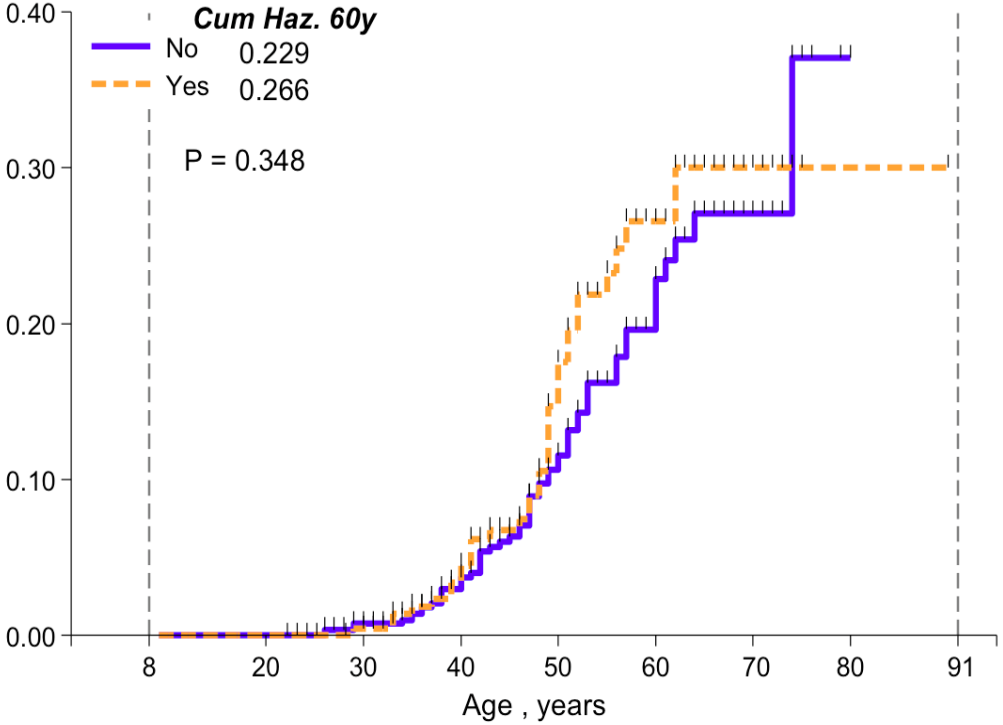



**RER3**

**UN MENARCA PRECOCE (≤12 ANNI) RAPPRESENTA UN FATTORE DI RISCHIO PER TUMORE MAMMARIO**

# ABORTI

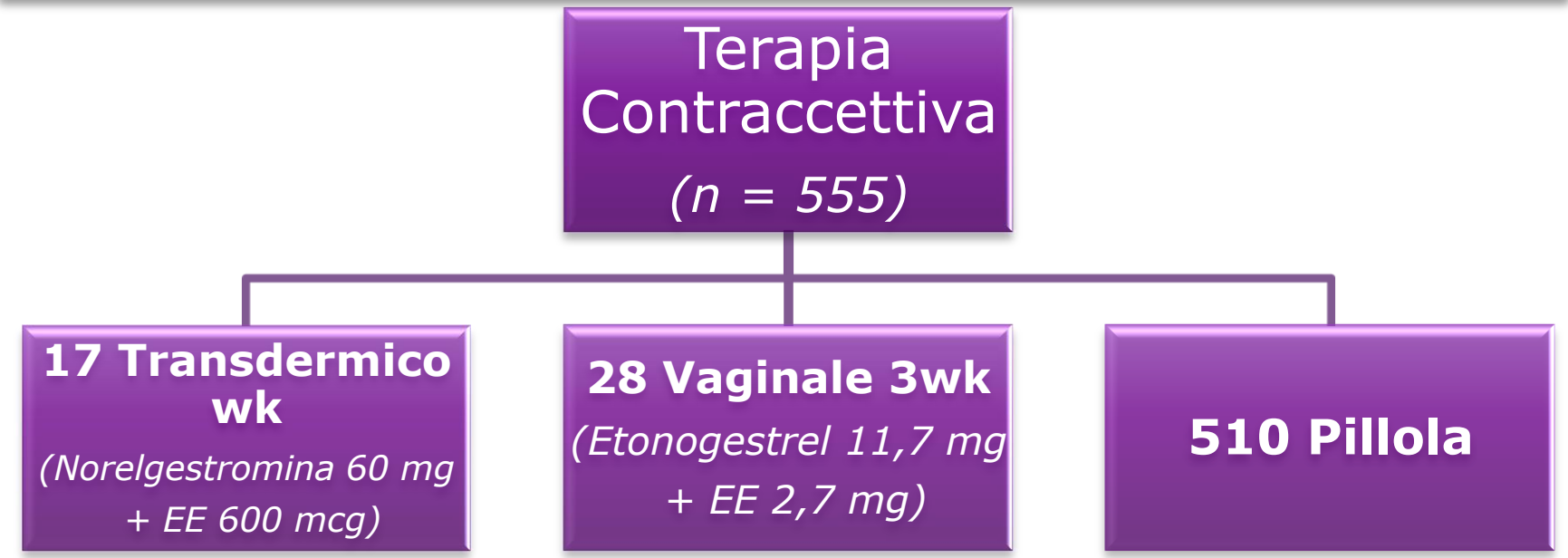
Diverse donne seguite dal nostro centro hanno riferito episodi di aborto
(da 1 fino a 8 episodi). Gli aborti sono tutti avvenuti tra la 5° e la 34° settimana.




**RER3**

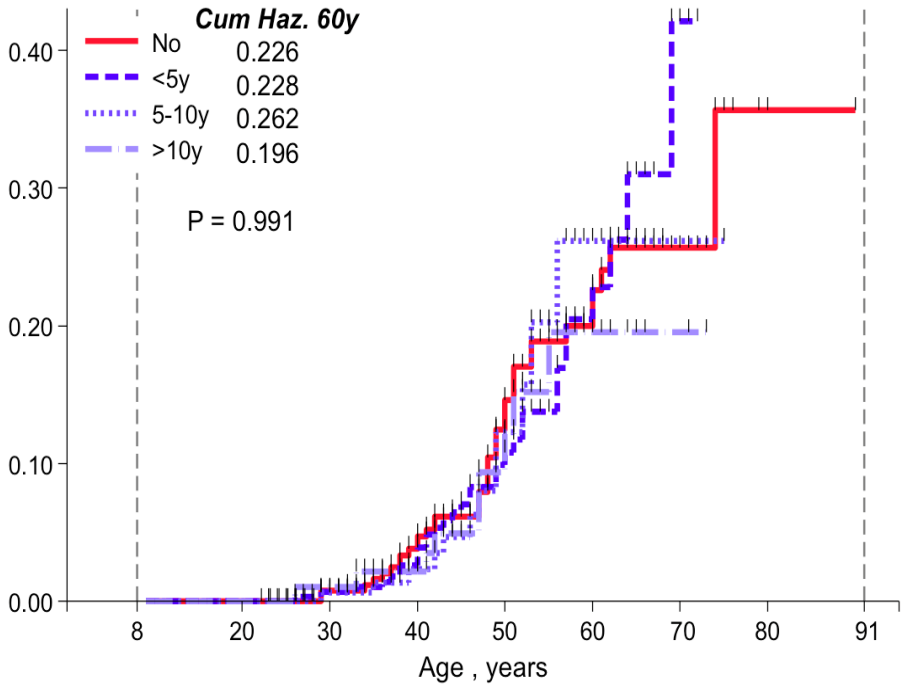
**NON È STATA RIPORTATA ALCUNA ASSOCIAZIONE TRA LA PRESENZA DI ABORTI E IL RISCHIO CUMULATIVO DI TUMORE MAMMARIO**

# TERAPIA CONTRACCETTIVA



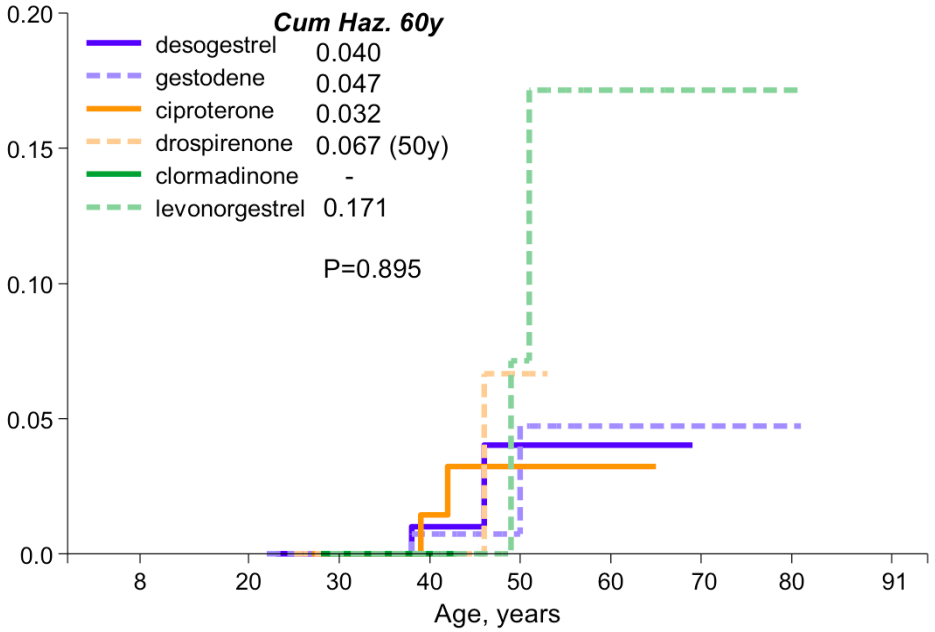

| | Desogestrel | Gestodene | Ciproterone | Drospirenone | Levonorgestrel | Clormadinone |
|---|---|---|---|---|---|---|
| Estrog. ≤ 20 mcg | 85 (57%) | 28 (13%) | - | 28 (29%) | 15 (44%) | - |
| Estrog. >20 mcg | 61 (41%) | 184 (87%) | 99 (100%) | 67 (71%) | 19 (56%) | 9 (100%) |
| Other /NA | 2 (1%) | - | - | - | - | |
| Total progest | 148 | 212 | 99 | 95 | 34 | 9 |

**NESSUNA DIFFERENZA STATISTICAMENTE SIGNIFICATIVA TRA CHI HA NON HA MAI ASSUNTO LA TERAPIA CONTRACCETTIVA E CHI L'HA ASSUNTA (≤ 5 ANNI, >5 E ≤ 10, > 10 ANNI).**



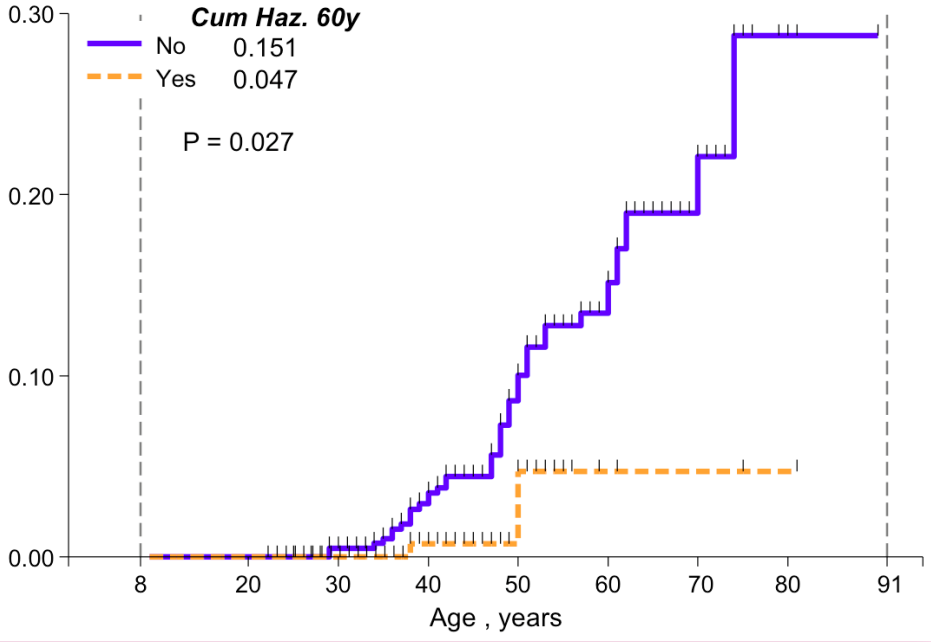

**RER3**

**NESSUNA DIFFERENZA TRA LE TERAPIE CHE CONTENEVANO ≤ 20 MCG DI ETINILESTRADIOLO E LE TERAPIE CON > DI 20 MCG**




Il confronto tra progestinici non ha mostrato alcuna differenza statisticamente significativa in termini di rischio cumulativo di tumore mammario.

Il gestodene nel confronto con le donne che non hanno mai assunto una terapia ormonale ha dato un risultato addirittura protettivo.



- UNO DEI PRIMI STUDI AD ANALIZZARE DONNE A INCREMENTATO RISCHIO FAMILIARE NON BRCA
- AMPIA DIMENSIONE DEL CAMPIONE
- INFORMAZIONI ANAMNESTICHE DETTAGLIATE
- INFORMAZIONI SU CONTRACCETTIVI DI ULTIMA GENERAZIONE

## *PUNTI DI FORZA*

- INFORMAZIONI ANAMNESTICHE INCOMPLETE
- ETA' GIOVANE DEL CAMPIONE (50,6 ANNI)
- PAZIENTI RER2 SOLO FINO AD ETA' DA SCREENING (45 ANNI)
- LIMITI NELLA RACCOLTA DELL'ANAMNESI FAMILIARE

# *PUNTI DEBOLI*

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