Rete Oncologica regionale e Percorsi di Patologia

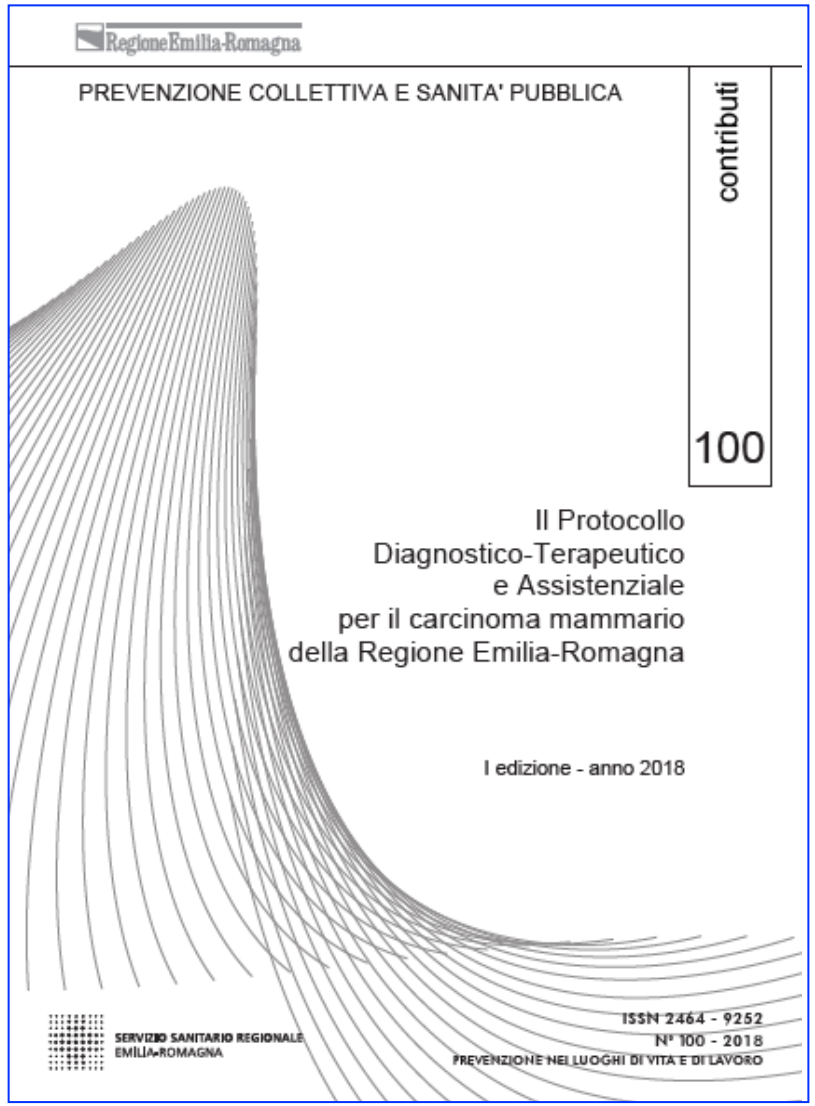
Percorso e Terapia - Mammella

Antonio Frassoldati – Ferrara

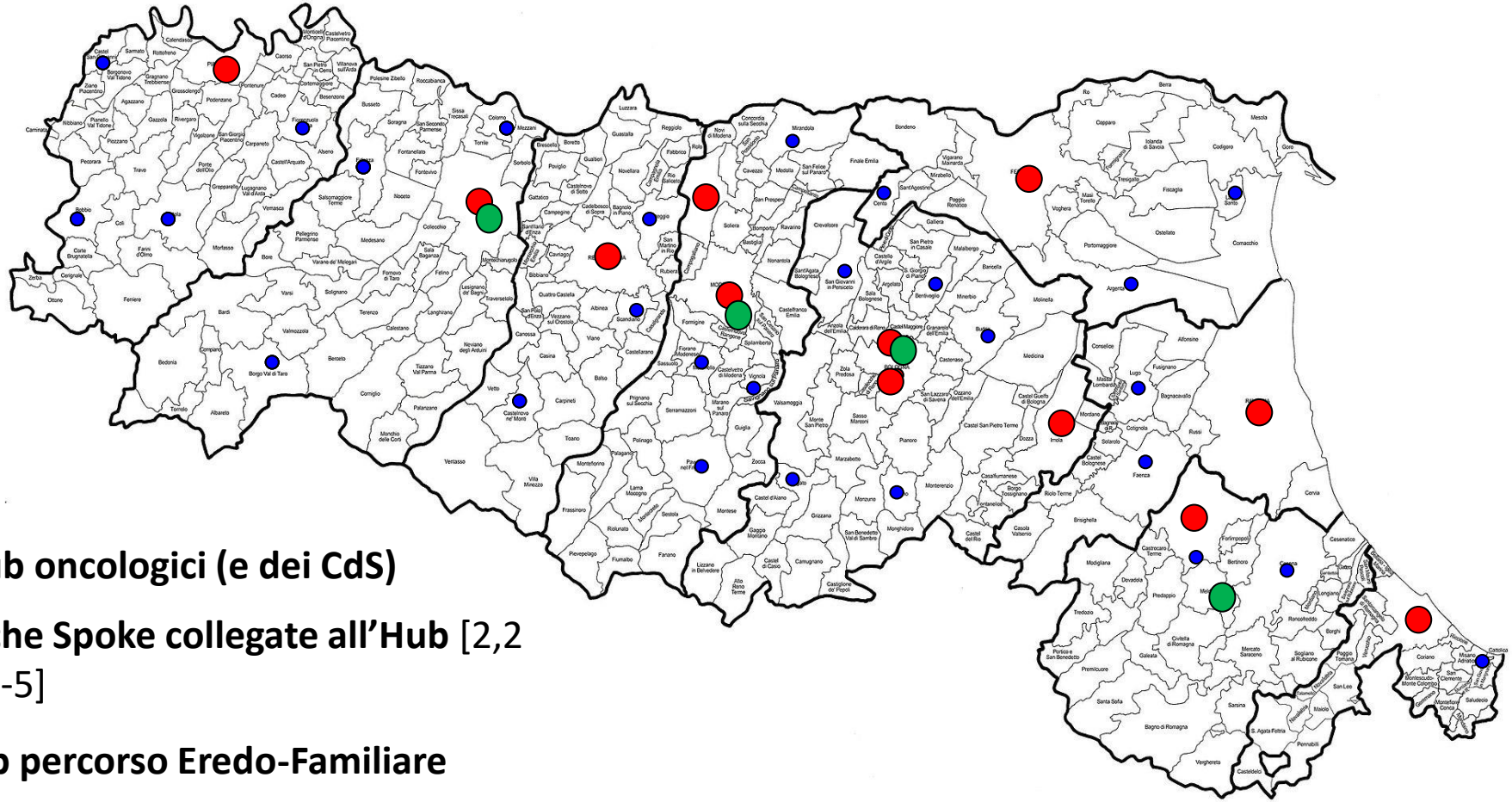
Guglielmo Ferrari – Reggio Emilia

Rete Regionale dei Centri di Senologia DGR 345 del 12 maggio 2018

- Identifica 12 Centri di Senologia con caratteristiche strutturali, organizzative e qualitative idonee
- documento formale che definisce il percorso, l'organizzazione e le funzioni dei servizi afferenti al CdS, fra cui;
  - massa critica minima di casistica (almeno 150 nuovi casi all'anno e bacino di 250.000 persone)
  - livelli di clinical competence di tutti i professionisti
  - presa in carico della donna assicurata da una continuità assistenziale tra CdS e territorio, integrata con la Medicina Generale;
  - coordinamento funzionale del team affidato all'Infermiere case-manager
  - integrazione a rete provinciale del programma di screening e della diagnostica clinica;
  - **protocollo assistenziale per le donne a rischio eredo-familiare**

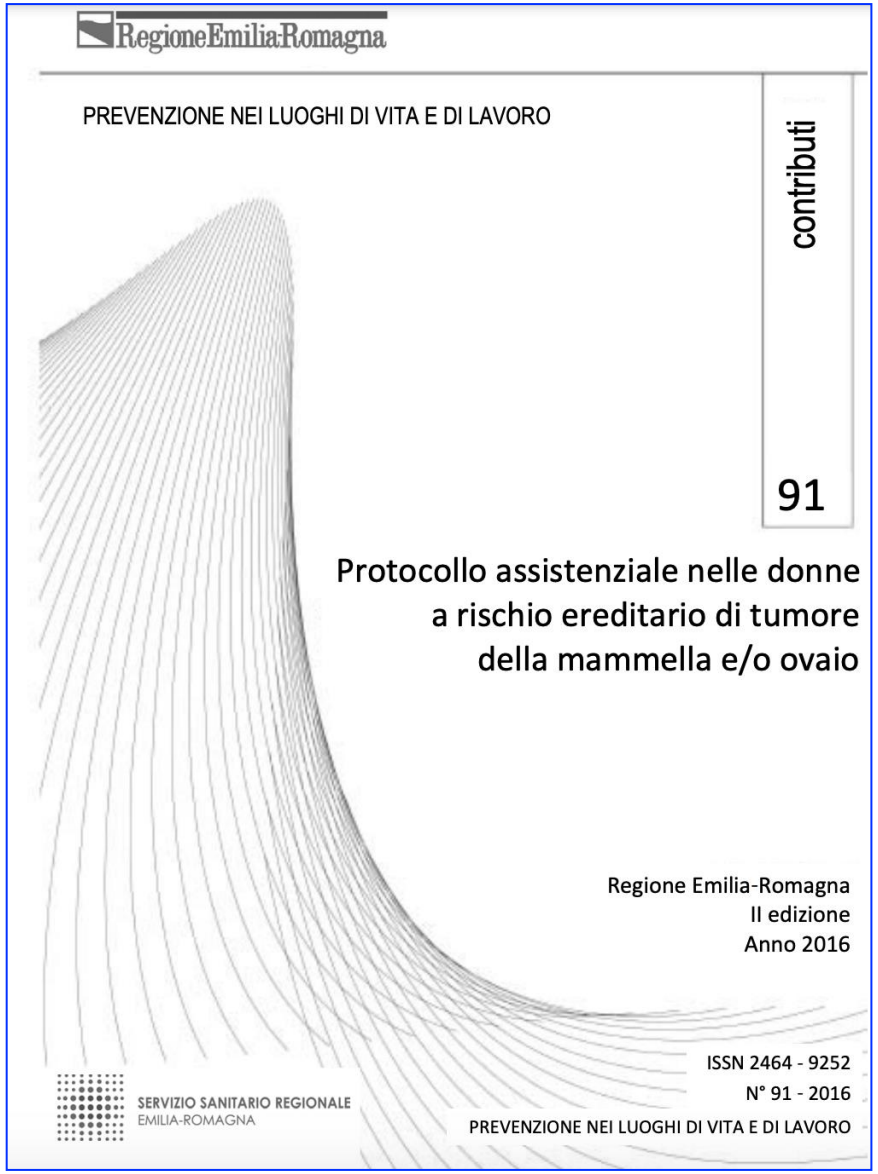


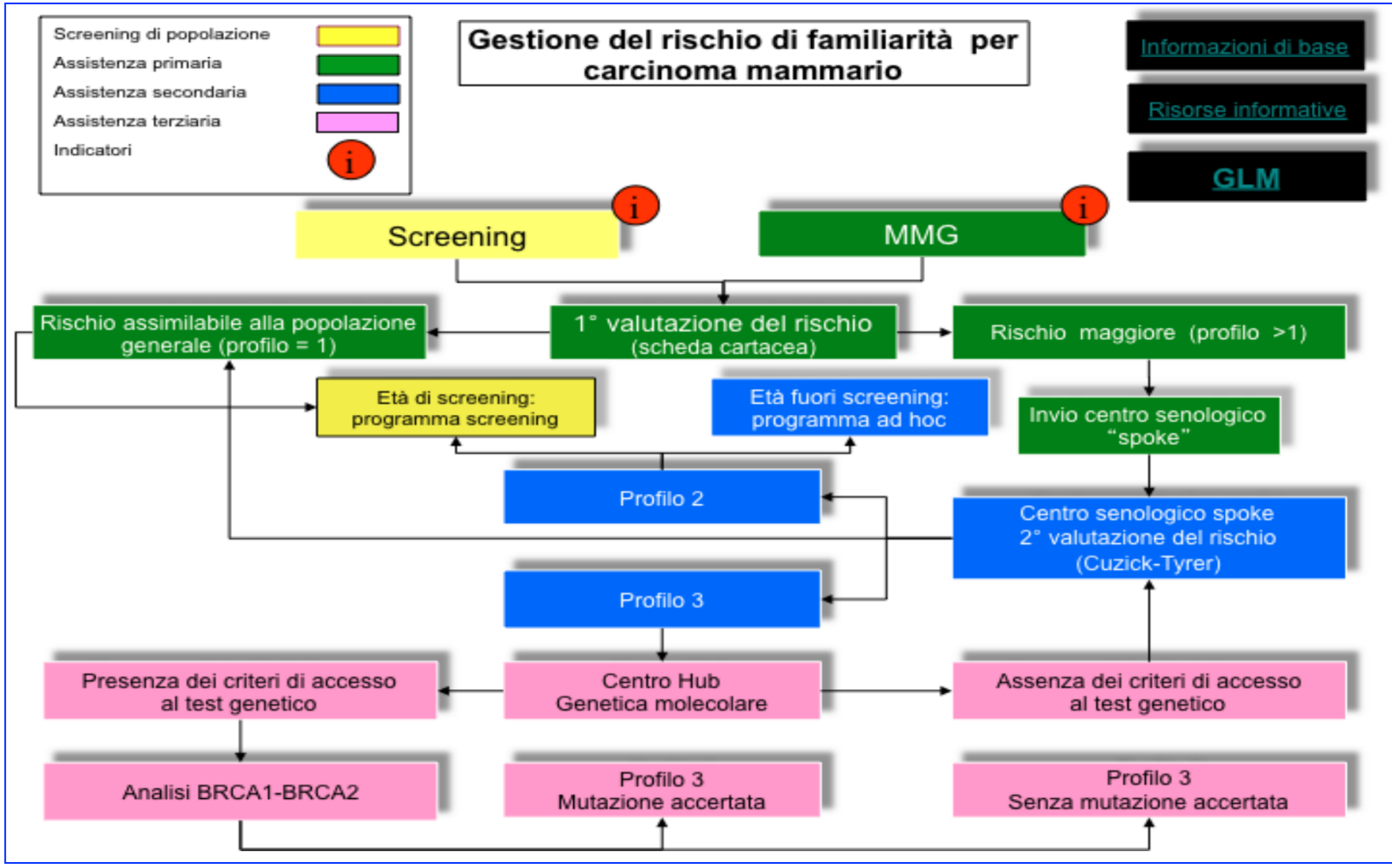
La mappa delle Oncologie nei CdS in Emilia Romagna



- **Sede dei 12 Hub oncologici (e dei CdS)**
- **Sedi Oncologiche Spoke collegate all'Hub** [2,2 media, range 0-5]
- **Sede dei 4 Hub percorso Eredo-Familiare** (DGR 220-2011)

Il modello regionale per la gestione delle donne a rischio eredo-familiare





Chi è realmente candidato ad eseguire il test genetico?

Aggiornamento Tabella 22 (precedentemente Tabella 26)

Storia personale di:
Variante patogenetica nota in un gene predisponente in un familiare
Uomo con carcinoma mammario
Donna con carcinoma mammario e carcinoma ovarico
Donna con carcinoma mammario ≤40 anni
Donna con carcinoma mammario triplo negativo
Donna con carcinoma mammario bilaterale < 50 anni
Donna con carcinoma mammario in stadio iniziale a recettori ormonali positivi e ≥ 4 linfonodi positivi
Donna con carcinoma mammario a recettori ormonali positivi con precedente CT neoadiuvante, residuo di malattia e CPS/EG score≥3
Donna con carcinoma mammario metastatico recettori ormonali positivi/HER2-negativo già sottoposta a chemioterapia con antracicline/taxani e trattamento endocrino (qualora possibili), in progressione dopo inibitori di CDK 4/6 per la malattia avanzata.
Storia personale di carcinoma mammario 46-50 anni e familiarità di primo grado* per:
Carcinoma mammario <50 anni
Carcinoma ovarico non mucinoso o borderline a qualsiasi età
Carcinoma mammario bilaterale
Carcinoma mammario maschile
Carcinoma del pancreas
Carcinoma della prostata
Storia personale di carcinoma mammario >50 anni e familiarità per carcinoma mammario, ovarico, pancreatico in 2 o più parenti in primo grado* tra loro (di cui uno in primo grado con lei)

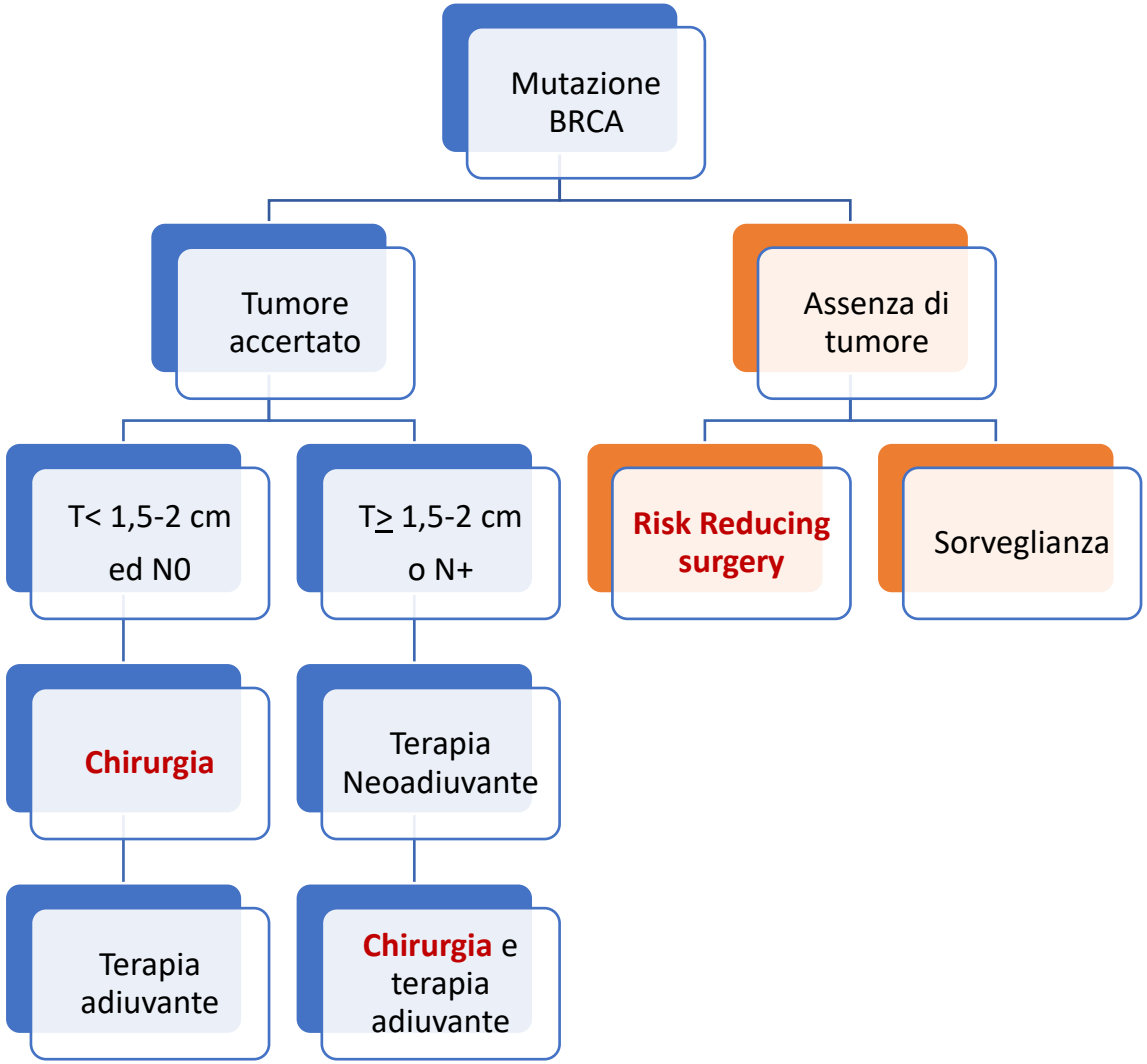
**Presenza di un familiare di primo grado (genitore, fratello/sorella, figlio/a) con le caratteristiche di malattia specificate. Per il lato paterno della famiglia, considerare anche familiari di secondo grado (nonna, zie).*

Il test BRCA a fini prognostici e predittivi di risposta alle terapie può essere prescritto dal genetista, dall'oncologo, dai chirurghi senologi con competenze oncologiche, che diventano responsabili anche di informare adeguatamente la paziente sugli aspetti genetici collegati ai risultati.

Linee Guida AIOM 2023

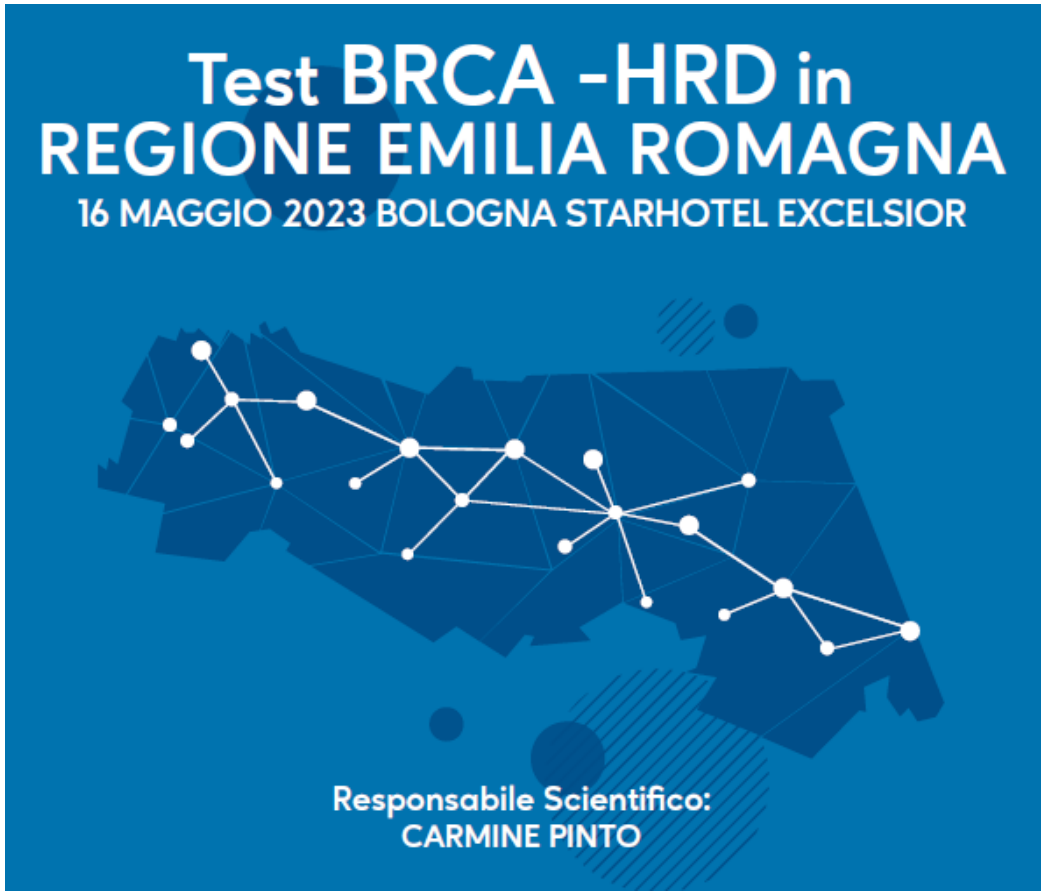
Percorsi di ricerca di mutazioni germinali di BRCA ai fini predittivi per la scelta della terapia

Gestione iniziale del percorso nella donna con mutazione BRCA



- **Punti di attenzione nella fase di malattia iniziale**
  - Tempi per la esecuzione del test genetico
  - Tempestività e tipo di intervento chirurgico
  - Terapia neoadiuvante vs adiuvante
  - Chirurgia dopo NAT
  - Tipo di terapia (neo)adiuvante (Sali di platino, PARPi, immunoterapia, abemaciclib)

La gestione chirurgica della paziente con mutazione BRCA



RISK REDUCING SURGERY IN HEREDITARY BREAST CANCER

GUGLIELMO FERRARI

BREAST UNIT

AUSL-IRCSS REGGIO EMILIA

	Penetrance			Measures		
Genes	ASCO	St. Gallen	NCCN	ASCO[a]	St. Gallen[b]	NCCN[a,c]
BRCA1	High	High	High	PM/TM+RRCM	TM+RRCM	TM+RRCM
BRCA2	High	High	High	PM/TM+RRCM	TM+RRCM	TM+RRCM
PTEN	High	–	High	–	–	Surveillance
PALB2	Moderate	High	High	Surveillance	TM+RRCM	Surveillance
BARD1	–	Moderate	Moderate	–	Surveillance	Surveillance
CHEK2	Moderate	Moderate	–	Surveillance	Surveillance	Surveillance
CDH1	High	Moderate	High	PM/TM+RRCM	Surveillance	Surveillance
STK11	High	Moderate	High	-	Surveillance	Surveillance
TP53	High	High	High	PM/TM+RRCM	Surveillance	TM+RRCM
ATM	Moderate	Low	Moderate	Surveillance	Surveillance	Surveillance

St. Gallen 2021 in GPV of **BRCA1, BRCA2, TP53, and PALB2** <40 years old at diagnosis 85% recommended a ‘‘ therapeutic mastectomy.’’ In women >60 years with high penetrance alterations, the panel was divided with 46% suggesting mastectomy and 54% suggesting breast surveillance, including MRI with or without antiestrogen prevention. They did not distinguish between asymptomatic women and women with BC (focused on early breast cancer).

St. Gallen 2021 in GPV of **BARD1, CHEK2,CDH1, and STK11** mastectomy is not considered the treatment of choice.

HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

BREAST CANCER PATIENTS WHO ARE IDENTIFIED AS HAVING A BRCA1/2 MUTATION AFTER THE DIAGNOSIS OF BC

PATIENTS WHO ARE IDENTIFIED AS HAVING A BRCA1/2 MUTATION AFTER SURGERY FOR BC

HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

Lifetime risk of developing breast cancer estimated to range from 45 to 88% up to the age of 70 years

BILATERAL RISK-REDUCING MASTECTOMY (BRRM) IS STRONGLY RECOMMENDED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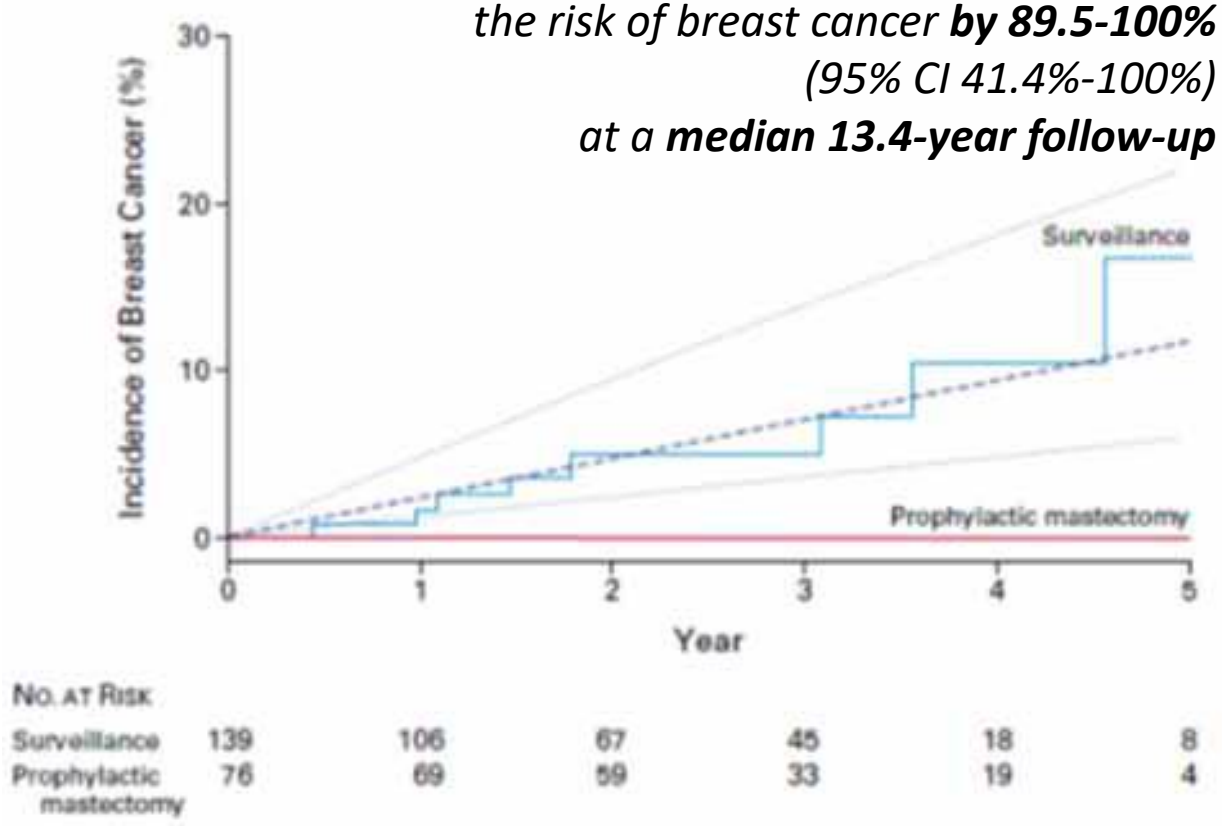
VOLUME 345 JULY 19, 2001 NUMBER 3

BREAST CANCER AFTER PROPHYLACTIC BILATERAL MASTECTOMY IN WOMEN WITH A *BRCA1* OR *BRCA2* MUTATION

HANNE MEIJERS-HEIJBOER, M.D., BERT VAN GEEL, M.D., PH.D., WIM L.J. VAN PUTTEN, M.SC.,

Bilateral mastectomy can reduce the risk of breast cancer ***by 89.5-100%*** *(95% CI 41.4%-100%) at a* ***median 13.4-year follow-up***



HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

BRRM: DIFFERENT SURGICAL TECHNIQUES

TOTAL MASTECTOMY (TM)

-**Historically TM** has been considered the preferred standard surgical procedure for prophylaxis, because the sparing of the skin and the nipple areola complex could leave a substantial amount of breast tissue.
-TM removes 95-99% of breast tissue

CONSERVATIVE MASTECTOMY (CM)

Skin- sparing mastectomy (SSM)

Nipple- sparing mastectomy (NSM)

Skin- reducing mastectomy

Bipedicled Nipple- sparing mastectomy

HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

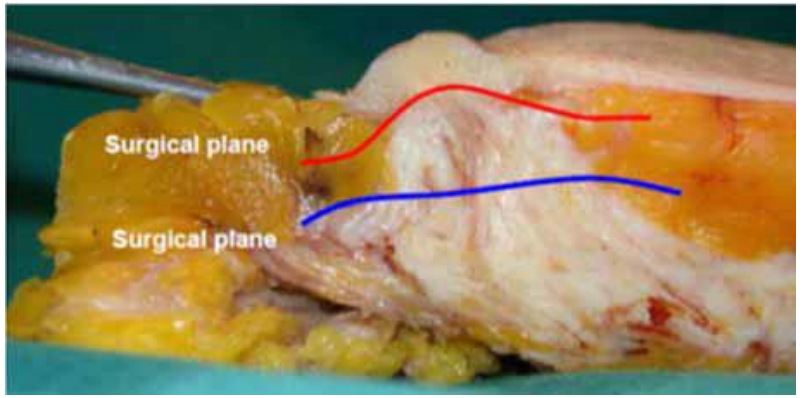
NIPPLE- SPARING MASTECTOMY (NSM)

Advantage of NSM: It allows to preserve the nipple-areola complex with better cosmetic result and less psychological impact.

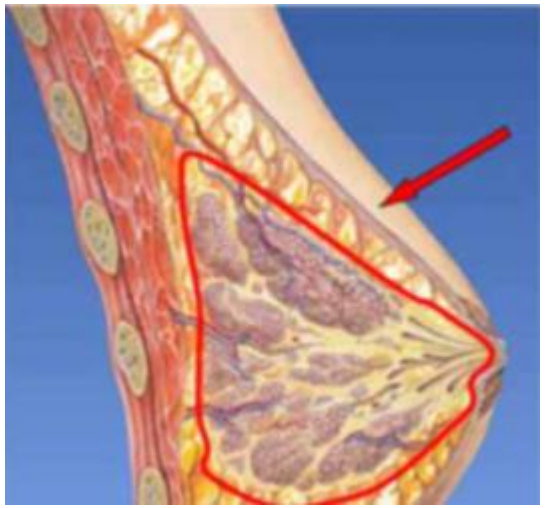
Indications: patients with small - medium breasts; minimal or moderate ptosis (NAC above or at the same level of the IMF); distance between mammary fold and areola > 5 cm

HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

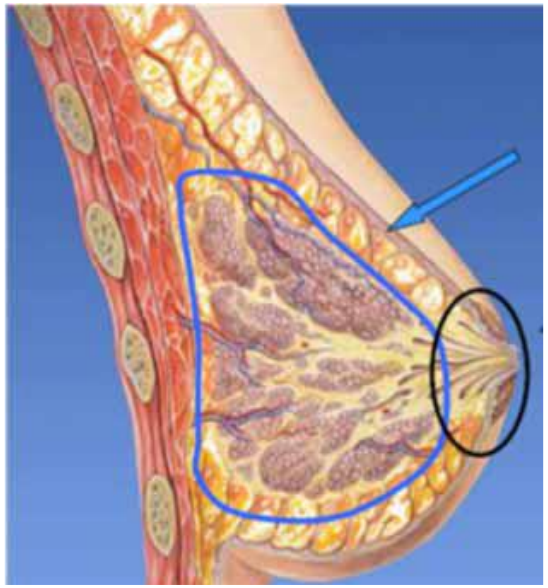
NIPPLE- SPARING MASTECTOMY (NSM)



Nipple – sparing mastectomy with complete removal of the mammary gland

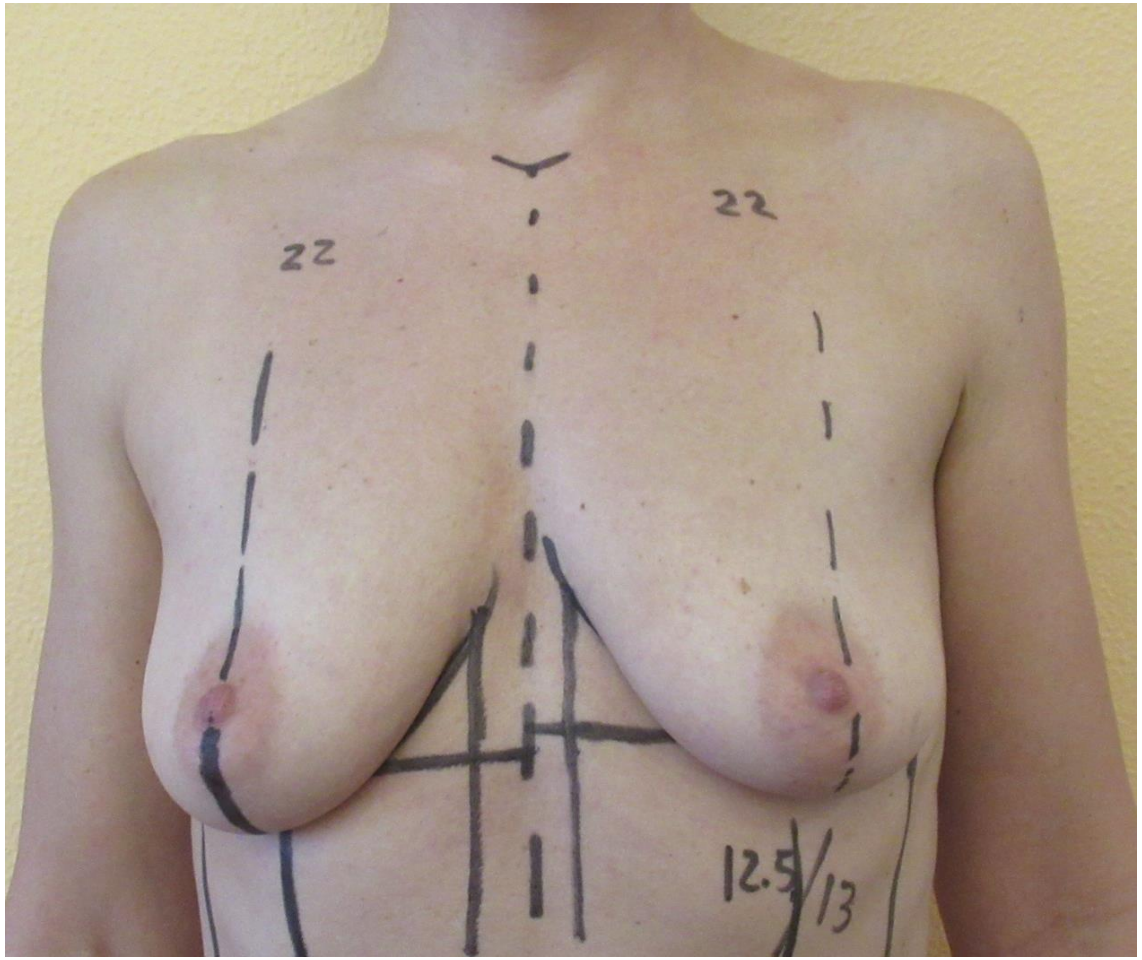


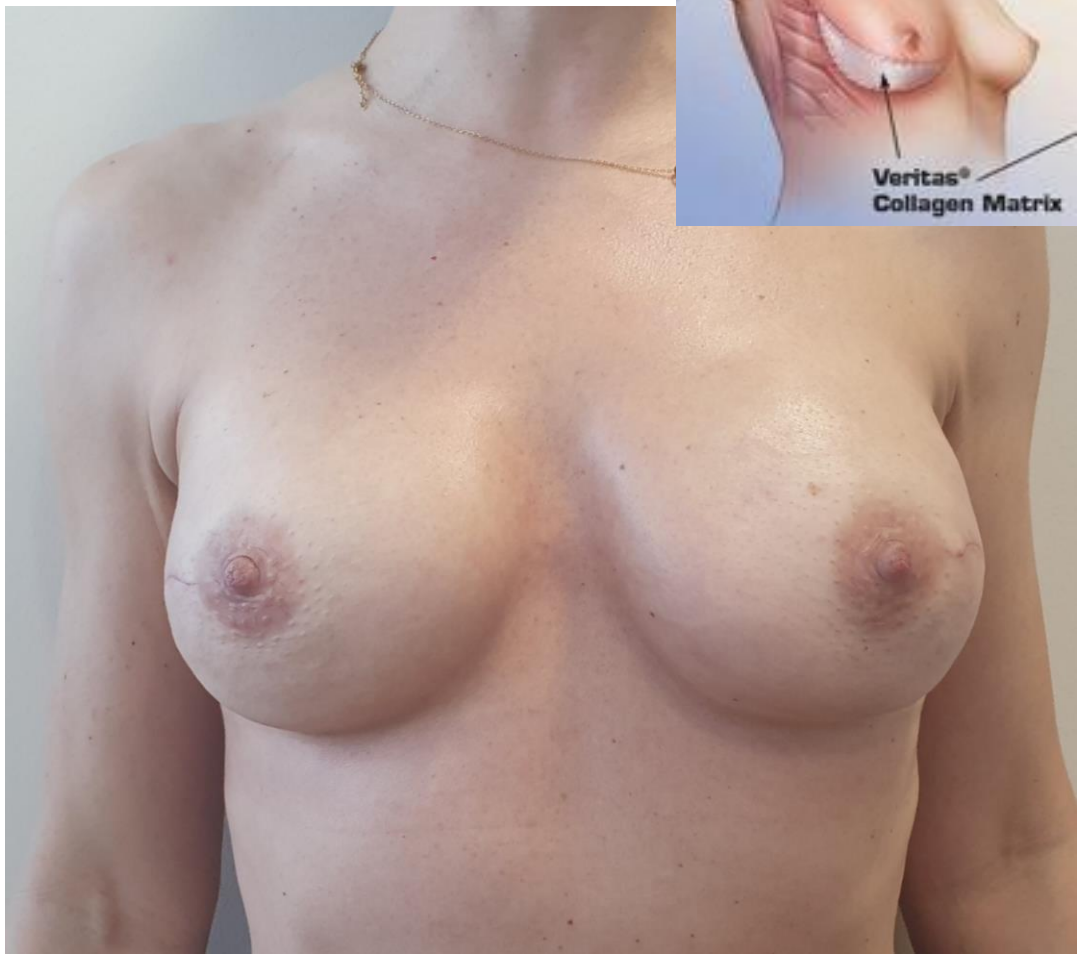
Nipple – sparing mastectomy with preservation of subareola glandular layer of 0.5-1cm

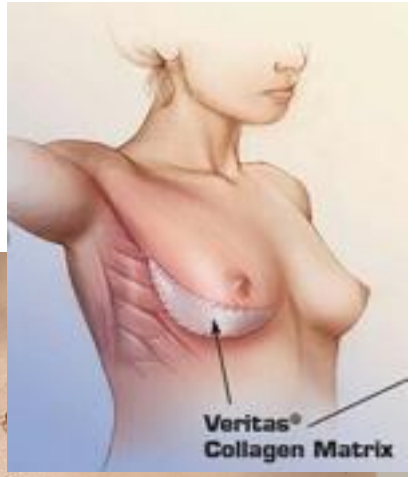


HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

NIPPLE- SPARING MASTECTOMY (NSM)







HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

NIPPLE- SPARING MASTECTOMY (NSM)

genes
MDPI

Review

Nipple Sparing Mastectomy as a Risk-Reducing Procedure for *BRCA*-Mutated Patients

Nicola Rocco [1,*], Giacomo Montagna [2,3], Carmen Criscitiello [4,5], Maurizio Bruno Nava [6], Francesca Privitera [7], Wafa Taher [8], Antonio Gloria [9] and Giuseppe Catanuto [7,10]

NSM as a risk-reducing procedure for BRCA-mutation carriers appears to be an oncologically safe procedure, comparable to the standard modified radical mastectomy with better patient-reported outcomes.

HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

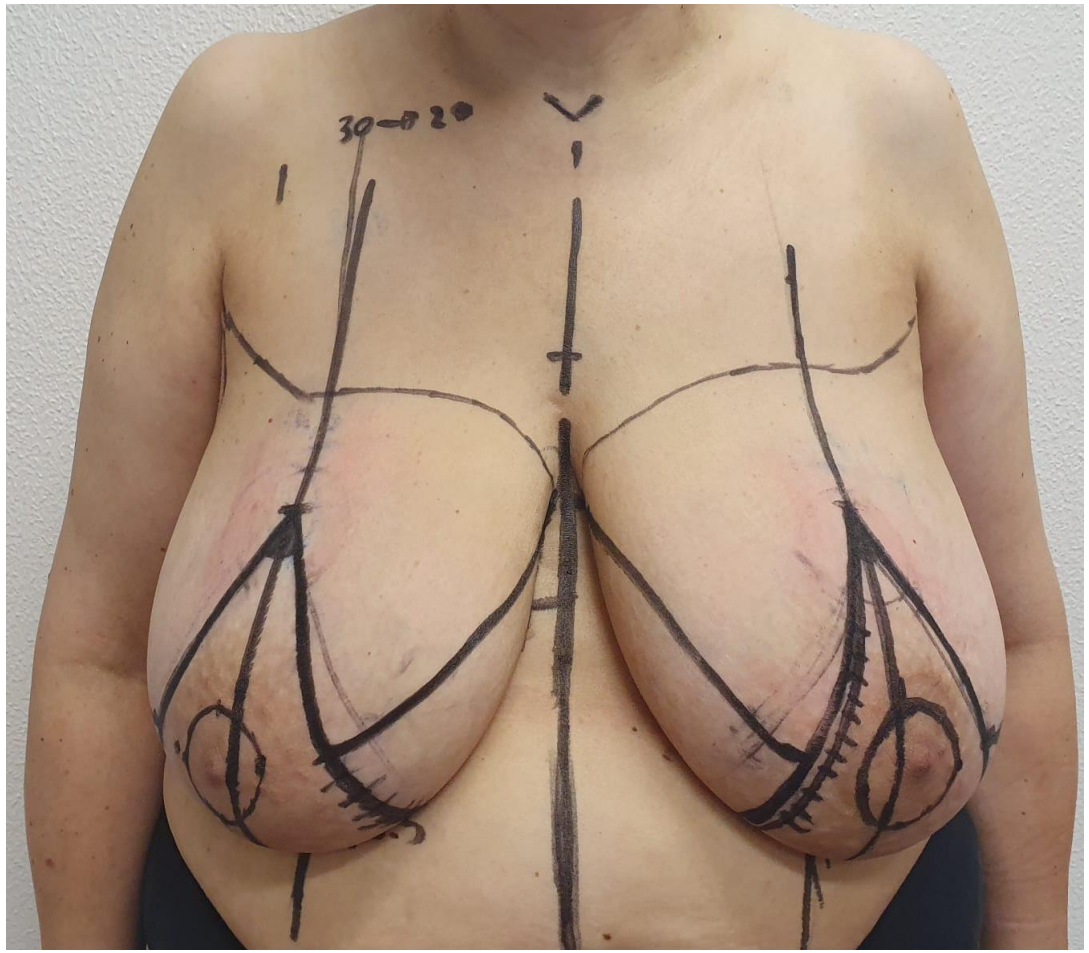
SKIN-REDUCING MASTECTOMY (SRM)

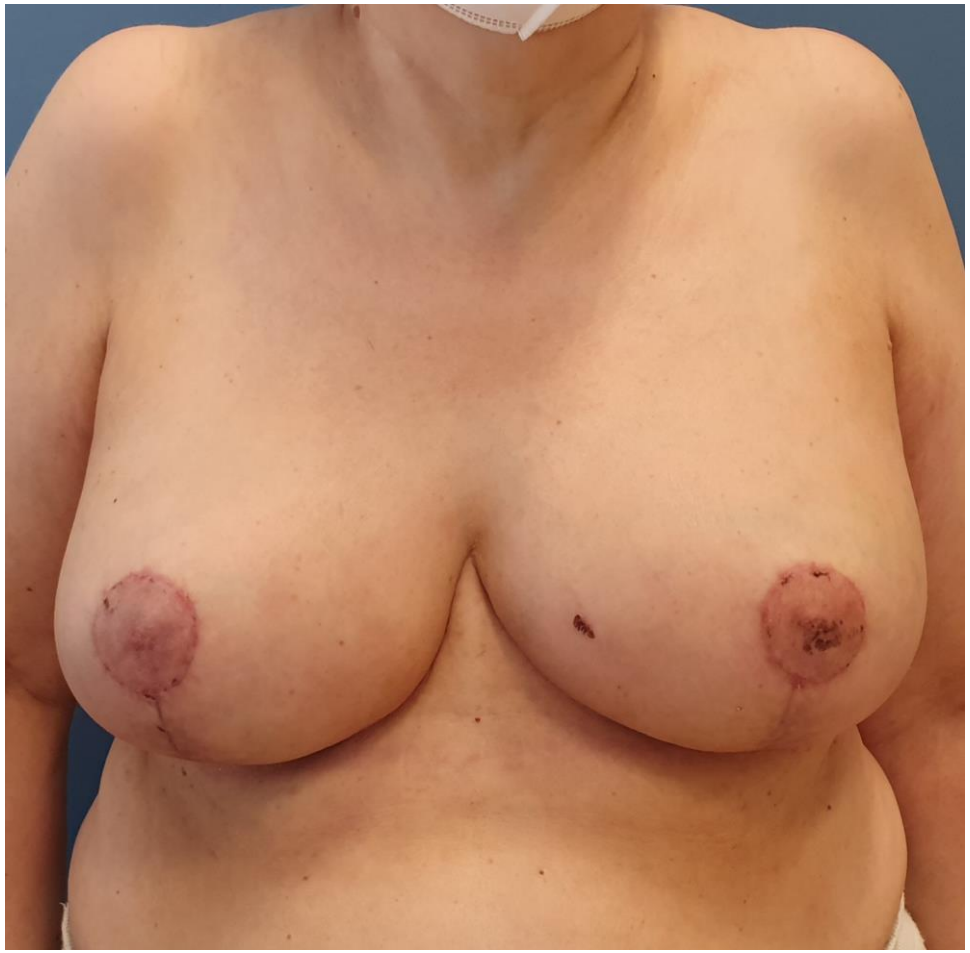
Advantage of SRM: Immediate reconstruction is possible, also in case of very large breast.

Indications: very large breast and important ptosis.

HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

SKIN-REDUCING MASTECTOMY (SRM)





HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

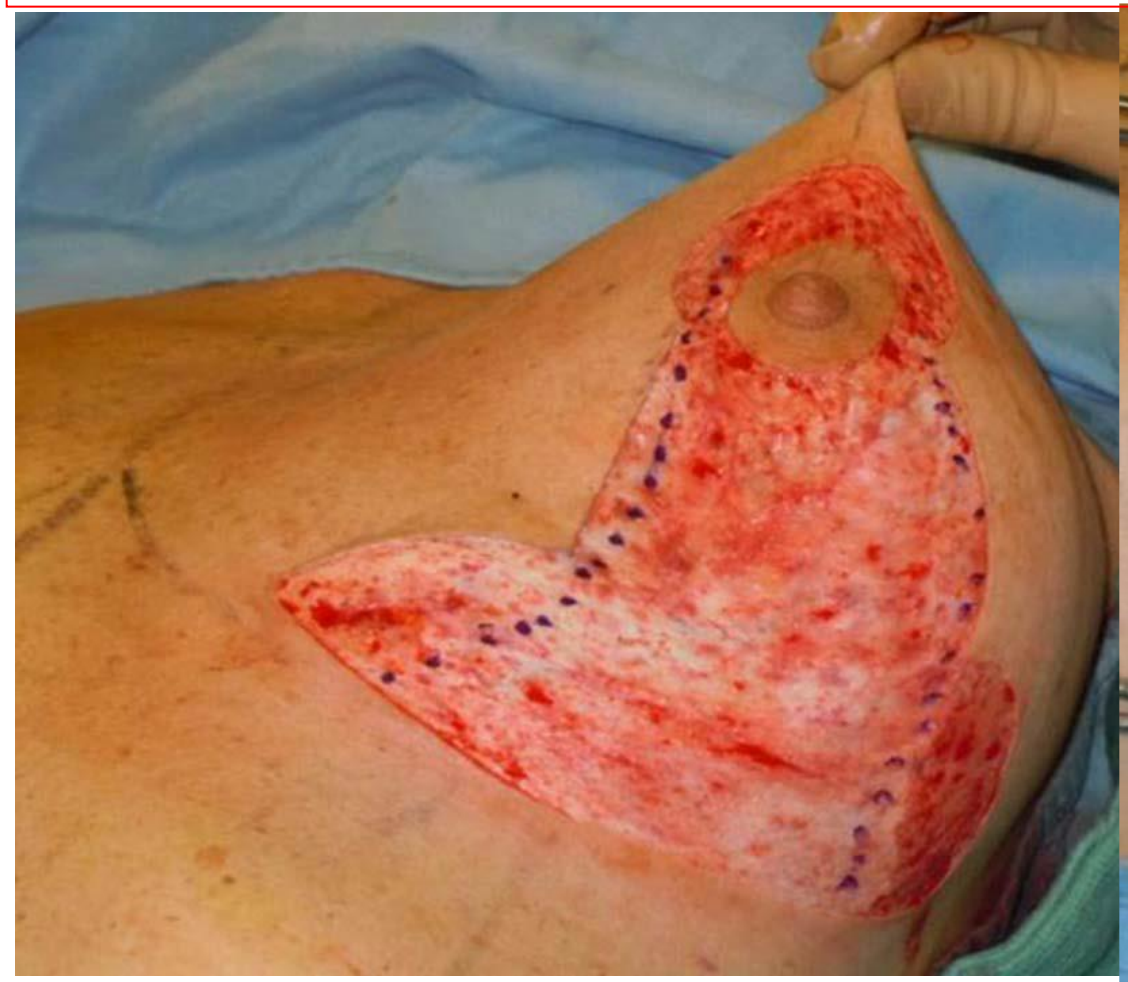
BIPEDICLED NIPPLE-SPARING MASTECTOMY

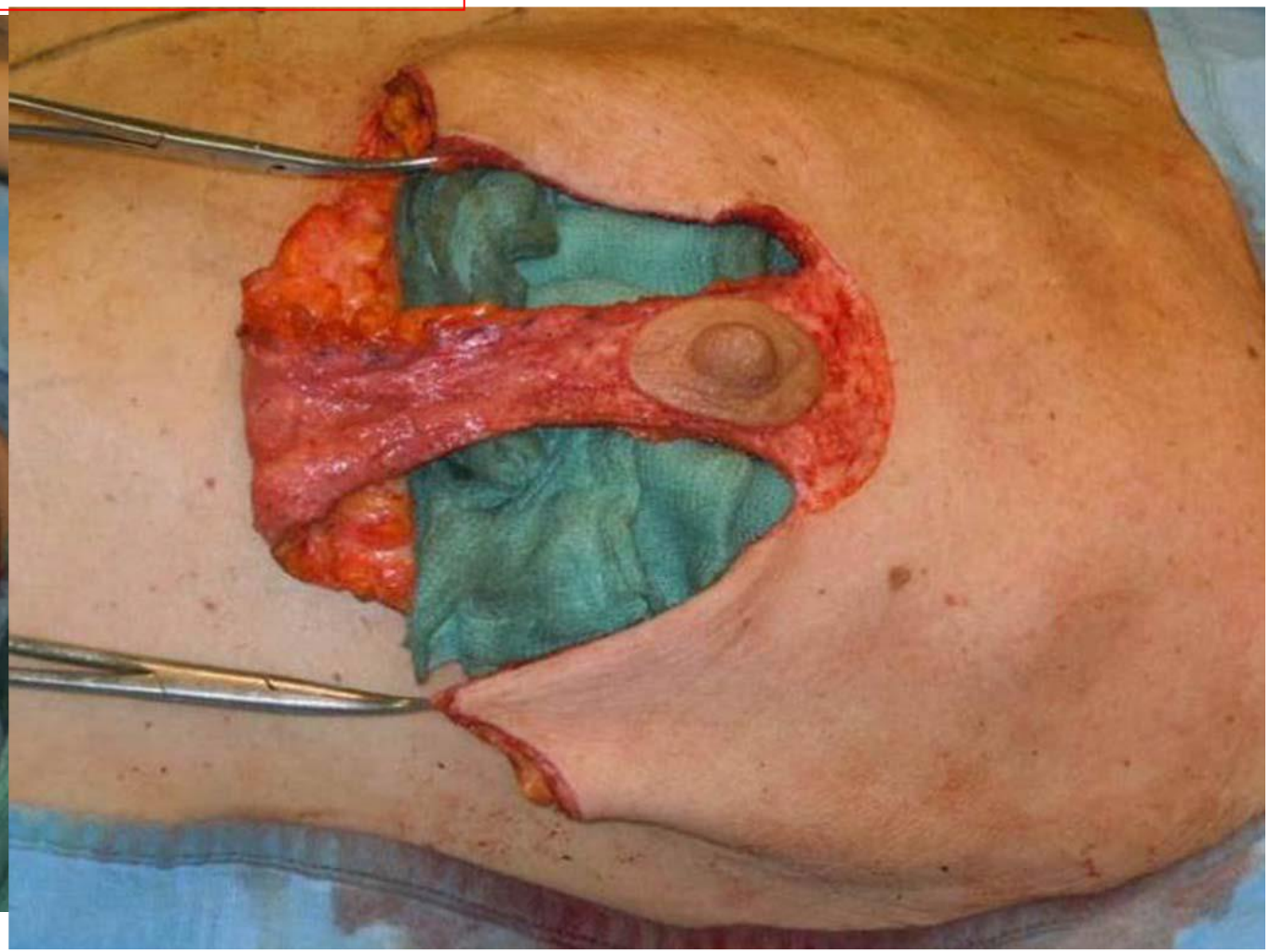
.

Indications: medium breast with moderate – large ptosis (NAC set below the IMF) and a distance between mammary fold and areola > 9 cm. Sternal notch-to-NAC distance of > than 22 cm and < OF 29 cm

HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

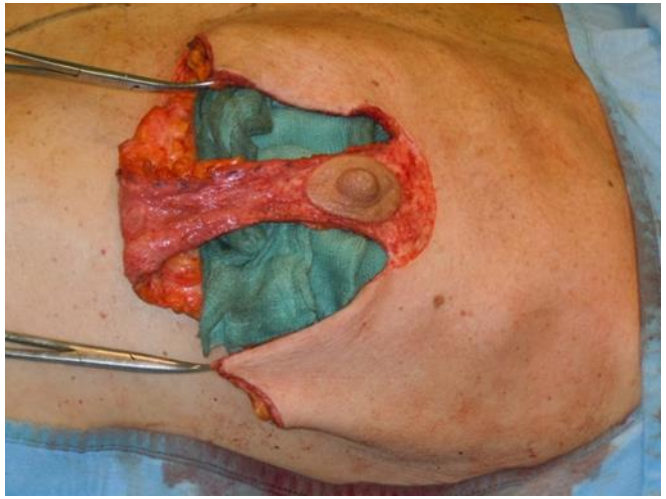
BIPEDICLED NIPPLE-SPARING MASTECTOMY

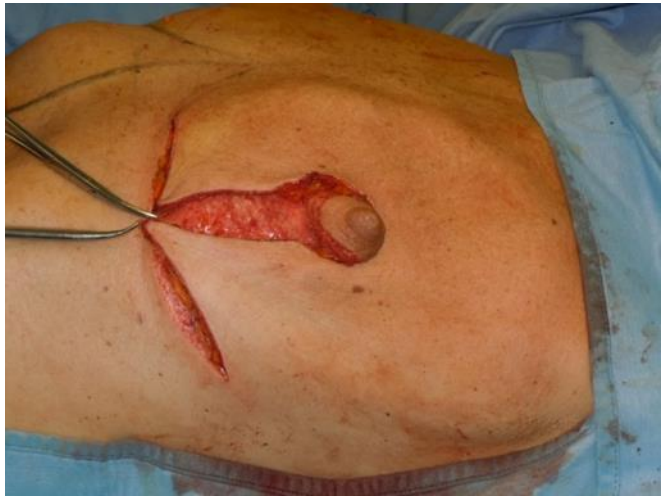


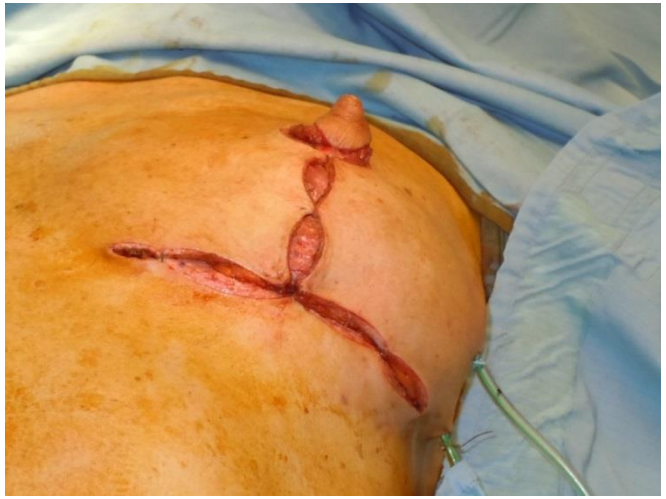


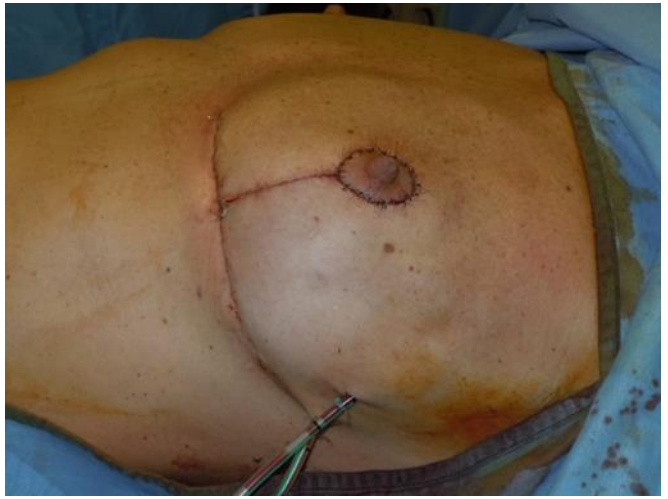
HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

BIPEDICLED NIPPLE-SPARING MASTECTOMY



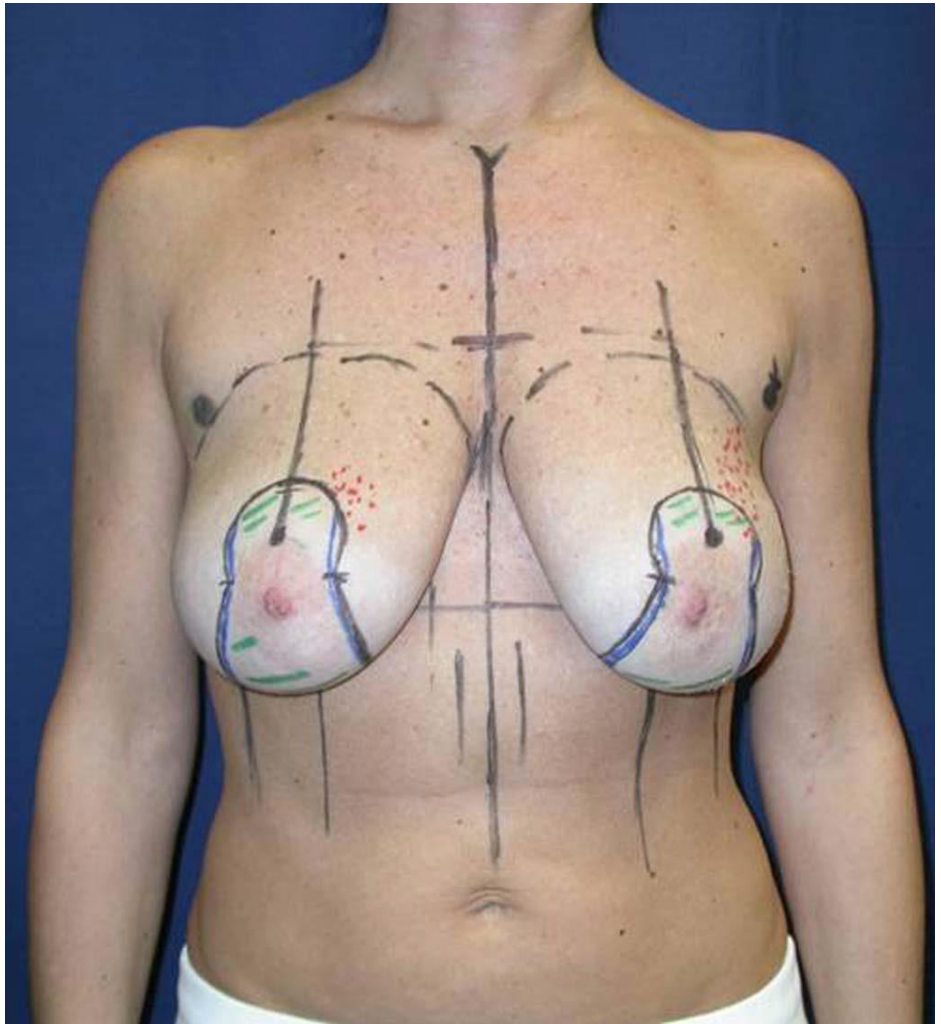


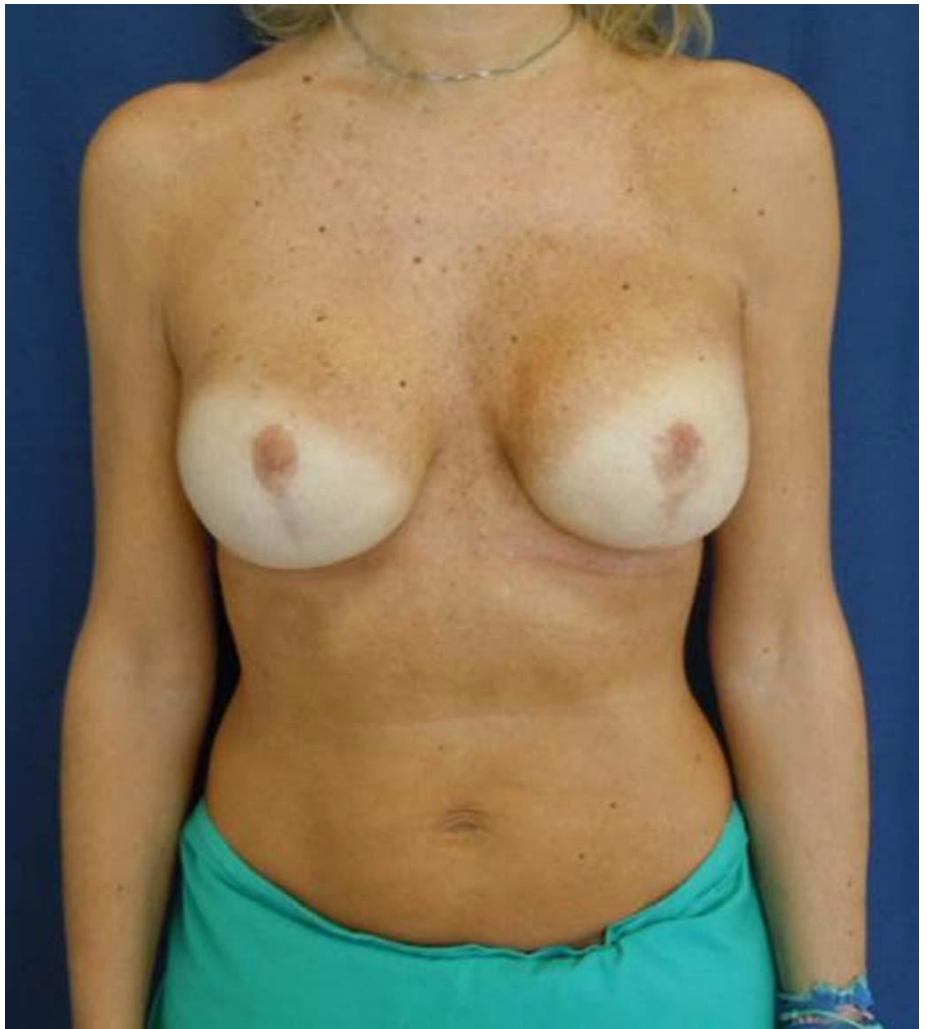




HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

BIPEDICLED NIPPLE-SPARING MASTECTOMY





HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

BIPEDICLED NIPPLE-SPARING MASTECTOMY

BREAST SURGERY

Bipedicled Nipple-Sparing Mastectomy Versus Traditional Nipple-Sparing Mastectomy

Comparison of 2 Alternative Techniques in Order to Save Nipple-Areola Complex

Giuseppe Falco, MD,[a] Annalisa Curcio, PhD, MD,[b] Francesco Marongiu, MD,[b] Federico Buggi, PhD, MD,[b] Matteo Mingozzi, MD,[b] Simone Mele, MD,[a] Guglielmo Ferrari, MD,[a] and Secondo Folli, MD[c]

Annals of Plastic Surgery • Volume 84, Number 4, April 2020

HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

Breast Cancer Research and Treatment (2019) 177:723–733
https://doi.org/10.1007/s10549-019-05345-2

EPIDEMIOLOGY

Check for updates

Survival after bilateral risk-reducing mastectomy in healthy *BRCA1* and *BRCA2* mutation carriers

Bernadette A. M. Heemskerk-Gerritsen[1] · Agnes Jager[1] · Linetta B. Koppert[2] · A. Inge-Marie Obdeijn[3] · Margriet Collée[4] · Hanne E. J. Meijers-Heijboer[5] · Denise J. Jenner[6] · Hester S. A. Oldenburg[7] · Klaartje van Engelen[8] · Jakob de Vries[9] · Christi J. van Asperen[10] · Peter Devilee[11] · Marinus J. Blok[12] · C. Marleen Kets[13] · Margreet G. E. M. Ausems[14] · Caroline Seynaeve[1] · Matti A. Rookus[6] · Maartje J. Hooning[1]

Received: 27 May 2019 / Accepted: 2 July 2019 / Published online: 13 July 2019

IS THERE A CLEAR SURVIVAL BENEFIT OF BRRM OVER BC SURVEILLANCE ?

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliera di Reggio Emilia
Arcispedale S. Maria Nuova

Istituto in tecnologie avanzate e modelli assistenziali in oncologia
Istituto di Ricovero e Cura a Carattere Scientifico

Test BRCA -HRD in REGIONE EMILIA ROMAGNA
16 MAGGIO 2023 BOLOGNA STARHOTEL EXCELSIOR
Responsabile Scientifico: CARMINE PINTO

OECI
Organisation of European Cancer Institutes

HEALTY WOMEN CARRIERS (

Breast Cancer Research and Treatment (2019) 177:723–733
https://doi.org/10.1007/s10549-019-05345-2

EPIDEMIOLOGY

Survival after bilateral risk-reducing mastectomy in healthy and *BRCA2* mutation carriers

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arriers

722/1712 *BRCA1* o

5.4%)

8 (1%) vs. 2

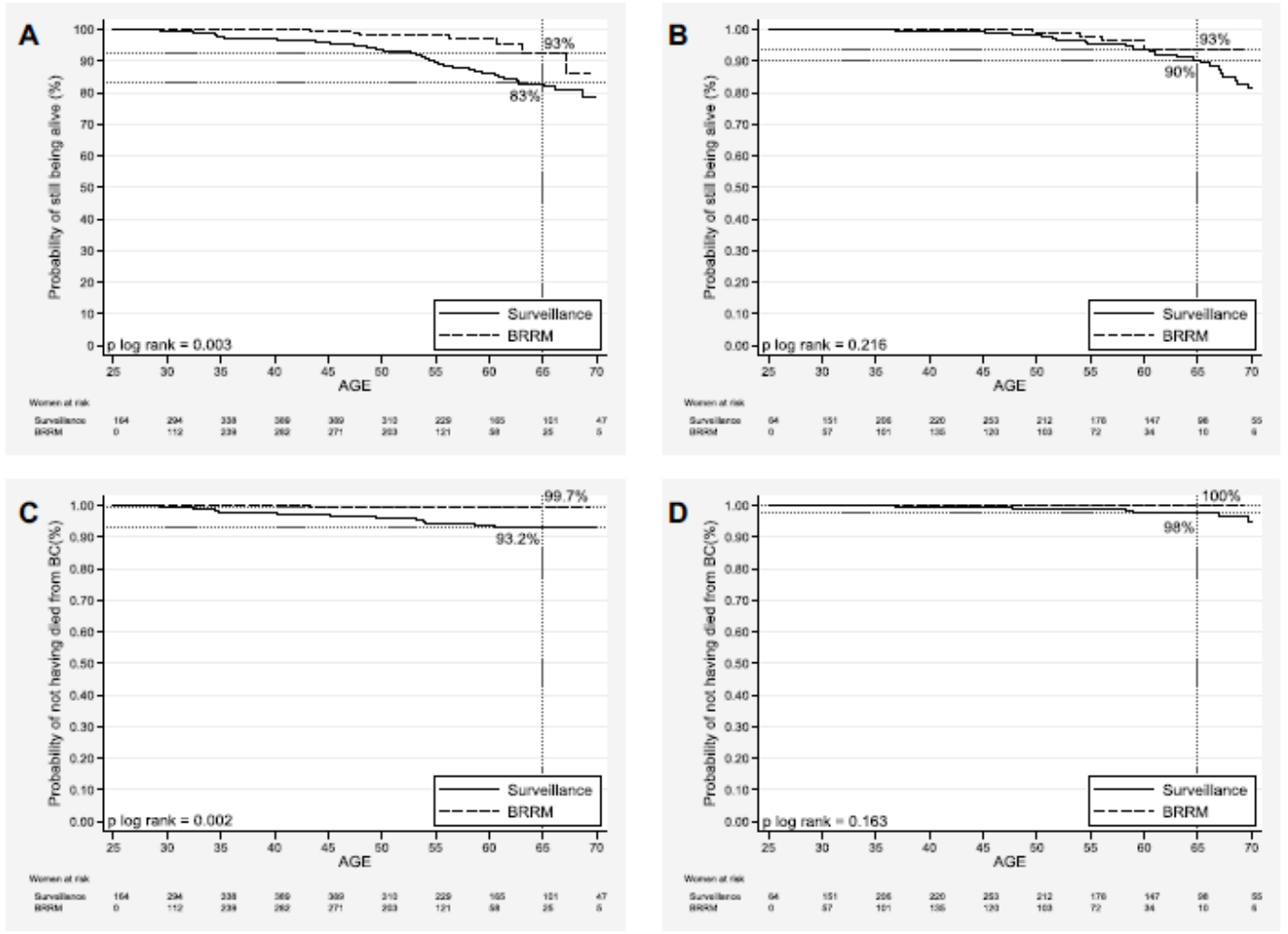

Fig. 2 Overall survival curves for *BRCA1* (**a**) and *BRCA2* (**b**) mutation carriers and breast cancer-specific survival curves for *BRCA1* (**c**) and *BRCA2* (**d**) mutation carriers opting for bilateral risk-reducing mastectomy (BRRM) versus staying under surveillance, using the Simon and Makuch method—which takes into account the change in an individual's variable status over time—with chronological age as the time variable

HEALTY WOMEN CARRIERS OF BRCA1/2 MUTATION (and PALB2 MUTATION)

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EPIDEMIOLOGY

Survival after bilateral risk-reducing mastectomy in healthy *BRCA1* and *BRCA2* mutation carriers

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Received: 27 May 2019 / Accepted: 2 July 2019 / Published online: 13 July 2019

THE CURRENT RESULTS SUGGEST THAT REGARDING BREAST CANCER-SPECIFIC MORTALITY, BC SURVEILLANCE MAY BE A REASONABLE AND BALANCED ALTERNATIVE TO BRRM FOR BRCA2 MUTATED PATIENTS

MORE INDIVIDUALIZED COUNSELING BASED ON BRCA MUTATION TYPE REGARDING THE DIFFICULT CHOICE BETWEEN BRRM AND BC SURVEILLANCE

BREAST CANCER PATIENTS WHO ARE IDENTIFIED AS HAVING A BRCA1/2 MUTATION AFTER THE DIAGNOSIS OF BC

NCCN National Comprehensive Cancer Network®

THE NCCN GUIDELINES® DISRECOMMEND BREAST- CONSERVING SURGERY (BCS) WITH RT FOR WOMEN WITH A KNOWN GENETIC PREDISPOSITION TO BREAST CANCER BECAUSE IT MAY INCREASE THE RISK OF IPSILATERAL BREAST TUMOR RECURRENCE (IBTR)

WOMEN CARRYING A GERMLINE VARIANT IN *BRCA1/2* GENES NOT ONLY HAVE A HIGH RISK OF BREAST CANCER BUT ARE ALSO AT INCREASED RISK OF DEVELOPING A SECOND PRIMARY BREAST CANCER, PARTICULARLY IN THE CONTRALATERAL BREAST.

BREAST CANCER PATIENTS WHO ARE IDENTIFIED AS HAVING A BRCA1/2 MUTATION AFTER THE DIAGNOSIS OF BC

Breast Cancer Res Treat (2014) 144:443–455
DOI 10.1007/s10549-014-2890-1

REVIEW

Surgical management of breast c carriers: a systematic review and

Antonis Valachis · Andreas D. Nearchou · Pehr Lind

Breast Cancer Research and Treatment (2019) 175:749–754
https://doi.org/10.1007/s10549-019-05199-8

EPIDEMIOLOGY

Check for updates

Risk of ipsilateral breast tumor recurrence in primary invasive breast cancer following breast-conserving surgery with *BRCA1* and *BRCA2* mutation in China

Wei Cao[1] · Yuntao Xie[1] · Yingjian He[1] · Jinfeng Li[1] · T

Ann Surg Oncol (2022) 29:4706–4713
https://doi.org/10.1245/s10434-022-11756-1

Annals of SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

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ORIGINAL ARTICLE – BREAST ONCOLOGY

Comparison of Outcomes Between BRCA Pathogenic Variant Carriers Undergoing Breast-Conserving Surgery Versus Mastectomy

Sarah Shubeck, MD, MS[1], Varadan Sevilimedu, MBBS, DrPH[2], Elizabeth Berger, MD, MS[3,4], Mark Robson, MD[5], Alexandra S. Heerdt, MD, MPH[1], and Melissa L. Pilewskie, MD[1]

Follow-up < 7,5 years

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliera di Reggio Emilia
Arcispedale S. Maria Nuova

Istituto in tecnologie avanzate e modelli assistenziali in oncologia
Istituto di Ricovero e Cura a Carattere Scientifico

Test BRCA -HRD in REGIONE EMILIA ROMAGNA
16 MAGGIO 2023 BOLOGNA STARHOTEL EXCELSIOR
Responsabile Scientifico: CARMINE PINTO

OECI
Organisation of European Cancer Institutes

BREAST CANCER PATIENTS WHO ARE IDENTIFIED AS HAVING A BRCA1/2 MUTATION AFTER THE DIAGNOSIS OF BC

Breast Cancer (2022) 29:394–401
https://doi.org/10.1007/s12282-022-01343-3

REVIEW ARTICLE

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Does breast-conserving surgery with radiotherapy in BRCA-mutation carriers significantly increase ipsilateral breast tumor recurrence? A systematic review and meta-analysis

Miyako Nara[1] · Sakiko Ishihara[1,2] · Atsuko Kitano[3] · Nobuko Tamura[4] · Tomoyuki Aruga[1] · Daiki Kobayashi[5] · Seigo Nakamura[6] · Hideko Yamauchi[7]

SIGNIFICANT DIFFERENCE IN THE INCIDENCE OF IPSILATERAL BREAST TUMOR RECURRENCE (IBTR) BETWEEN BRCA-MUTATION CARRIERS WHO UNDERWENT BCS AND CONTROLS WITH SPORADIC BREAST CANCER??

BREAST CANCER PATIENTS WHO ARE IDENTIFIED AS HAVING A BRCA1/2 MUTATION AFTER THE DIAGNOSIS OF BC

No difference in IBTR risk was found between BRCA-mutation carriers and controls with sporadic cancer in studies with a median follow-up time < 7 years (five studies, 2923 patients)

Higher IBTR risk was reported in BRCA-mutation carriers in studies with a median follow-up ≧ 7 years (eight studies, 2566 patients)

The IBTR risk was higher in patients with a follow-up time of ten years or longer

The data on the IBTR risk after post-operative radiation, postoperative adjuvant therapy or risk-reducing salpingo-oophorectomy for ovarian cancer prevention are still insufficient.

BREAST CANCER PATIENTS WHO ARE IDENTIFIED AS HAVING A BRCA1/2 MUTATION AFTER THE DIAGNOSIS OF BC

DOI: 10.1002/cam4.2836

ORIGINAL RESEARCH

Cancer Medicine Open Access WILEY

Outcomes and risk of subsequent breast events in breast-conserving surgery patients with BRCA1 and BRCA2 mutation

Fugui Ye[1] | Liang Huang[1] | Guantian Lang[1,2] | Xin Hu[1] | Genhong Di[1] | Zhimin Shao[1,3] | Ayong Cao[1]

Ye and colleagues reported that women with BRCA1 and/or BRCA2 genetic mutations were significantly more likely to experience a contralateral breast cancer following BCS, with 9.5% of carriers and only 0.7% of non-carriers having a CBC diagnosed in their median follow-up of 61 and 70 months, respectively (p\0.001).

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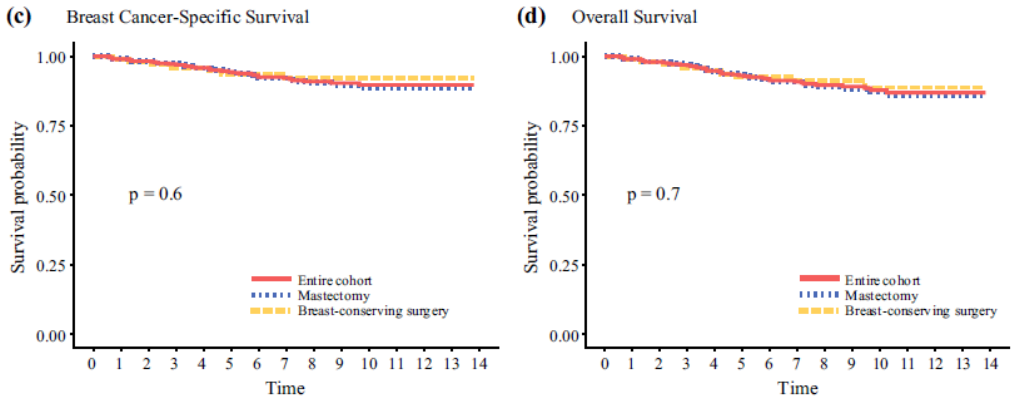
[1]Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY; [2]Biostatistics Service, Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY; [3]Department of Surgery, Yale University School of Medicine, New Haven, CT; [4]Yale Comprehensive Cancer Center, Ne
[5]Breast Medicine Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York,



BREAST CANCER PTIENTS WHO ARE IDENTIFIED AS HAVING A BRCA1/2 MUTATION AFTER THE DIAGNOSIS OF BC

BILATERAL RISK-REDUCING MASTECTOMY (BRRM) IS STILL RECOMMENDED

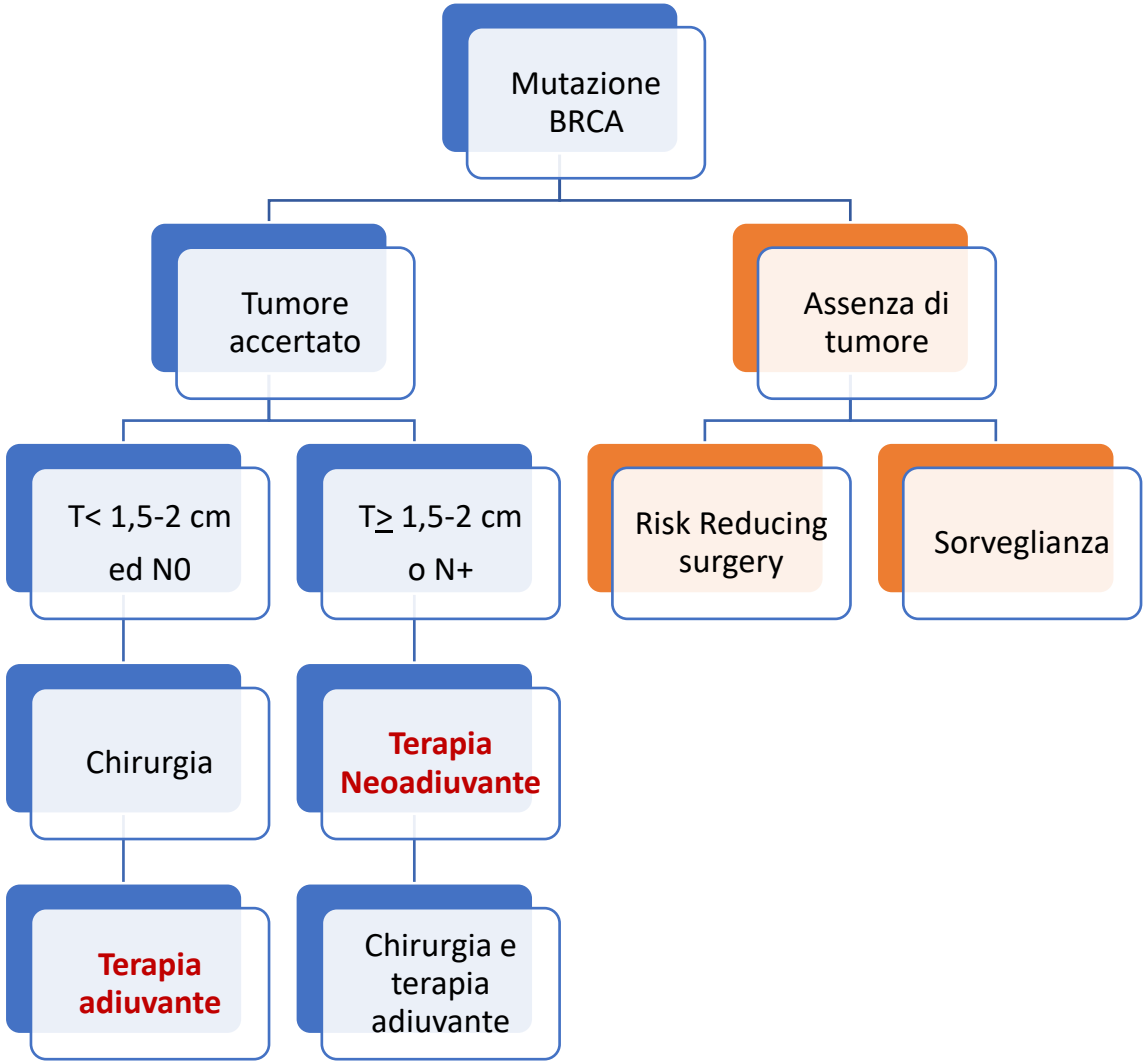
BCS SHOULD BE OFFERED AS AN OPTION IF INDICATED

PATIENTS WHO ARE IDENTIFIED AS HAVING A BRCA1/2 MUTATION AFTER SURGERY FOR BC

NIBC/NCBC → **BRRM**

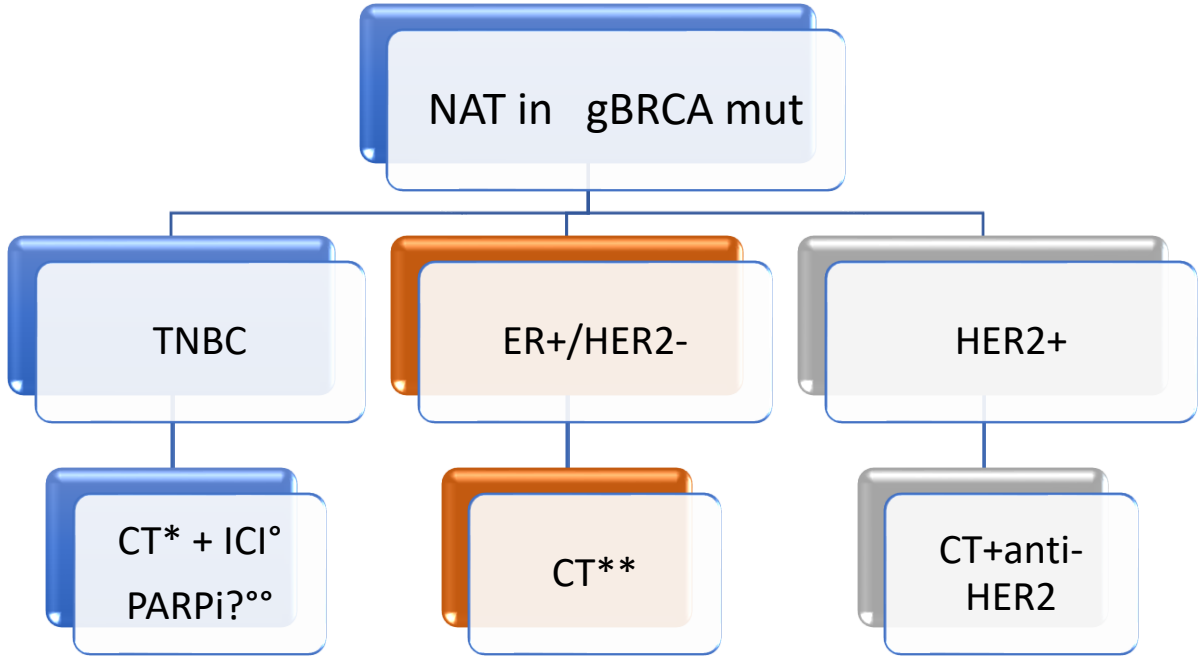
HEALTHY → **FOLLOW-UP**

Gestione iniziale del percorso nella donna con mutazione BRCA



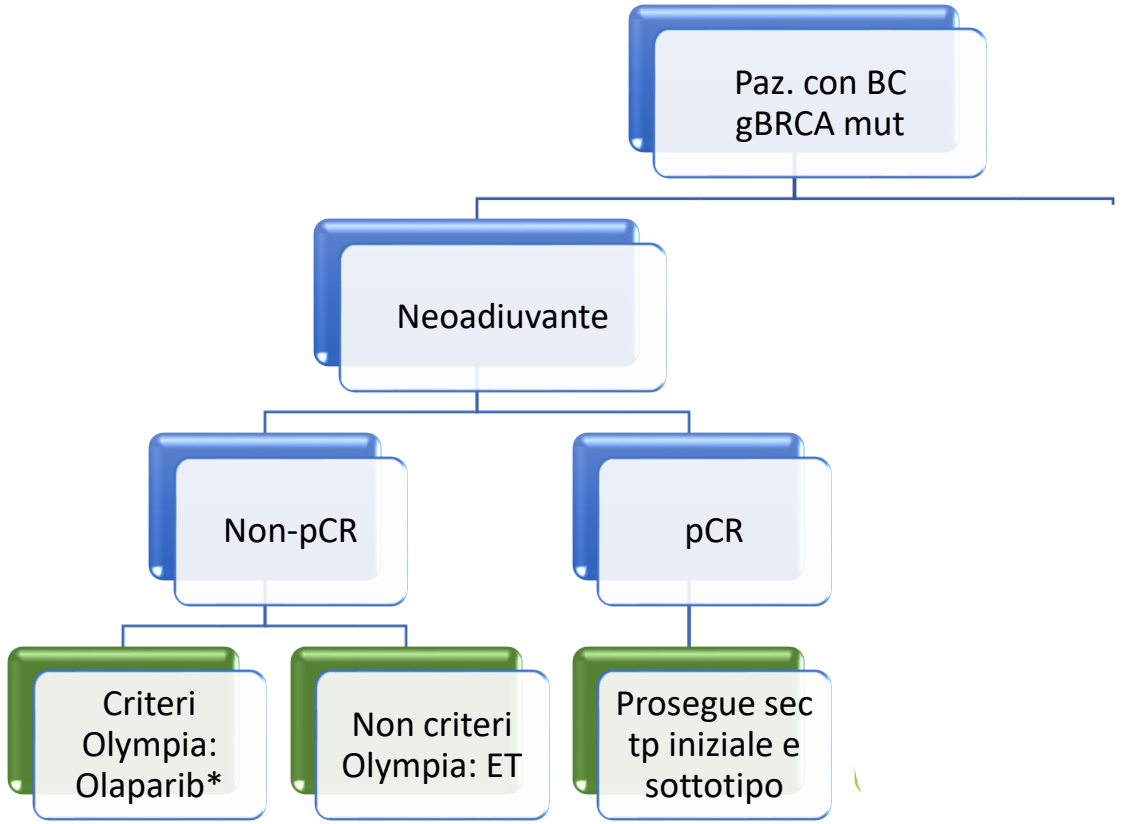
- **Punti di attenzione nella fase di malattia iniziale**
  - Tempi per la esecuzione del test genetico
  - Tempestività e tipo di intervento chirurgico
  - Terapia neoadiuvante vs adiuvante
  - Chirurgia dopo NAT
  - Tipo di terapia (neo)adiuvante (Sali di platino, PARPi adj, immunoterapia, abemaciclib adj)

Terapia neoadiuvante nella paziente con mutazione BRCA e tumore in fase iniziale



*Ruolo dei Sali di Platino ?: indipendente da BRCA su pCR *[frequenza elevata di metilazione di BRCA in early TNBC]*, e pCR correla con EFS; molto efficace anche Antra-Ciclo, spt in ER+.
° KN-522 non specifico per gBRCA-mut BC; quale tp ADJ in non pCR?
°°Dati promettenti, talazoparib non rimborsato
**se N+, stadio ≥ IIb, Gn 3 → x possibile modulazione tp adiuvante in base a risposta e CPS-EG (≥3)

Terapia adiuvante post-NAT nella paziente con gBRCAmut e Early BC



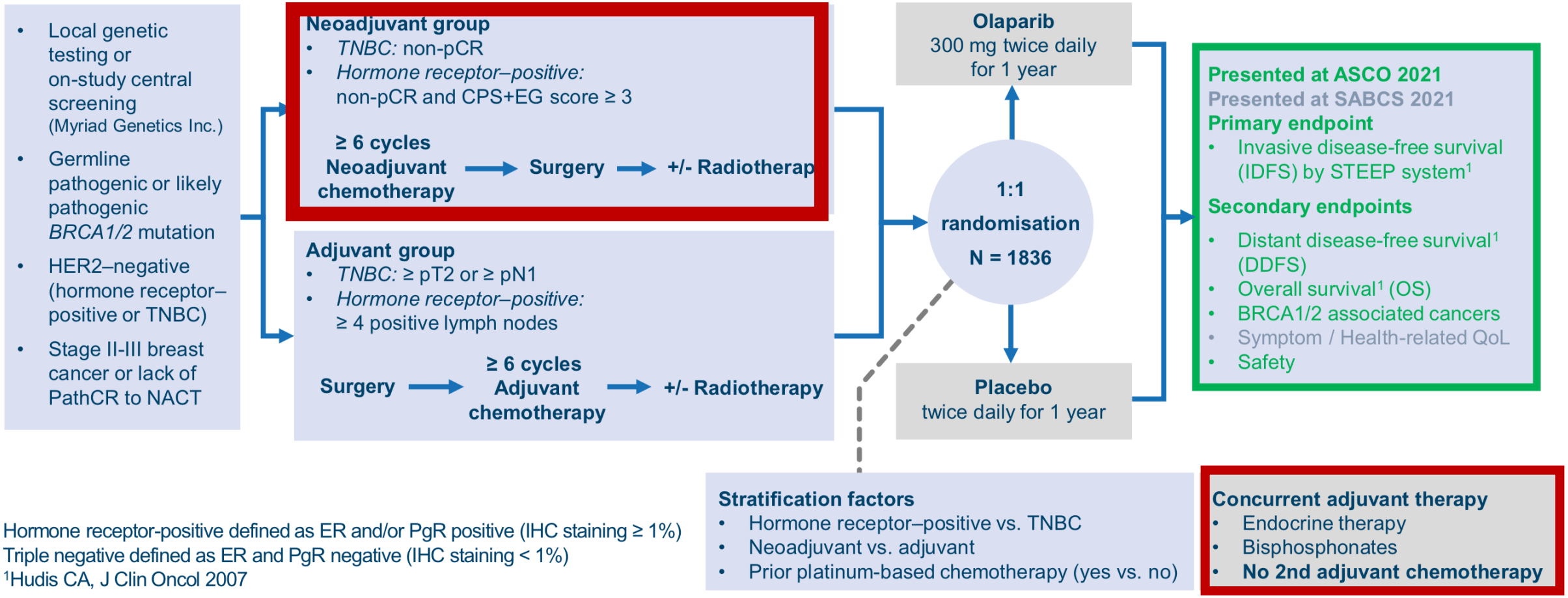
*__in ER+,__ preferibile rispetto ad abema *(se anche criteri MonarchE) – (Abema dopo Ola x 1 aa? Abema fino a 16 mesi da CH; ET possibile in combinazione con Ola);* **in TN**, da preferire a pembro *(resistenza a pembro in non-pCR? 3y EFS 67% vs ola iDFS 88%)* ed a cape *(non trasferibile il dato CreateX, ma PARPi > cape in mBC)*

**se non criteri Olympia: valutare uso di Sali di platino *(accesso a PARPi in mBC)*

° se criteri Olympia

Olaparib adiuvante post-neoadiuvante

OLYMPIA: TRIAL SCHEMA



Hormone receptor-positive defined as ER and/or PgR positive (IHC staining ≥ 1%)
Triple negative defined as ER and PgR negative (IHC staining < 1%)
[1]Hudis CA, J Clin Oncol 2007

Post-neoadiuvante – ER+: non-pCR & CPS-EG ≥ 3

Neoadjuvant Therapy Outcomes Calculator

This software calculates the anticipated 5-year distant metastasis-free survival and disease-specific survival for breast cancer patients following treatment with neoadjuvant chemotherapy. The scoring systems provide a novel means for evaluating prognosis in these patients by incorporating the pretreatment clinical stage and post-treatment pathologic stage (CPS score) as well as estrogen receptor status and tumor grade (CSP+EG score). Please note that this calculator is not applicable for patients presenting with distant metastatic (M1) disease or for patients who go on to develop M1 disease.

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Clinical Stage
Clinical Staging for Breast Cancer

TNM Stage: Select Clinical Stage

Pathologic Stage
Pathologic Staging for Breast Cancer

TNM Stage: Select Pathologic Stage

Estrogen Receptor Status

Select Estrogen Receptor Status

Nuclear Grade

Select Nuclear Grade

calculate | clear

Clinical-Pathologic Scoring System	
Total Score:	
5-year Distant Metastasis Free Survival:	95% CI:
5-year Disease Specific Survival:	95% CI:

Clinical-Pathologic Scoring System incorporating estrogen receptor status and nuclear grade	
Total Score:	
5-year Distant Metastasis Free Survival:	95% CI:
5-year Disease Specific Survival:	95% CI:

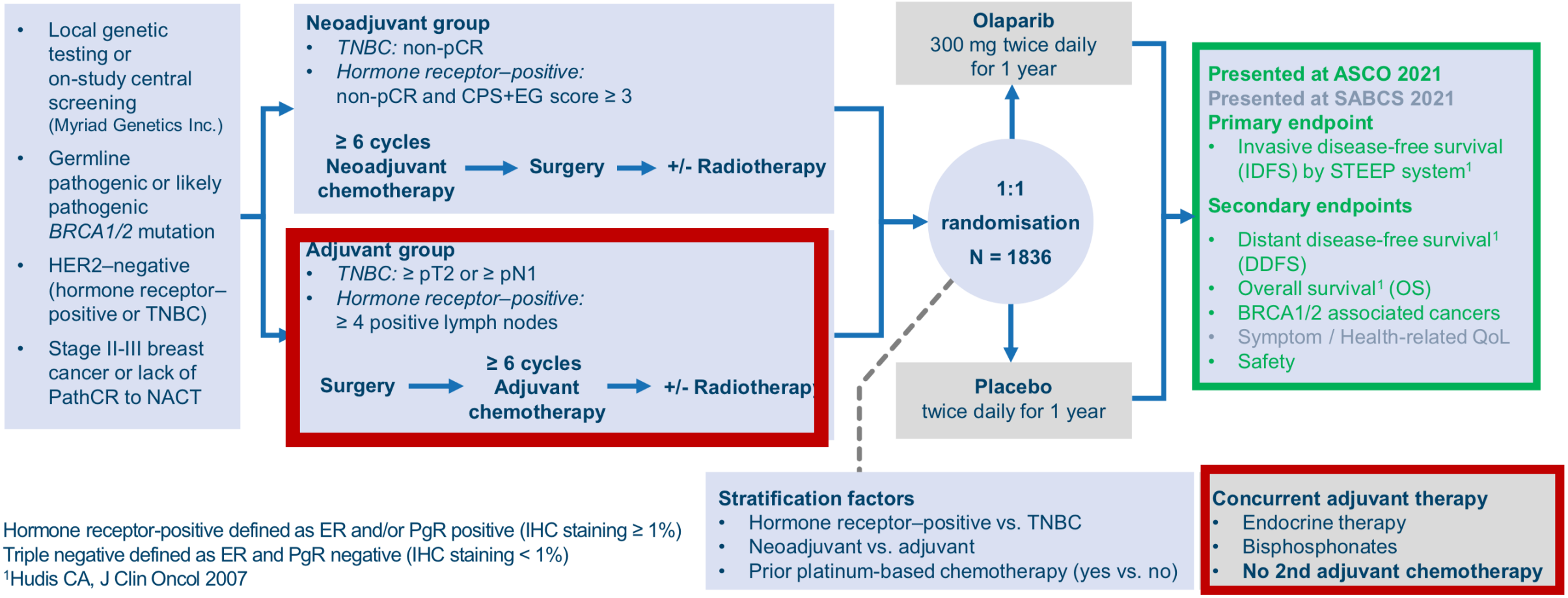
The CPS&EG score is a staging system for disease specific survival in patients with breast cancer treated with neoadjuvant chemotherapy.[1] This incorporates pretreatment clinical stage, estrogen receptor status, nuclear grade and post-neoadjuvant chemotherapy pathological stage.

Calculation instructions: Add the points for Clinical Stage + Pathologic Stage + ER status + Nuclear grade to derive a sum (CPS&EG score) between 0 and 6.

Stage/feature		Points
Clinical Stage (AJCC staging [1])	0	0
	IIA	0
	IIB	1
	IIIA	1
	IIIB	2
	IIIC	2
Pathologic Stage (AJCC staging [1])	0	0
	I	0
	IIA	1
	IIB	1
	IIIA	1
	IIIB	1
	IIIC	2
Receptor status	ER negative [2]	1
Nuclear grade [3]	Nuclear grade 3	1

Olaparib adiuvante

OLYMPIA: TRIAL SCHEMA



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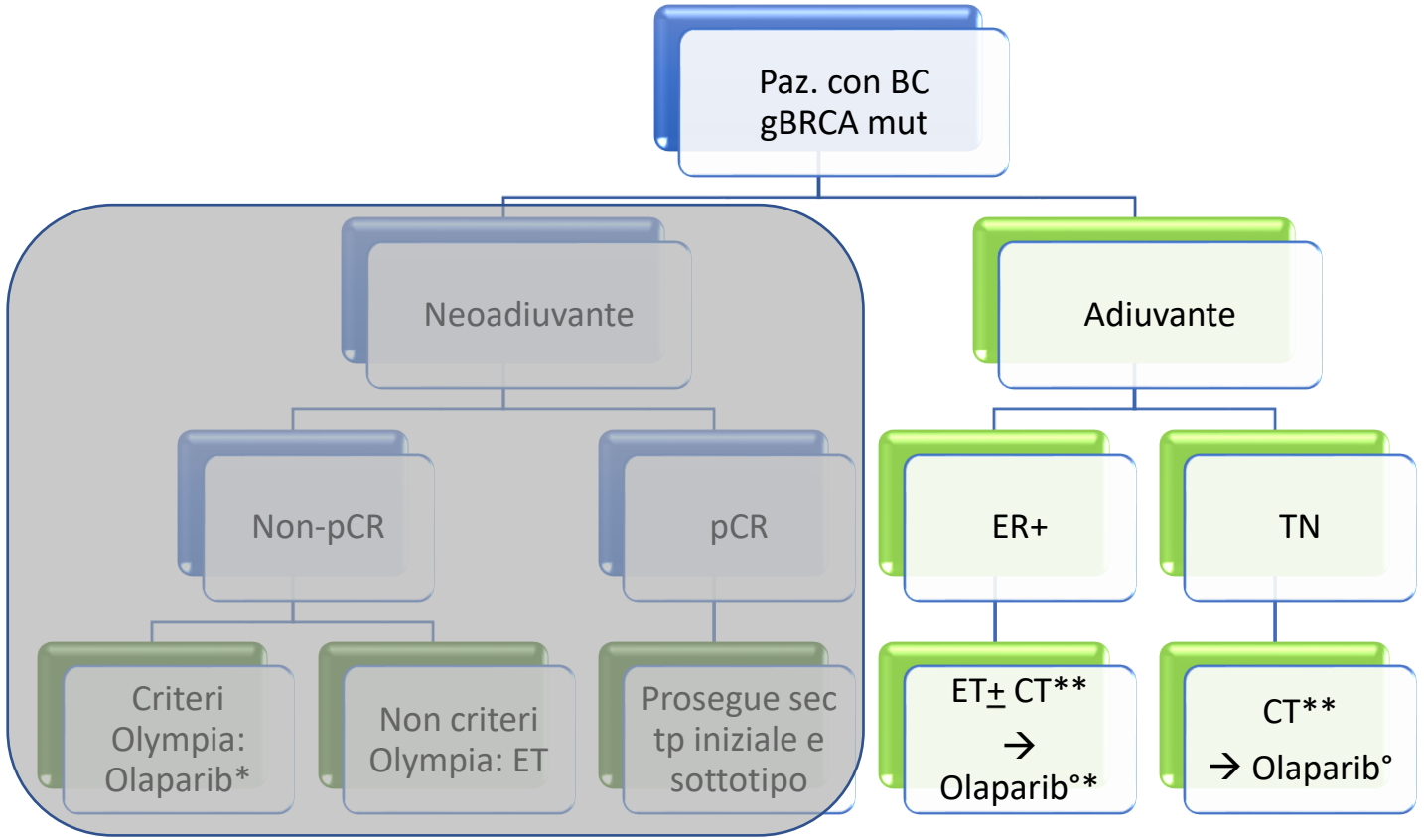
Terapia adiuvante nella paziente con gBRCAmut e Early BC



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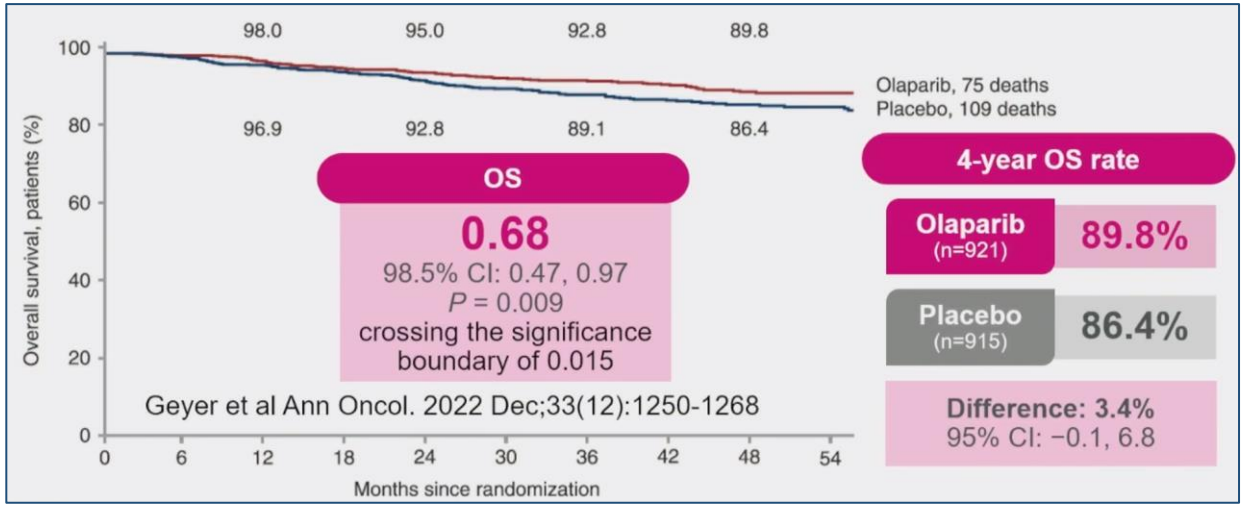
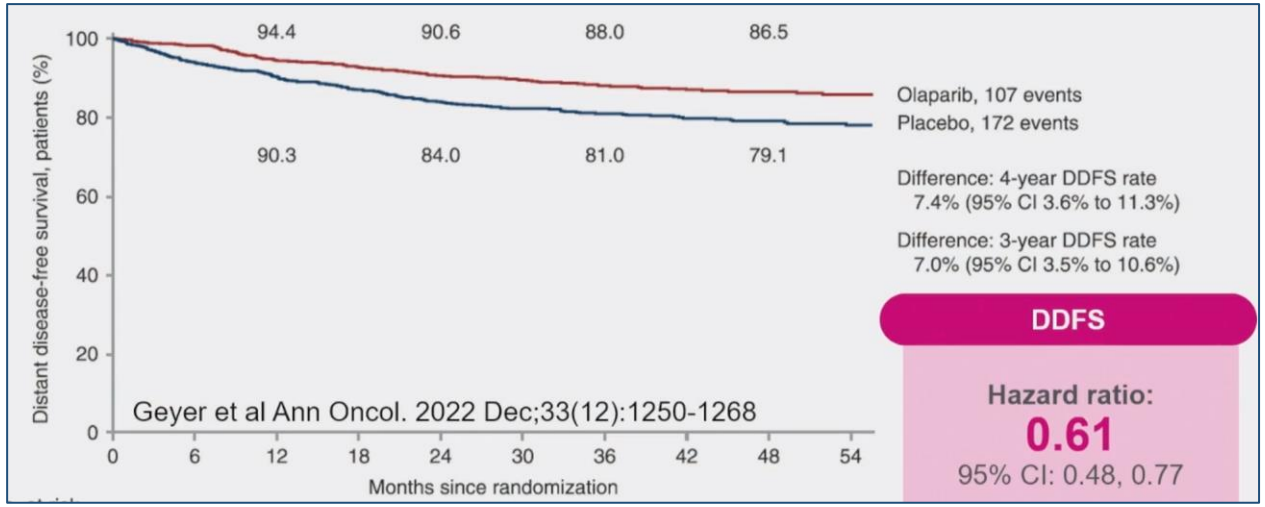
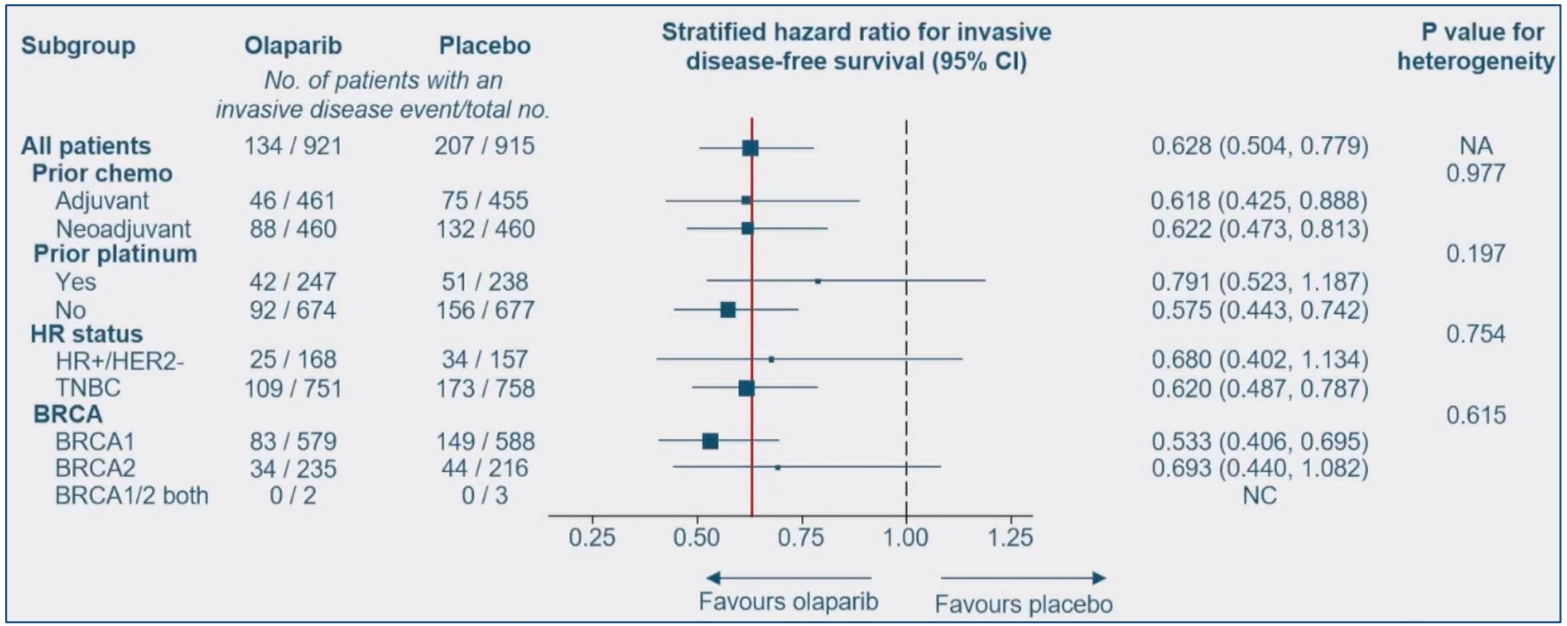
**se non criteri Olympia: valutare uso di Sali di platino *(accesso a PARPi in mBC)*

° se criteri Olympia, dopo CT

Miglioramento della sopravvivenza con olaparib







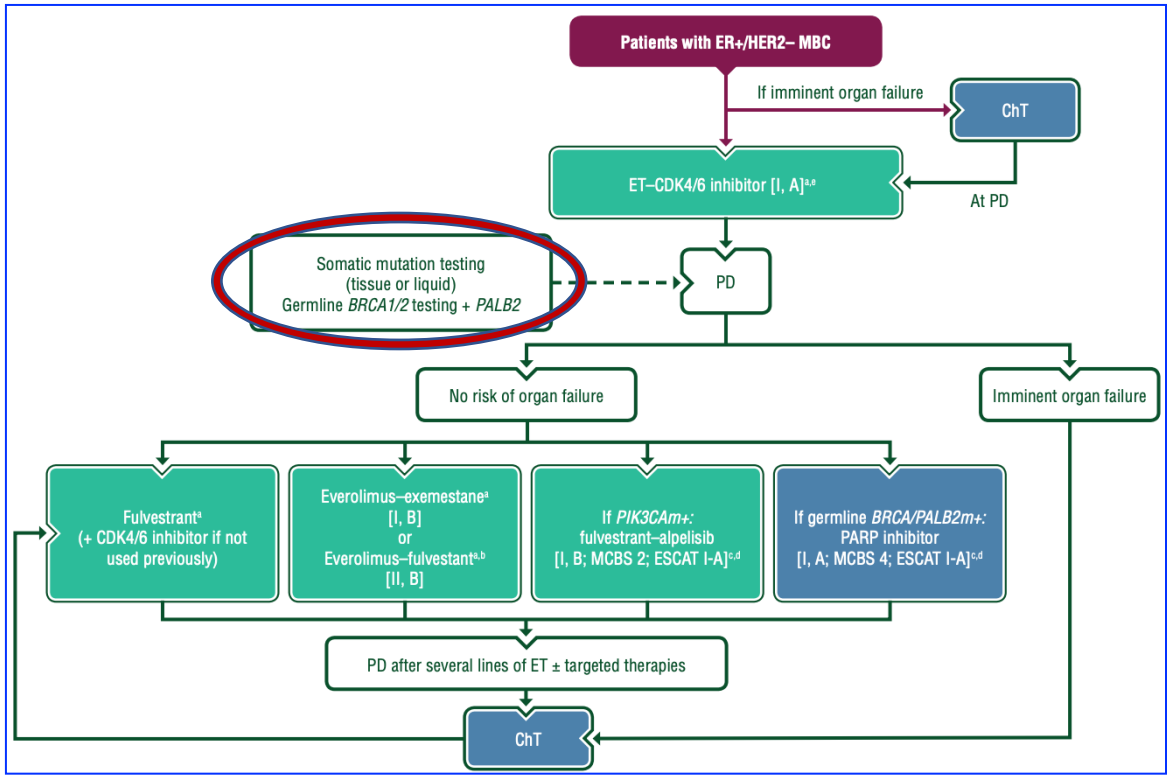
Test di interazione negativi per tutti i sottogruppi

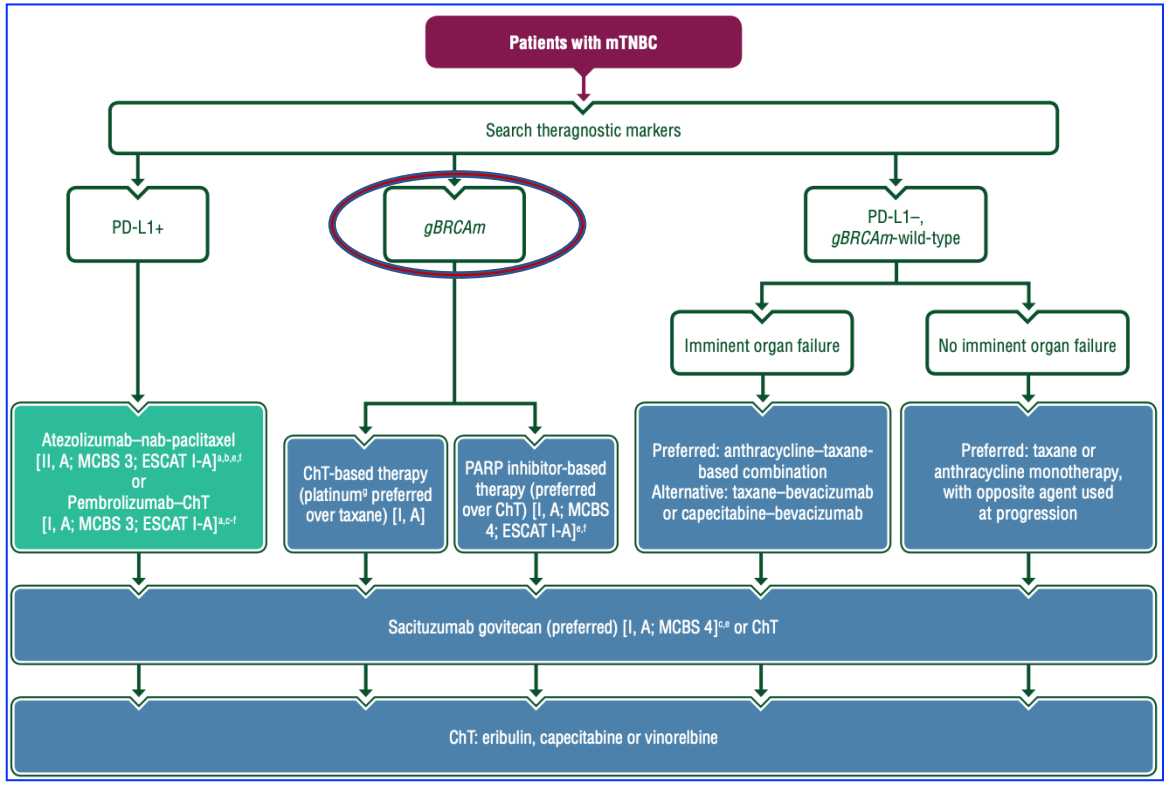
Terapia adiuvante con inibitori di PARP

- In Italia olaparib adiuvante non è al momento approvato da AIFA e pertanto **non è rimborsato** da parte del Sistema Sanitario Nazionale.

- Al momento è disponibile **l'uso compassionevole** di Olaparib (a partire da Maggio 2022) per il trattamento adiuvante di pazienti con neoplasia della mammella in stadio precoce, HER2-negativo e con mutazioni germinali nei geni BRCA1/2, che presentino caratteristiche istopatologiche ad alto rischio e che abbiano completato il trattamento loco-regionale e la chemioterapia (neo/adiuvante).

Strategia terapeutica nel carcinoma mammario avanzato





Linee Guida ESMO 2021

Olaparib e Talazoparib nel mBC con mutazione gBRCA

- Locally advanced breast cancer and/or metastatic disease appropriate for systemic single cytotoxic chemotherapy
- gBRCAm
- ECOG 0-2
- ≤3 prior lines of chemotherapy for locally advanced/metastatic disease
- HER2-negative
- Prior platinum permitted if:
  - In (neo-)adjuvant setting: disease-free interval of ≥6 months after the last dose
  - In advanced setting: no objective disease progression while receiving platinum
- Previous treatment with a taxane, an anthracycline, or both, unless this treatment was contraindicated

Randomise 2:1

Talazoparib (n=287)
1 mg/day 21 day cycles *po*

Therapy of physician's choice (TPC) (n=144)
(capecitabine, eribulin, gemcitabine or vinorelbine)

Primary endpoint:
- PFS (BICR)

Secondary endpoints include:
- ORR
- OS
- Safety and tolerability
- PK

Exploratory endpoint:
- HRQoL

Patients stratified according to:
- *Number of prior chemotherapy regimens (0 vs. 1,2,3)*
- *Triple negative status (HR+ vs. TNBC)*
- *History of CNS metastasis (y/n)*

- gBRCAm mBC
- **TNBC or HER2-negative, ER/PR positive**
- ≤2 prior chemotherapy lines for mBC
- Previous treatment with anthracycline and taxane in either the (neo)adjuvant or metastatic setting
- Hormone receptor positive (HR+) disease progressed on ≥1 endocrine therapy, or not suitable
- If patients have received platinum therapy there should be:
  - No evidence of progression during treatment in the advanced setting
  - At least 12 months since (neo)adjuvant treatment and randomisation
- ECOG PS 0-1
- At least one lesion that can be assessed by RECIST v1.1

FSI May 2014:[3]
Global Study in 19 countries and approximately 141 sites[1]

Randomise 2:1
n=302[4]

Stratification by:[2]
- *Prior chemotherapy regimens for metastatic breast cancer*
- *Hormonal receptor (HR) status*
- *Prior platinum therapy*

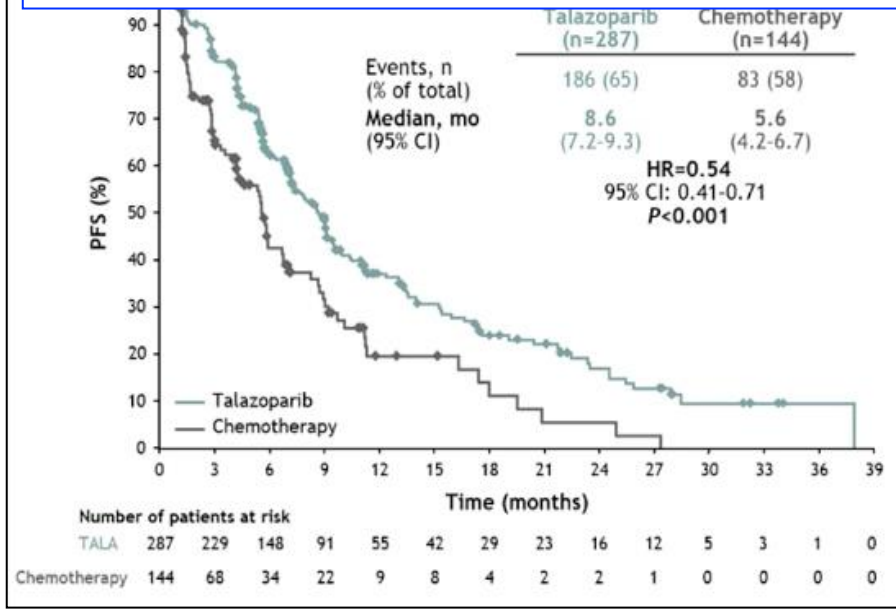
Olaparib
300mg*po bid

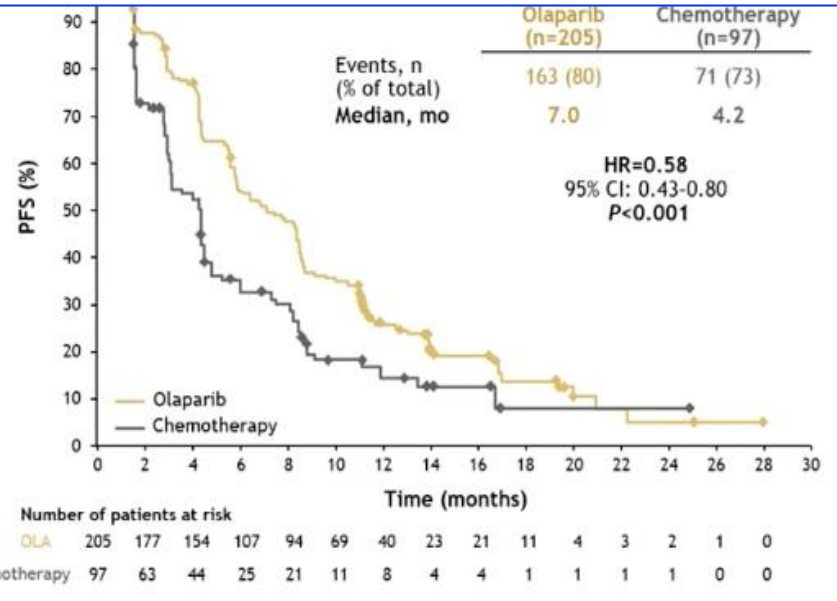
Treatment of Physician's Choice
(TPC)
(capecitabina, vinorelbine, eribulina)

Primary endpoint
- PFS (RECIST 1.1, Independent Review)

Secondary endpoints
- OS
- PFS2
- ORR
- PFS, PFS2 and OS based on Myriad gBRCAm status
- HRQoL (EORTC-QLQ-C30)
- Safety and tolerability

Riduzione del rischio di progressione del 46-48%





Talazoparib: NEJM 2018, Ann Oncol 2020

Olaparib: NEJM 2017, Ann Oncol 2019

PARP-inibitori: Rimborsabilità in Italia mBC con mutazione gBRCA

Autorizzazione più ampia (HER2-; non riferimenti a platino), ma rimborsabilità limitata a:

- **Talazoparib** è indicato come monoterapia per il trattamento di pazienti adulti con mutazioni germinali BRCA1/2, affetti da carcinoma mammario HER2-negativo localmente avanzato o metastatico. I pazienti devono essere stati precedentemente trattati con una antraciclina e/o un taxano nel contesto (neo)adiuvante, localmente avanzato o metastatico, ad eccezione dei pazienti non idonei per tali trattamenti. *Le pazienti con carcinoma mammario **HR-positivo** devono essere state precedentemente trattate con terapia endocrina o ritenuti non idonei alla terapia endocrina e **devono aver ricevuto una linea di trattamento con inibitori CDK4/6**. **Le** pazienti con carcinoma mammario **negativo ai recettori ormonali devono essere state** precedentemente **trattate con chemioterapia a base di platino**, ad eccezione dei pazienti non idonei per tale trattamento*

- **Olaparib** è indicato, in monoterapia, per il trattamento di pazienti adulti con cancro della mammella, localmente avanzato o metastatico, **HER2 negativo, HR-negativo** e con mutazioni della linea germinale BRCA1/2. *Le pazienti **devono essere state** precedentemente **trattate con** un'antraciclina e un taxano e con **platino nel setting (neo)adiuvante o metastatico***, a meno che non fossero eleggibili per questi trattamenti

Conclusioni

- Il protocollo regionale per il rischio eredofamiliare offre una gestione completa di valutazione del rischio
- La Rete dei Centri di Senologia permette una gestione omogenea delle pazienti con carcinoma mammario con mutazione gBRCA
- La modalità di valutazione delle mutazioni ha oggi significato anche predittivo per la scelta dei trattamenti
- Il gruppo multidisciplinare deve valutare la necessità del test, e non solo il genetista è coinvolto nella fase di informazione della paziente.
- I casi con mutazione BRCA sono sottostimati, e le opzioni terapeutiche disponibili richiamano ad una maggiore attenzione al problema
- Il pannello di geni da analizzare è più ampio di quanto oggi previsto.

- **Il percorso complessivo deve essere programmato anche in funzione delle opzioni terapeutiche disponibili**