


XXXII CONGRESSO NAZIONALE AIRO  
XXXIII CONGRESSO NAZIONALE AIRB  
XII CONGRESSO NAZIONALE AIRO GIOVANI

# AIRO2022

Radioterapia di precisione per un'oncologia innovativa e sostenibile

BOLOGNA, 25-27 NOVEMBRE  
PALAZZO DEI CONGRESSI

 Associazione Italiana  
Radioterapia e Oncologia clinica

 Società Italiana di Radiobiologia

 Associazione  
Italiana  
Radioterapia  
e Oncologia  
clinica  




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## **In quali pazienti eseguire il test germinale e perché Come monitorare l'efficacia dei trattamenti**

**Luca Eolo Trodella**

**Radioterapia oncologica**

**Fondazione Campus Bio-Medico**

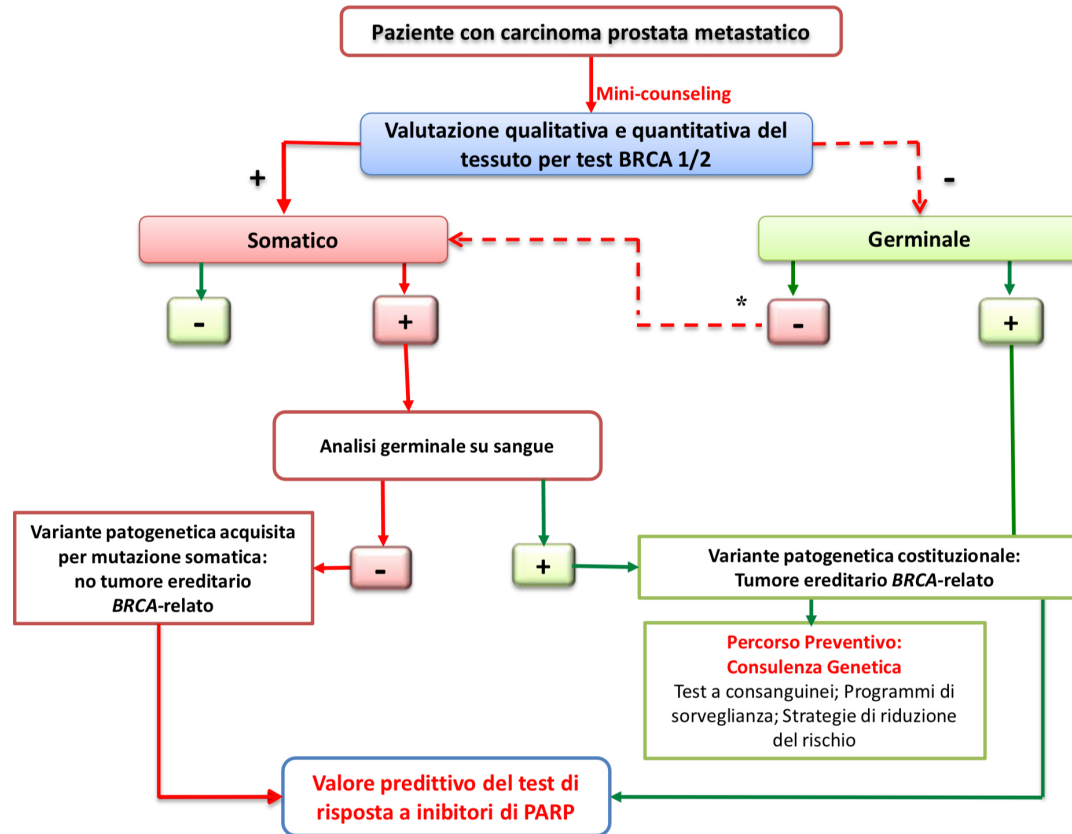
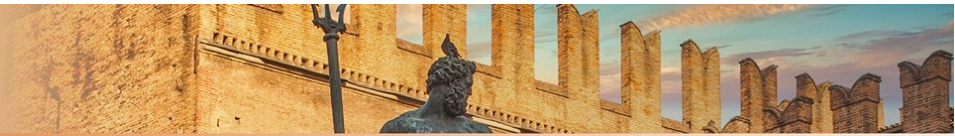


## DICHIARAZIONE

Relatore: Luca Eolo Trodella

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE )**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE )**
- Partecipazione ad Advisory Board **(NIENTE DA DICHIARARE)**
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE )**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro



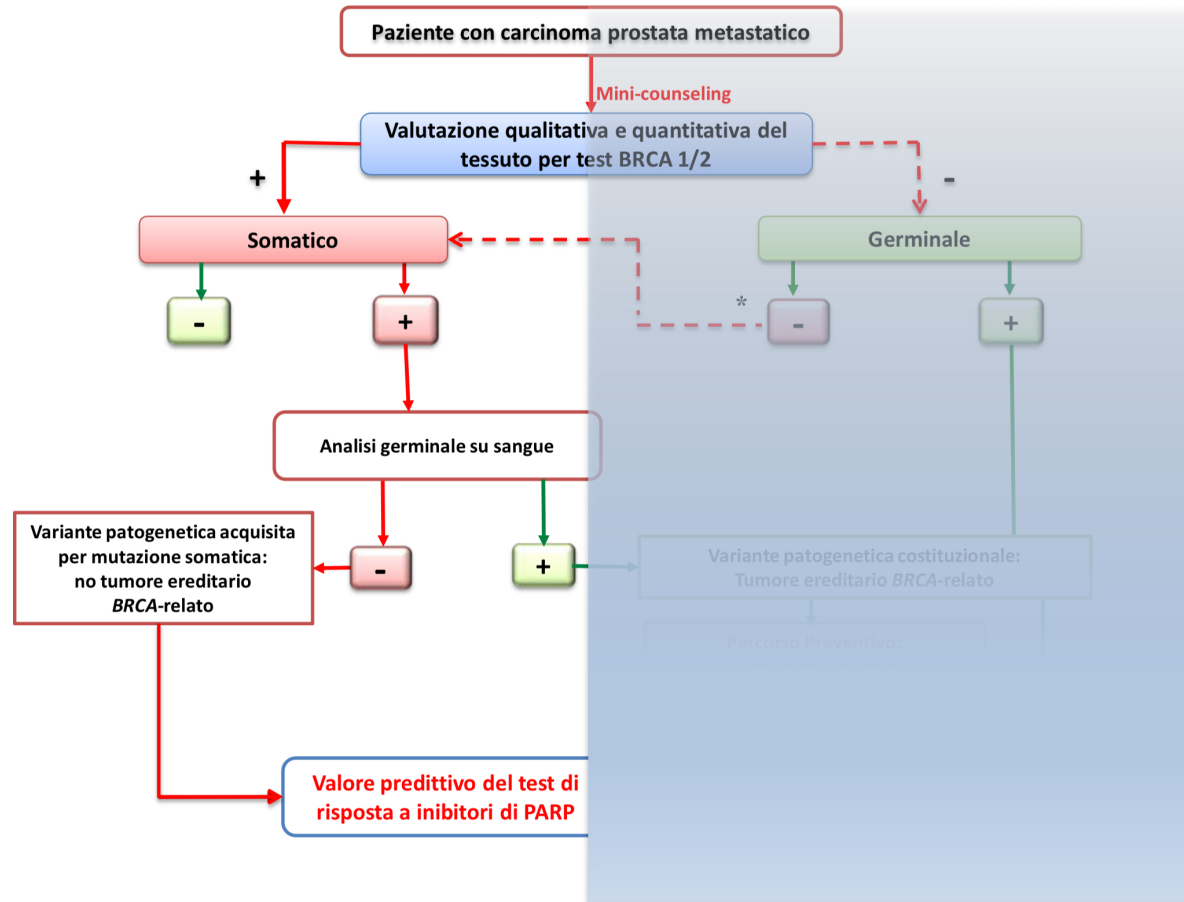
\* Da considerare la re-biopsia a negatività del germinale

Raccomandazioni AIOM  
 Analisi Mutazionale BRCA mPCa  
 Edizione Febbraio 2021



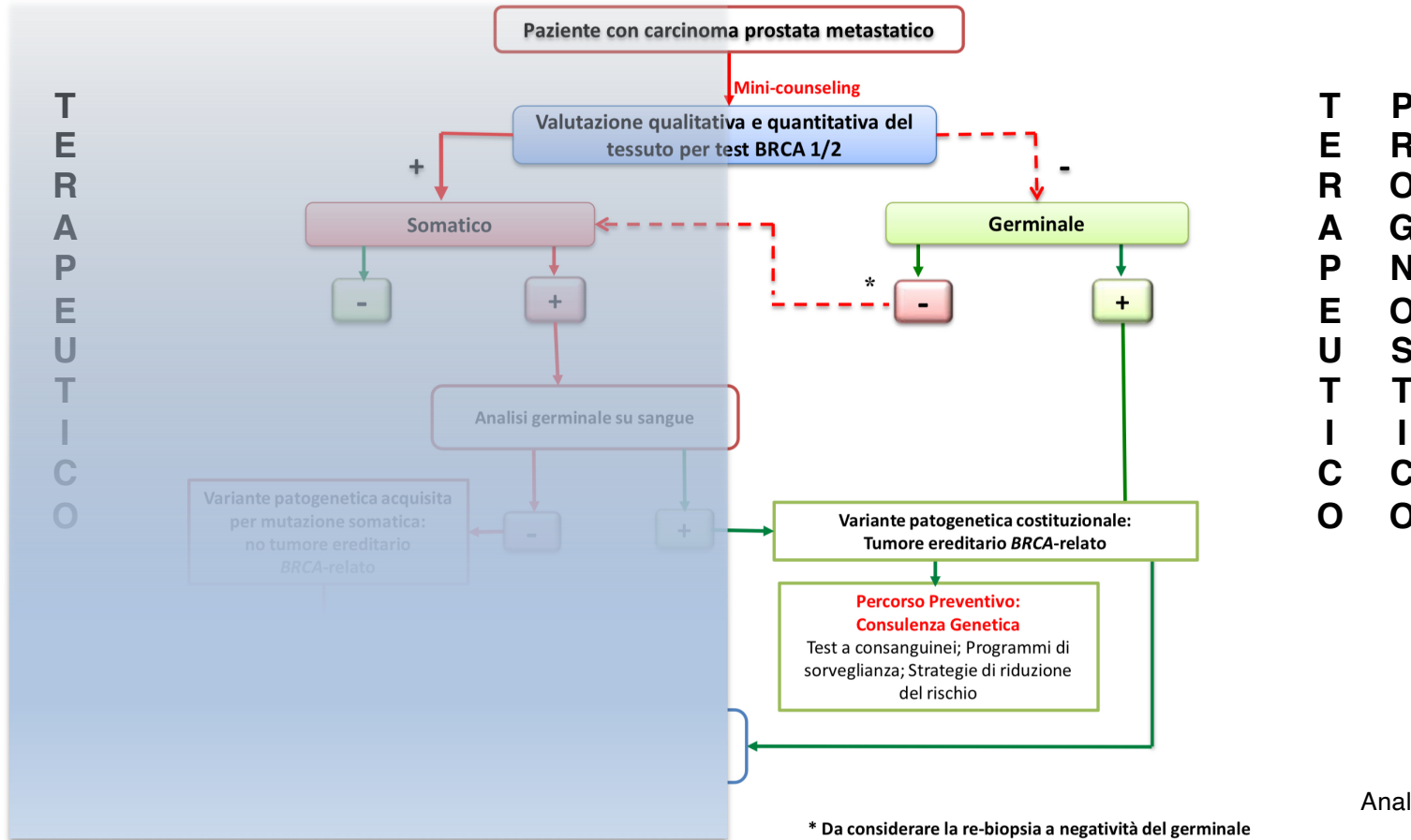
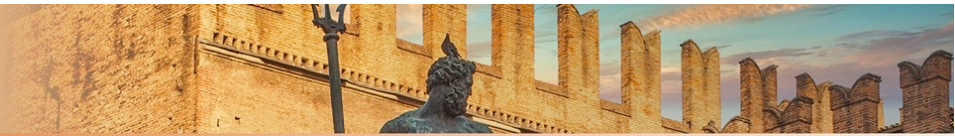


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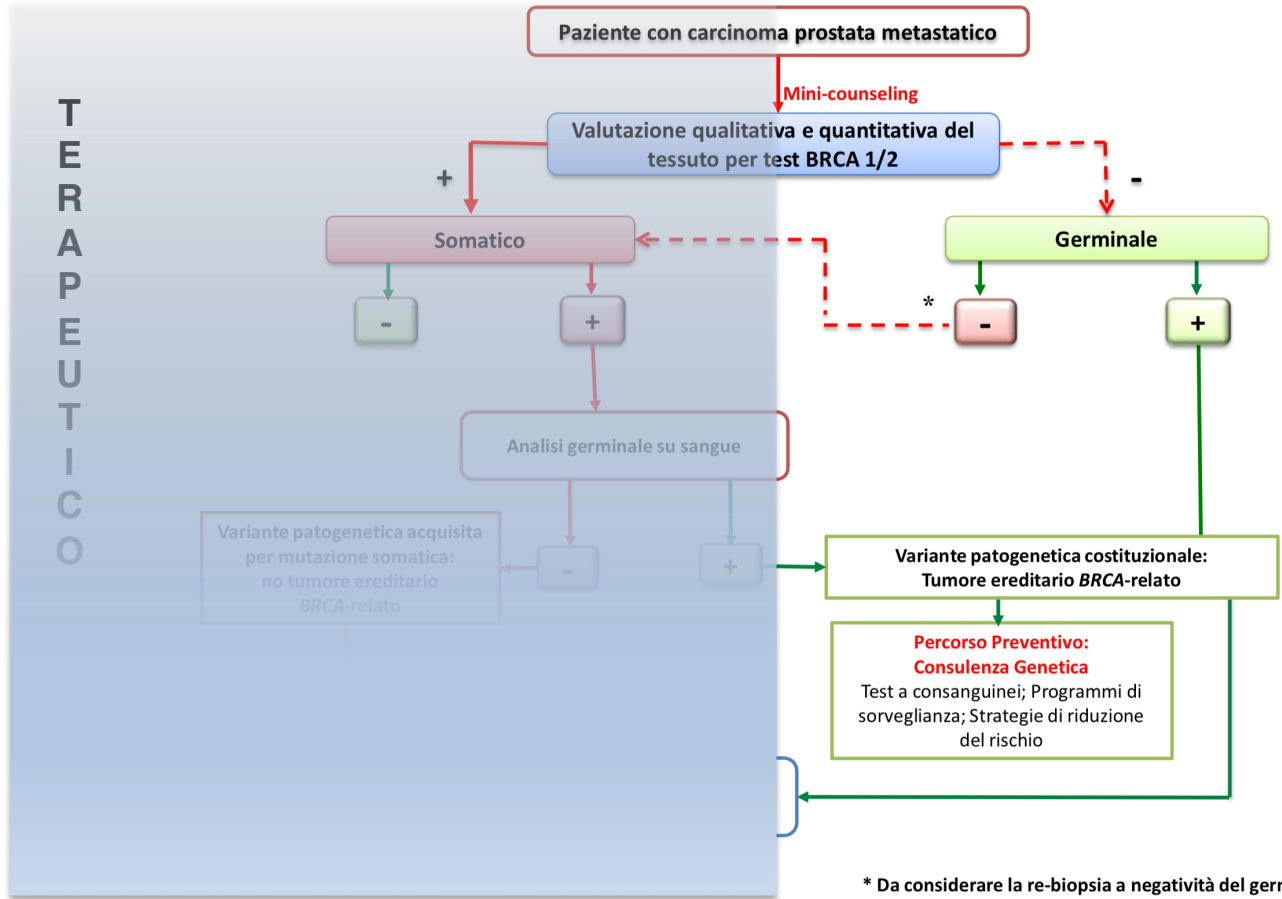
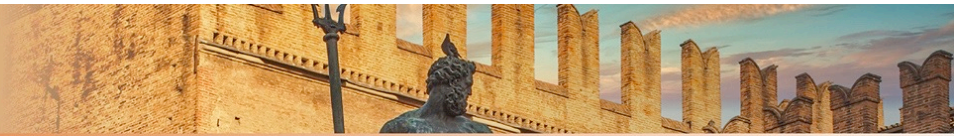
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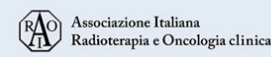




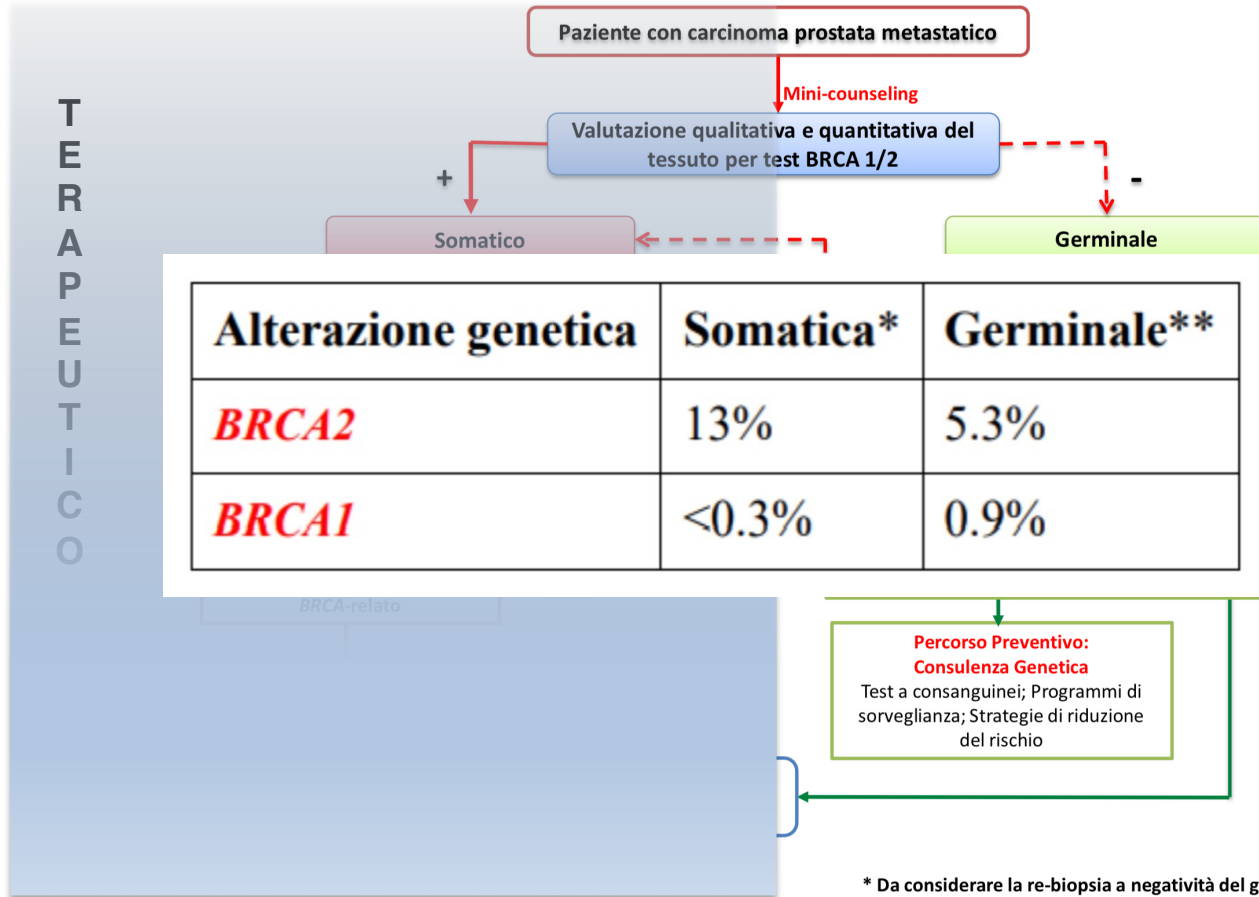
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Raccomandazioni AIOM  
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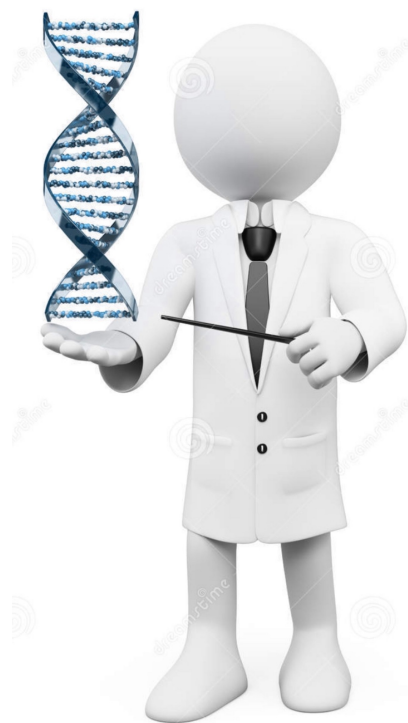
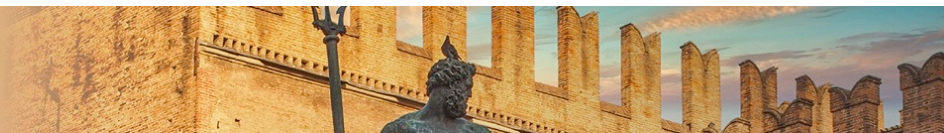




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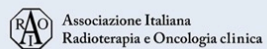
Radioterapia di precisione per un'oncologia innovativa e sostenibile



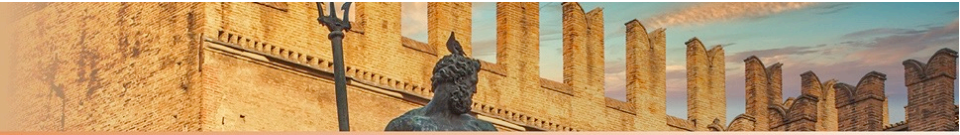
## GENETISTA



## TEAM MULTIDISCIPLINARE



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## American College of Medical Genetics guidelines

1. Three or more first-degree relatives with prostate cancer; or
2. Two or more first-degree relatives diagnosed with prostate cancer at age 55 years; or
3. Gleason grade  $>7$  prostate cancer and a family history of 2 individuals with breast, ovarian, or pancreatic cancer.

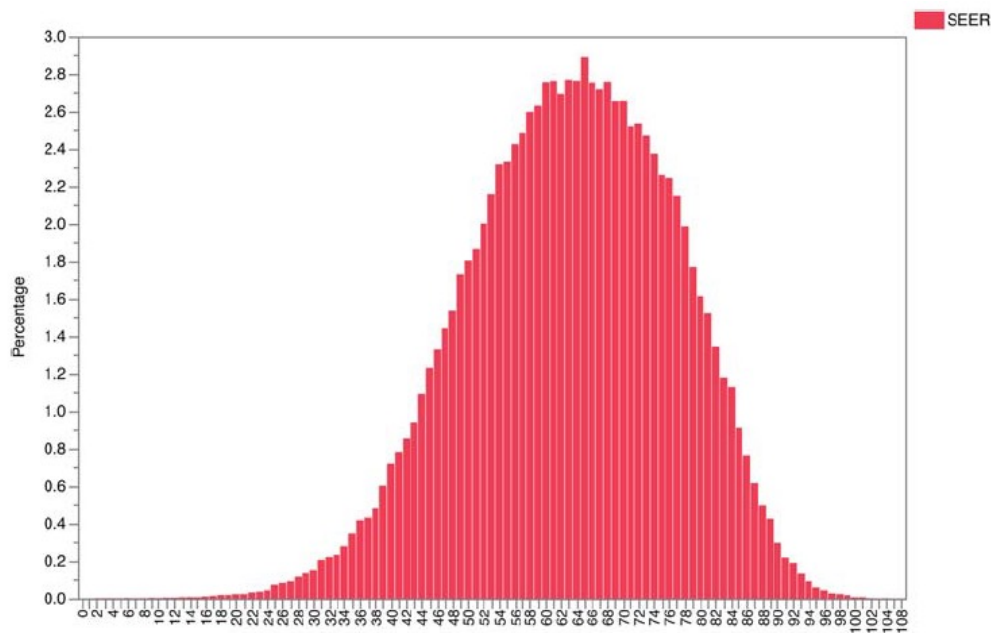
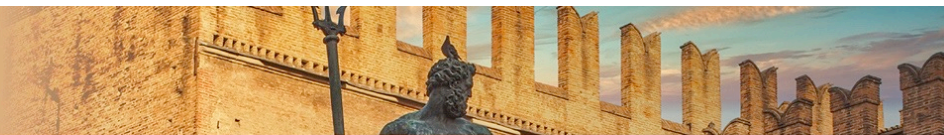
## Johns Hopkins group

1. Three or more first-degree relatives with prostate cancer, or
2. Three successive generations of prostate cancer, or
3. Two relatives with prostate cancer diagnosed at age 55 years.

## National Comprehensive Cancer Network

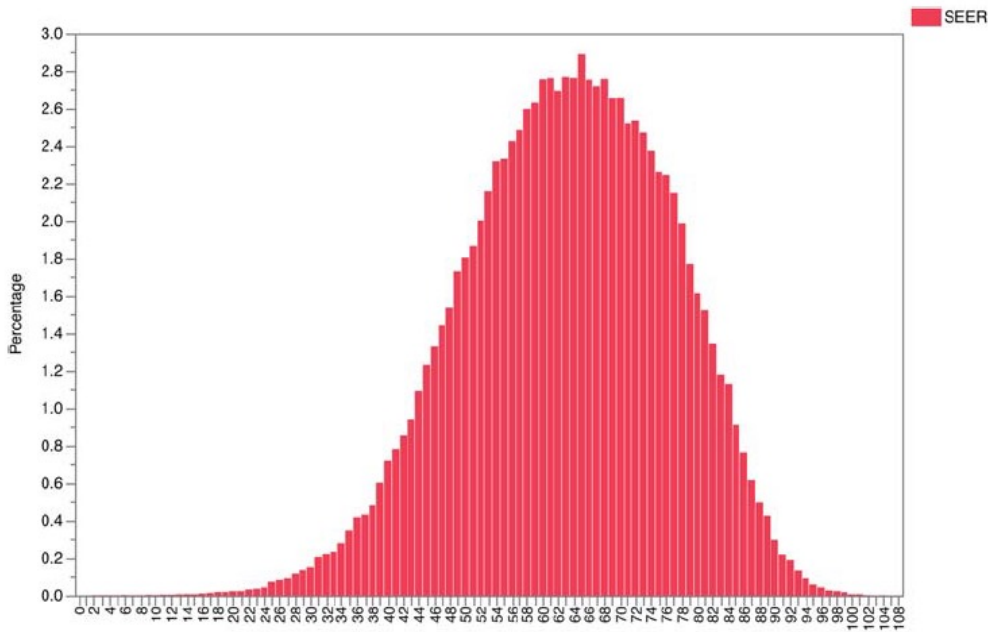
1. A history of Gleason grade  $\geq 7$  prostate cancer regardless of age and 1 close relative with breast cancer (age 50 years) and/or invasive ovarian cancer; or
2. Patients with prostate cancer (Gleason  $\geq 7$ ) who have 2 relatives with breast, pancreatic, or prostate cancer (Gleason  $\geq 7$ ) diagnosed at any age; or
3. A personal history of metastatic prostate cancer (radiographic evidence) of or biopsy-proven disease.

Zhen JT, et al, *Cancer*. 2018 Aug 1;124(15):3105-3117

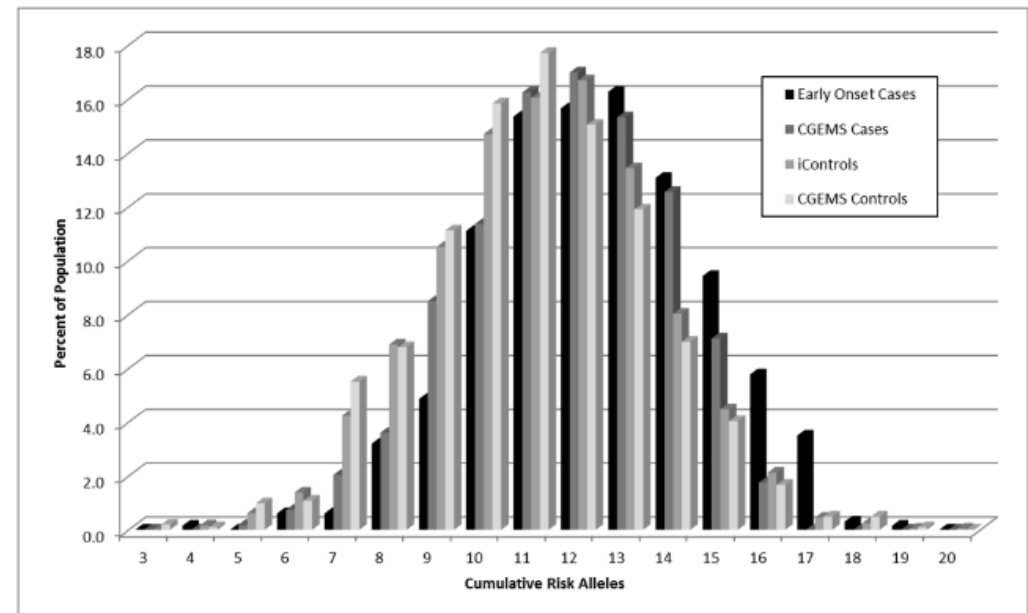


The bottom decile of prostate cancer cases are diagnosed in men aged 55 years

Zhen JT, et al, *Cancer*. 2018 Aug 1;124(15):3105-3117



The bottom decile of prostate cancer cases are diagnosed in men aged 55 years



The total number of risk alleles observed in each subject (measured as the sum of risk alleles across 13 SNPs) was strongly associated with EO PCa ( $p = 2.1 \times 10^{-33}$ )

Zhen JT, et al, *Cancer*. 2018 Aug 1;124(15):3105-3117  
 Lange EM et al, *Prostate*. 2012 February 1; 72(2): 147-156



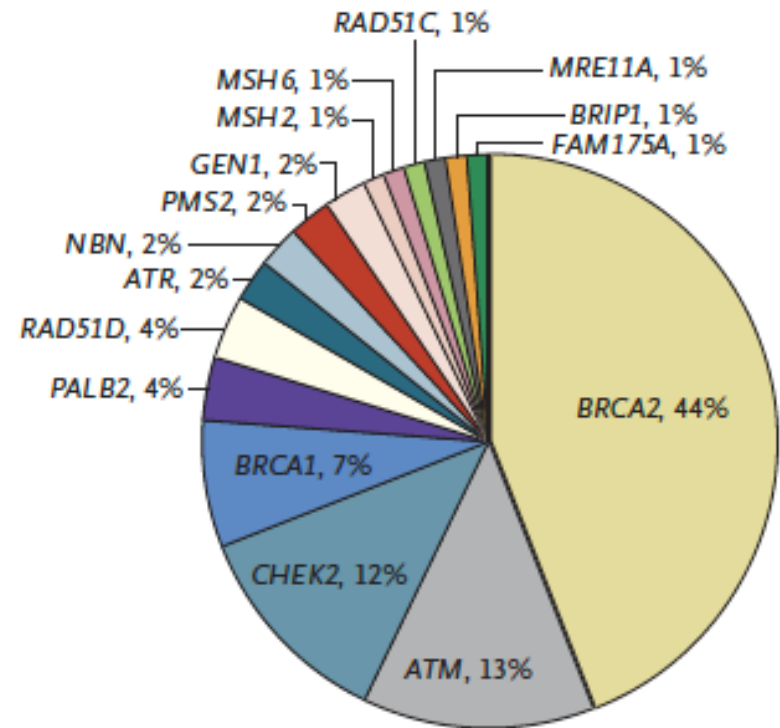
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer

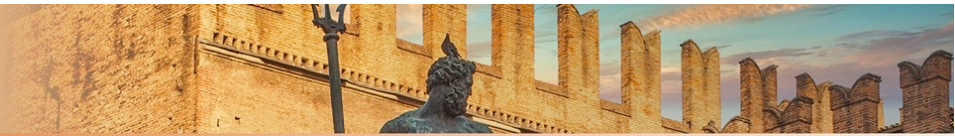
692 men with documented metastatic prostate cancer who were unselected for family history of cancer or age at diagnosis

A total of 84 germline DNA-repair gene mutations that were presumed to be deleterious were identified in 82 men (**11.8%**)



Pritchard CC, et al, N Engl J Med 2016;375:443-53





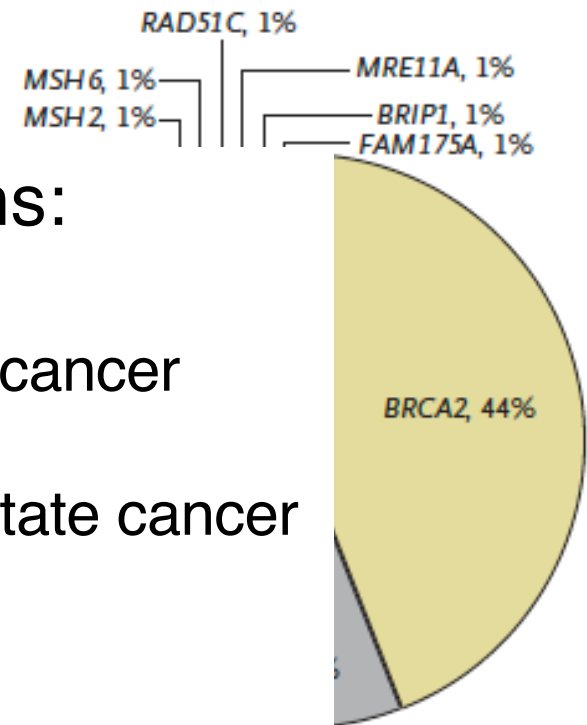
ORIGINAL ARTICLE

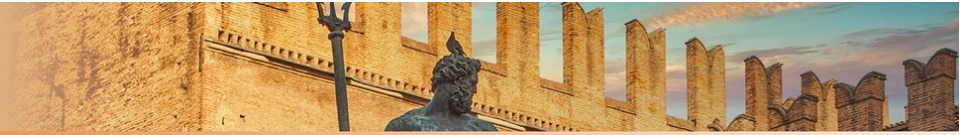
## Inherited DNA repair mutations in Men with M1 prostate cancer

692 men with documented M1 prostate cancer were unselected for germline DNA repair gene testing

A total of 84 germline DNA repair mutations were presumed to be deleterious (11.8%)

- 11,8 %: in men with M1 prostate cancer
- 4,6 %: in men with localized prostate cancer
- 2,6 %: general population





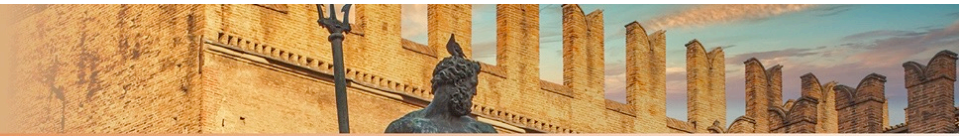
Il test germinali dovrebbe essere preso in considerazione in uno dei seguenti scenari:

- Storia personale di cancro alla prostata ad esordio precoce ( $\leq 55$  anni)
- Storia personale di cancro alla prostata metastatico al momento della diagnosi
- In presenza di parenti di primo grado con diagnosi di tumore prostatico (tre o più)
- Carcinoma prostatico Grade Group IV o V, e/o istotipo duttale (anche dopo prostatectomia) e/o una storia familiare di  $\geq 2$  individui con carcinoma mammario, ovarico o pancreatico

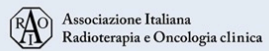
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## Quali pazienti?



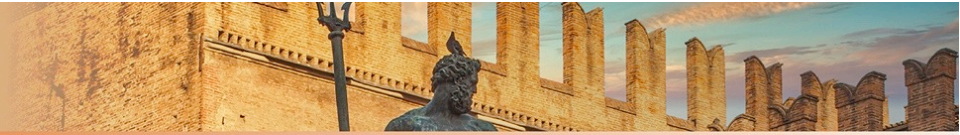
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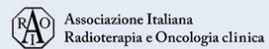
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## Quali pazienti: OK

## Perché?



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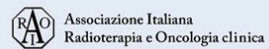
VOLUME 31 • NUMBER 14 • MAY 10 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Germline *BRCA* Mutations Are Associated With Higher Risk of Nodal Involvement, Distant Metastasis, and Poor Survival Outcomes in Prostate Cancer

2019 Pca patients  
79 carriers vs 1940 no carriers  
**Evaluation of disease @ diagnosis**



Castro E et al, *J Clin Oncol* 31:1748-1757, 2013

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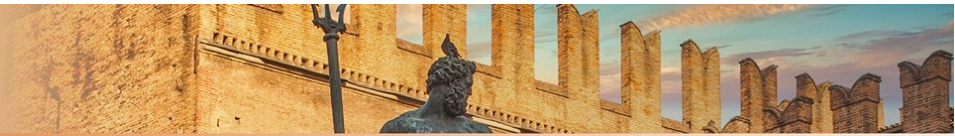


## Germline *BRCA* Mutations Are Associated With Higher Risk of Nodal Involvement, Distant Metastasis, and Poor Survival Outcomes in Prostate Cancer

2019 Pca patients  
 79 carriers vs 1940 no carriers  
**Evaluation of disease @ diagnosis**

STATUS	Gleason Score $\geq$ 8		T3-T4 stage		Nodal involvement		M+ @ diagnosis	
	Carriers	No carriers	Carriers	No carriers	Carriers	No carriers	Carriers	No carriers
Carriers	35%	P=.00003	37%	P= .003	15%	P=.0005	18%	P=.005
No carriers	15%		28%		5%		9%	





EUROPEAN UROLOGY 76 (2019) 831–842

available at [www.sciencedirect.com](http://www.sciencedirect.com)  
 journal homepage: [www.europeanurology.com](http://www.europeanurology.com)



Prostate Cancer

## Interim Results from the IMPACT Study: Evidence for Prostate-specific Antigen Screening in BRCA2 Mutation Carriers



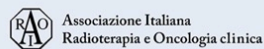
Men aged 40–69 yr with a germline pathogenic BRCA1/2 mutation and male controls testing negative for a familial BRCA1/2 mutation were recruited.

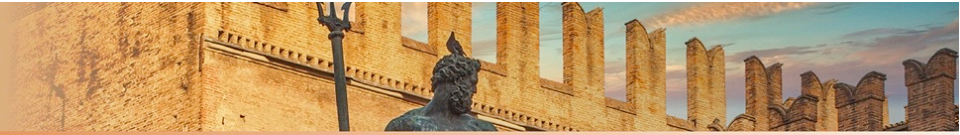
**Participants underwent PSA screening for 3 yr, and if PSA>3.0 ng/ml, men were offered prostate biopsy.**

3027 patients (919 BRCA1 carriers, 709 BRCA1 noncarriers, 902 BRCA2 carriers, and 497 BRCA2 noncarriers).

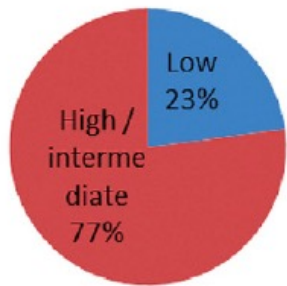
527 men had PSA>3.0 ng/ml, 357 biopsies were performed, and 112 PrCa cases were diagnosed

Cancer **incidence rate** per 1000 person years **was higher in BRCA2 carriers** than in noncarriers (19.4 vs 12.0; p = 0.03)

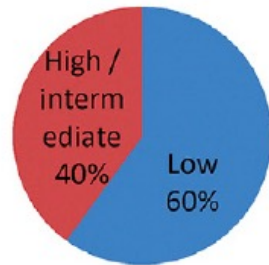




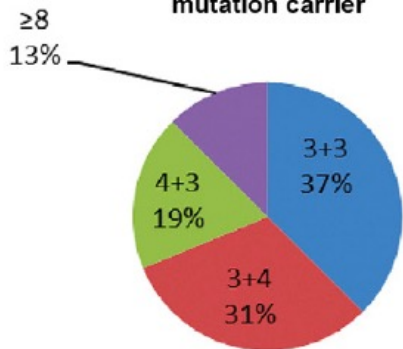
**Overall risk category- *BRCA2* mutation carrier**



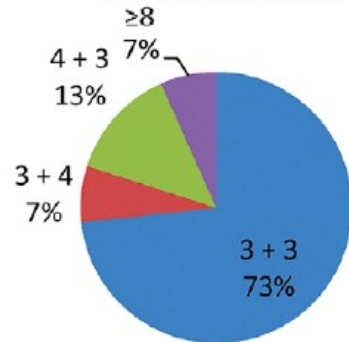
**Overall risk category—*BRCA2* mutation noncarrier**



**Overall Gleason score -*BRCA2* mutation carrier**

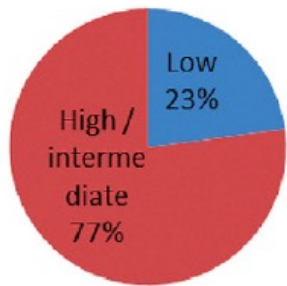


**Overall Gleason score—*BRCA2* mutation noncarrier**

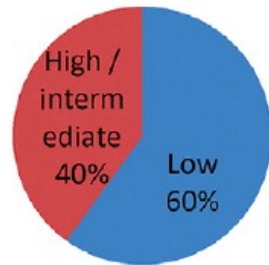




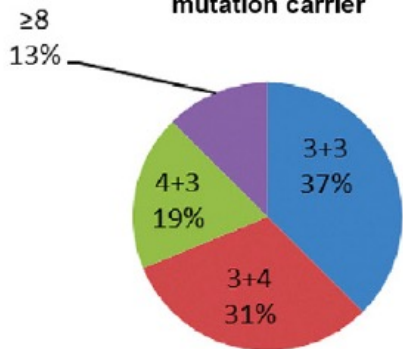
**Overall risk category- *BRCA2* mutation carrier**



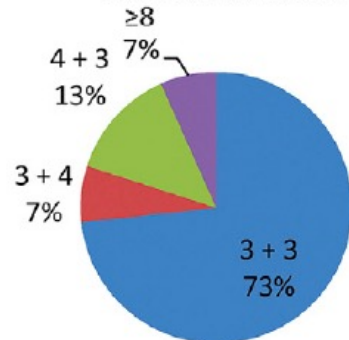
**Overall risk category—*BRCA2* mutation noncarrier**



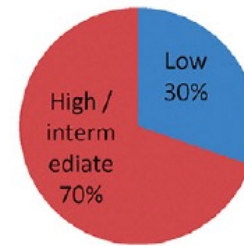
**Overall Gleason score -*BRCA2* mutation carrier**



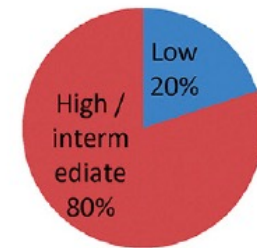
**Overall Gleason score—*BRCA2* mutation noncarrier**



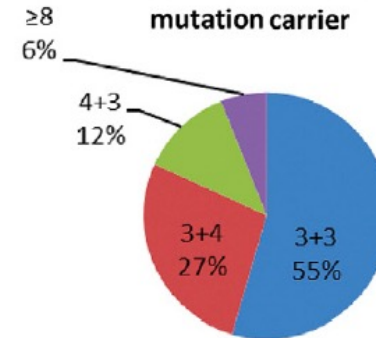
**Overall risk category—*BRCA1* mutation carrier**



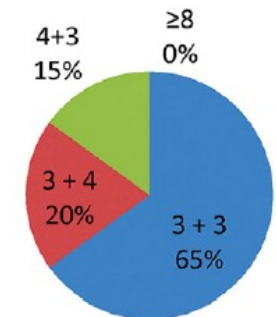
**Overall risk category—*BRCA1* mutation noncarrier**



**Overall Gleason score - *BRCA1* mutation carrier**



**Overall Gleason score—*BRCA1* mutation noncarrier**

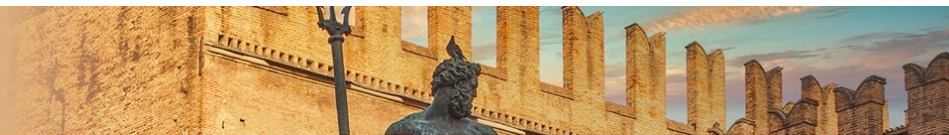


Page EC et al, EUROPEAN UROLOGY 76 ( 2019 ) 831 –842

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## Come monitorare l'efficacia dei trattamenti



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EUROPEAN UROLOGY 68 (2015) 186-193

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journal homepage: [www.europeanurology.com](http://www.europeanurology.com)

**EAU**  
European Association of Urology




Platinum Priority – Prostate Cancer  
Editorial by Ola Bratt and Niklas Loman on pp. 194-195 of this issue

**Effect of BRCA Mutations on Metastatic Relapse and Cause-specific Survival After Radical Treatment for Localised Prostate Cancer**

1302 patients with local/locally advanced PCa  
67 BRCA carriers  
RP for 535 patients (35 BRCA)  
RT for 767 patients (32 BRCA)  
Median follow-up was 64 mo.



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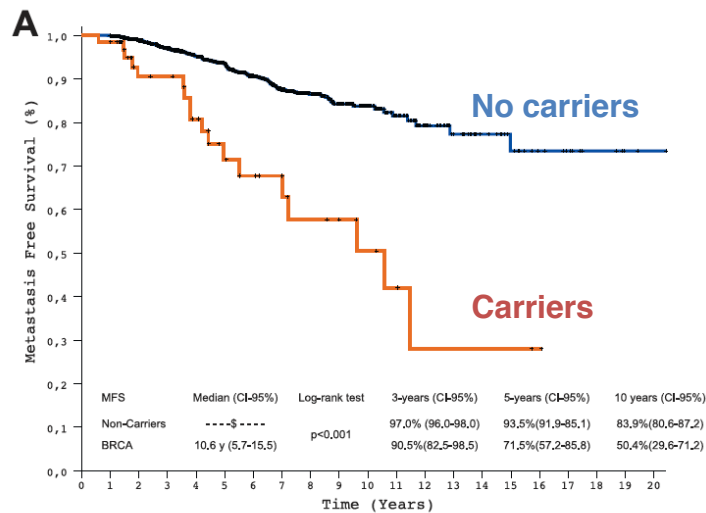
Page EC et al, EUROPEAN UROLOGY 68 ( 2015 ) 186-193

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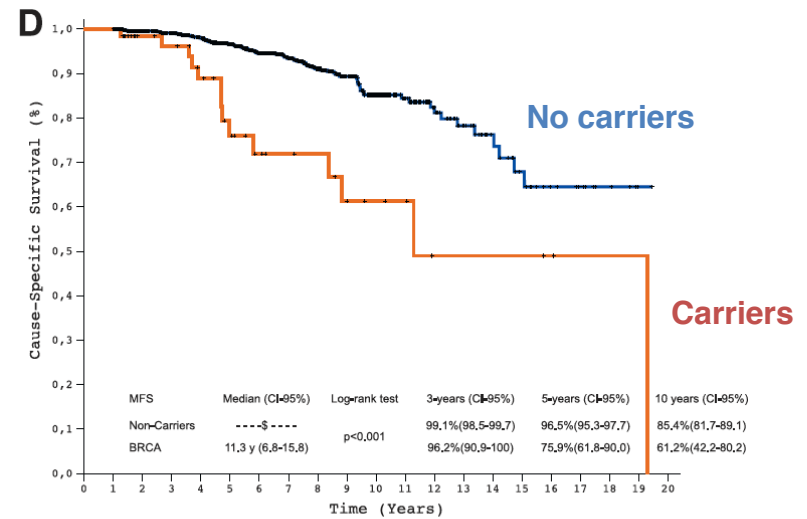


### Effect of BRCA Mutations on Metastatic Relapse and Cause-specific Survival After Radical Treatment for Localised Prostate Cancer



Patients at Risk	Baseline	3 years	5 years	8 years	10 years	12 years	15 years	20 years
Non-Carriers	1235	865	646	285	140	57	18	1
BRCA	67	39	20	12	7	2	1	0

1302 patients with local/locally advanced PCa  
 67 BRCA carriers  
 RP for 535 patients (35 BRCA)  
 RT for 767 patients (32 BRCA)  
 Median follow-up was 64 mo.



Patients at Risk	Baseline	3 years	5 years	8 years	10 years	12 years	15 years	20 years
Non-Carriers	1235	889	675	316	154	67	21	1
BRCA	67	43	22	12	8	3	2	0

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# I pazienti con mutazione germinale di BRCA1-2 sottoposti a trattamenti locali con intento radicale con assenza di malattia dovrebbero essere sottoposti ad un follow up intensivo



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