

EAU26

LONDON, GB

13-16 March 2026

Cutting-edge Science at
Europe's largest Urology Congress



Impact of Germline Mutations in Homologous Recombination Genes on Efficacy of Radium-223 in mCRPC: Results from PRORADIUM study

González GineLL., de Velasco G., Romero-Laorden N., Lozano R., Tello D., Conteduca V., Ovejero M., Villa-Guzman J.C., Villatoro R., Puente J., Esteban J., Almagro E., Gómez A., Sanz S., Herrera B., Rodríguez-Antolín A., Castellanos D., Lorente D., Olmos D., Castro E.

AM26-4358

 **ibima** Instituto de Investigación
Biomédica de Málaga

cnio stop cancer

 Instituto de Salud
Carlos III

i+12
Instituto de Investigación
Hospital 12 de Octubre

Cris
contra el cáncer

 Prostate Cancer
Foundation
Curing Together.

 **BAYER**

 **EAU** European
Association
of Urology

Conflict of Interest Disclosure

- This work was supported by funding from Bayer

INTRODUCTION

Ra233 → alpha-emission → DNA double-strand breaks (DSBs) → HR-mediated repair¹.



mCRPC with pathogenic **germline** mutations in **HR genes** (gHR+) **compromise** this repair **mechanism** and are associated a **poorer outcomes**².

Retrospective studies: Radium-223 (Ra223) in mCRPC → **improved outcomes** when germline and somatic **HR alterations** → Prospective validation³.

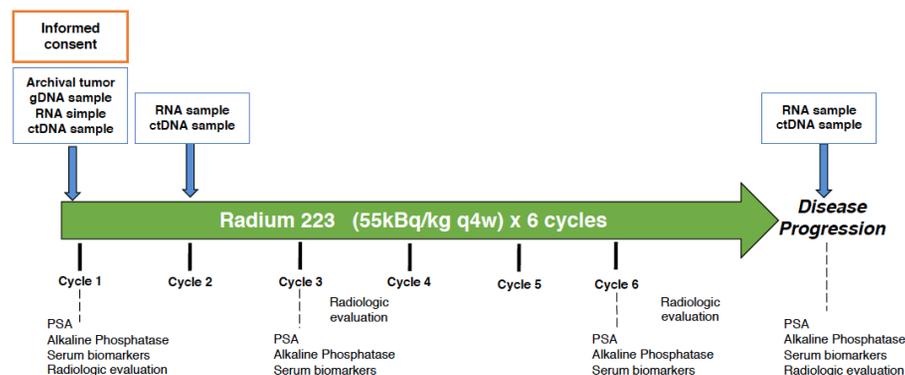
OBJECTIVE

Prospectively assess the predictive value of germline HR gene mutations on clinical outcomes following Ra223 treatment in mCRPC patients.

MATERIALS & METHODS

PRORADIUM (NCT022925702) is a **prospective**, multicentre, **observational cohort study** of mCRPC patients treated with standard-of-care **Ra223**.

169 participants underwent comprehensive **germline genetic testing** for **DNA damage repair pathway mutations** via targeted multigene panel sequencing.



- Primary endpoint: **alkaline phosphatase (ALP) response** ($\geq 30\%$ decline from baseline) at **12 weeks**.
- Secondary endpoints: PSA response rate at 12 weeks ($\geq 50\%$ decline from baseline), Time to PSA progression (TTPP), clinical and radiographic progression free survival (cPFS and rPFS) and cause specific survival (CSS) from treatment with Radium.

RESULTS

Baseline characteristics of patients

	gHR -	gHR+	p-value
Age at Ra223, years			0.040
Median (range)	75.0 (48.0-90.6)	67.5 (45.7-86.3)	
ECOG, n (%)			0.200
ECOG 0	33 (21.4%)	1 (6.7%)	
ECOG 1	99 (64.3%)	11 (73.3%)	
ECOG 2	22 (14.3%)	3 (20.0%)	
N° Prior treatment lines for mCRPC			0.230
0-1 line	57 (37%)	11 (73.3%)	
2 lines	60 (38.9%)	2 (13.3%)	
3 lines	29 (18.8%)	2 (13.3%)	
4 lines	8 (5.2%)		
Prior Taxane or Prior NHA			0.230
Any of them	5 (3.4%)	1 (6.7%)	
Prior NHA	50 (32.5%)	6 (40.0%)	
Prior taxane	9 (5.8%)	2 (13.3%)	
Prior NHA and Taxane	90 (58.4%)	6 (40.0%)	
Bone Pain at baseline			0.360
No	41 (26.6%)	2 (9.1%)	
Yes	113 (73.4%)	13 (86.7%)	
Bone disease extension			0.220
Low volume	30 (19.5%)	6 (40%)	
Intermediate volume	106 (68.8%)	7 (46.7%)	
High volumen/Superscan	18 (11.7%)	2 (13.3%)	
Lymph nodes extension			1.000
No	115 (74.7%)	11 (73.3%)	
Yes	38 (25.3%)	4 (26.7%)	
Baseline PSA, ng/mL			0.445
Median (range)	61.4 (0.03-1670)	122.2 (1.8-1300)	
Baseline ALP, U/L			0.415
Normal	72 (46.7%)	5 (35.7%)	
>UNL	81 (52.6%)	9 (64.3%)	
Missing	2	1	
Baseline LDH, U/L			0.443
Normal	68 (44.1%)	7 (58.3%)	
>UNL	75 (48.7%)	5 (41.7%)	
Missing	11	3	
Baseline Albumin			1.000
≥ 3.5 g/dL	114 (74.1%)	11 (84.6%)	
< 3.5 g/dL	20 (12.9%)	2 (15.4%)	
Missing	20	2	
Baseline Haemoglobin			0.893
≥ 12 g/dL	100 (64.9%)	10 (66.7%)	
<12 g/dL	54 (35.1%)	5 (33.3%)	

59.2%
≥5 cyc.
Rad233

15/169 patients gHR+ (8.8%)

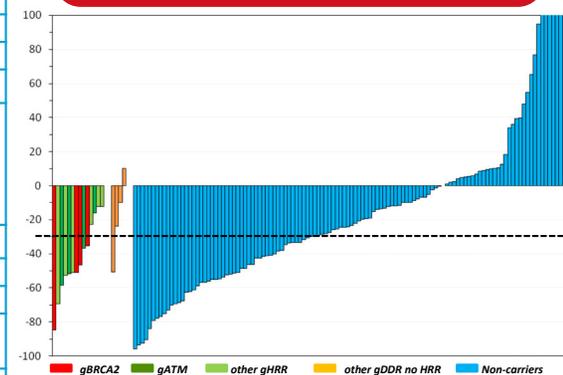
5 BRCA2
4 ATM
1 BRCA1
1 CHEK2
1 BRCA1+CHEK2
1 BRIP1
1 NBN
1 BLM

Responses to Ra223 by gHR status

	gHR -	gHR +	p-value
ALP response @t 12 weeks	n=124	n=14	
ALP50	30 (24.2%)	7 (50.0%)	0.055
ALP30	49 (39.5%)	10 (71.4%)	0.022
ALP conversion @t 12 weeks			
Normal	51 (41.1%)	5 (35.7%)	
>UNL to normal	19 (15.3%)	4 (28.6%)	0.953
Normal to >UNL	10 (8.1%)	0	
>UNL	44 (35.5%)	5 (35.7%)	
Best ALP response	n=124	n=14	
ALP50	40 (32.3%)	7 (50.0%)	0.232
ALP30	64 (51.7%)	10 (71.4%)	0.142
ALP conversion @t any time			
Normal	51 (41.1%)	5 (35.7%)	
>UNL to normal	19 (15.3%)	4 (28.6%)	0.953
Normal to >UNL	10 (8.1%)	0	
>UNL	44 (35.5%)	5 (35.7%)	
PSA response 12 weeks	n=126	n=11	
PSA50	8 (6.3%)	1 (9.1%)	0.540
PSA30	13 (10.3%)	2 (18.2%)	0.344
Best confirmed PSA response	n=131	n=11	
PSA50	14 (11.2%)	2 (18.2%)	0.358
PSA30	24 (18.3%)	2 (18.2%)	1.000

TTP, rPFS and cPFS
↓
similar in both groups

≥30% decline in ALP in
71.4% of gHR+ vs
39.5% gHR- (p=0.022)

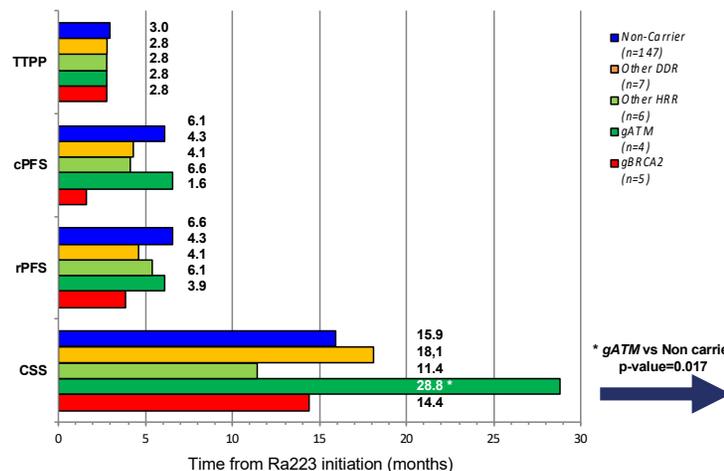
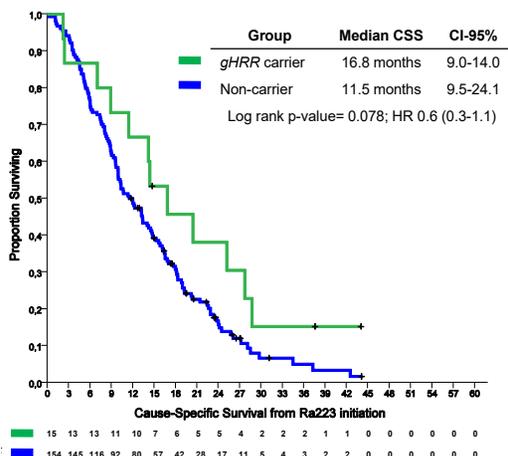


Change in ALP levels at 12 weeks by HR status

RESULTS

Cause-specific survival by gHR status

Trend to improved CSS in gHR+ (16.8 vs 11.5 m, p=0.078)



CSS ↑ in gATM (28.8 vs 15.9 m, p=0.017)

CONCLUSIONS

Germline HR mutations were associated with improved ALP response and a trend towards more prolonged cause specific survival, suggesting a benefit from Ra223 in some gHR+ patients, particularly those with germline ATM mutations.

These findings support further investigation of HR gene status as a predictive biomarker for Ra223 response in mCRPC.