Abstract Session 31 - Systemic treatment of metastatic prostate cancer
Sunday 23 March 2025, 13:45 - 15:15, Purple Area, Room 2

EAU25
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Europe's largest Urology Congress

Impact of bone protecting agents on the efficacy and safety of enzalutamide vs combination of Radium-223 and enzalutamide in asymptomatic or mildly symptomatic patients with bone metastatic castration-resistant prostate cancer (mCRPC): safety analysis from EORTC-GUCG 1333/PEACE-3, an EORTC/CTI/CUOG/LACOG/UNICANCER randomized phase III study

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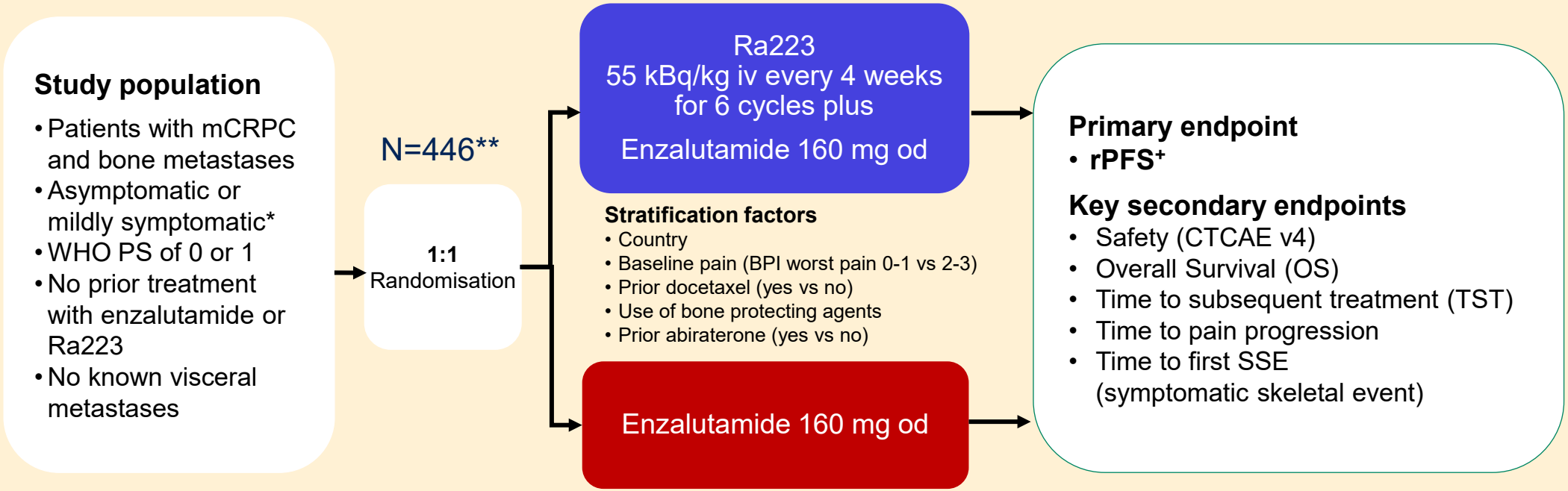
Disclosures:

- **Consulting or advisory roles:** AbbVie, Astellas, AstraZeneca, Bayer, Janssen, Knight, Myovant, Novartis, Pfizer, Sanofi
- **Honoraria:** AbbVie, Astellas, AstraZeneca, Bayer, Bristol Myers Squibb, Janssen, Knight, Merck, Novartis, Pfizer, Sanofi
- **Research funding to institution: Abbvie,** Astellas, AstraZeneca, Bayer, Bristol Myers Squibb, Janssen, Merck, Novartis, Pfizer, Sanofi

PEACE-3 STUDY DESIGN



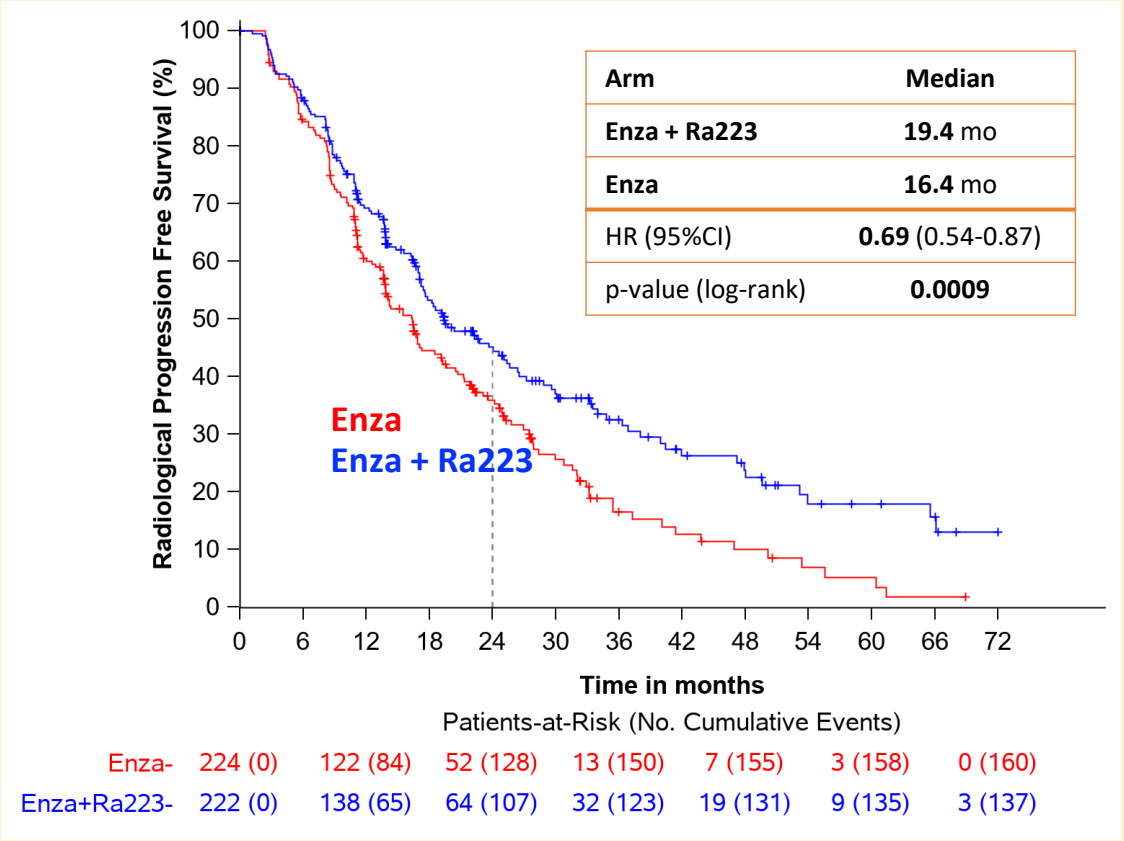
*defined as brief pain inventory WP24 score < 4
** original target accrual N=560, adapted for slow accrual
*** of these 119, four patients did not start protocol treatment

+ rPFS = radiological progression free survival by investigator assessment according to modified Prostate Cancer Working Group 3 (PCWG3) criteria

On 18 MAR 2018, with 119 = 27% of 446 patients enrolled, an urgent safety letter (USL) made co-administration of zoledronic acid or denosumab obligatory.***

Top line RESULTS

Primary endpoint: rPFS

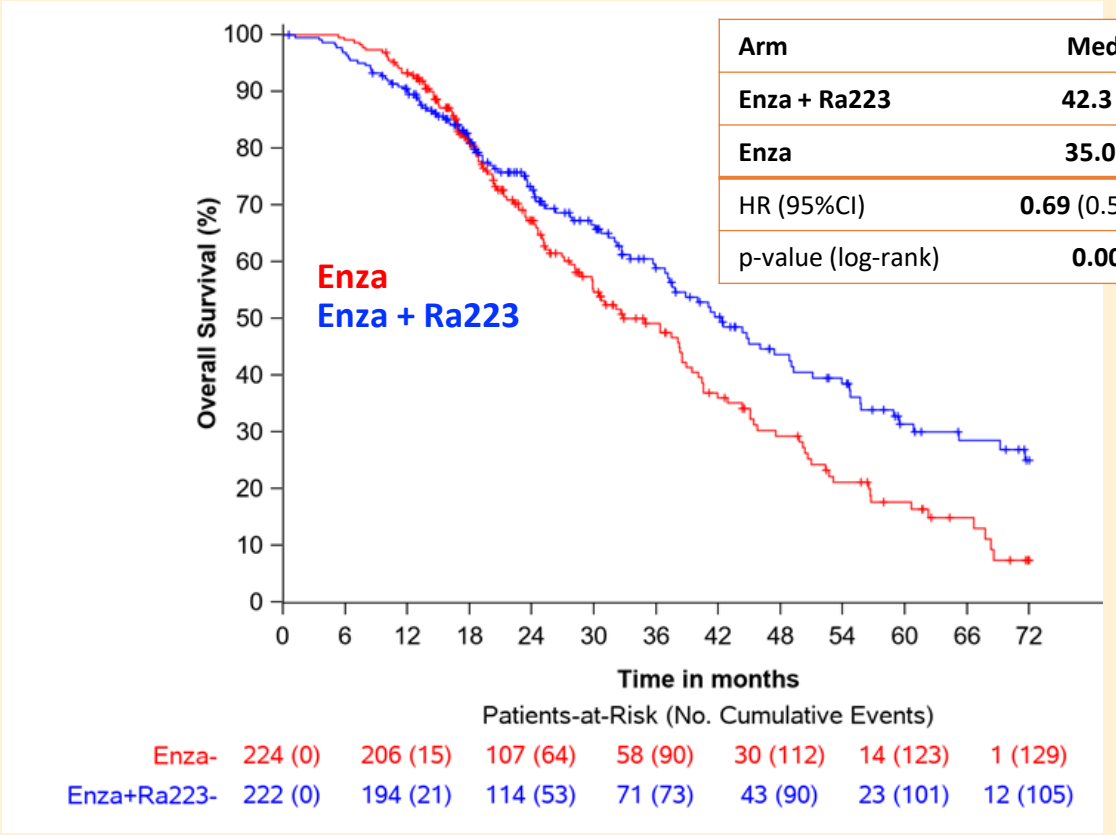


Arm	Median
Enza + Ra223	**19.4** mo
Enza	**16.4** mo
HR (95%CI)	**0.69** (0.54-0.87)
p-value (log-rank)	**0.0009**

Patients-at-Risk (No. Cumulative Events)

Enza-	224 (0)	122 (84)	52 (128)	13 (150)	7 (155)	3 (158)	0 (160)
Enza+Ra223-	222 (0)	138 (65)	64 (107)	32 (123)	19 (131)	9 (135)	3 (137)

Secondary endpoint: OS
(interim analysis at 80% of events)

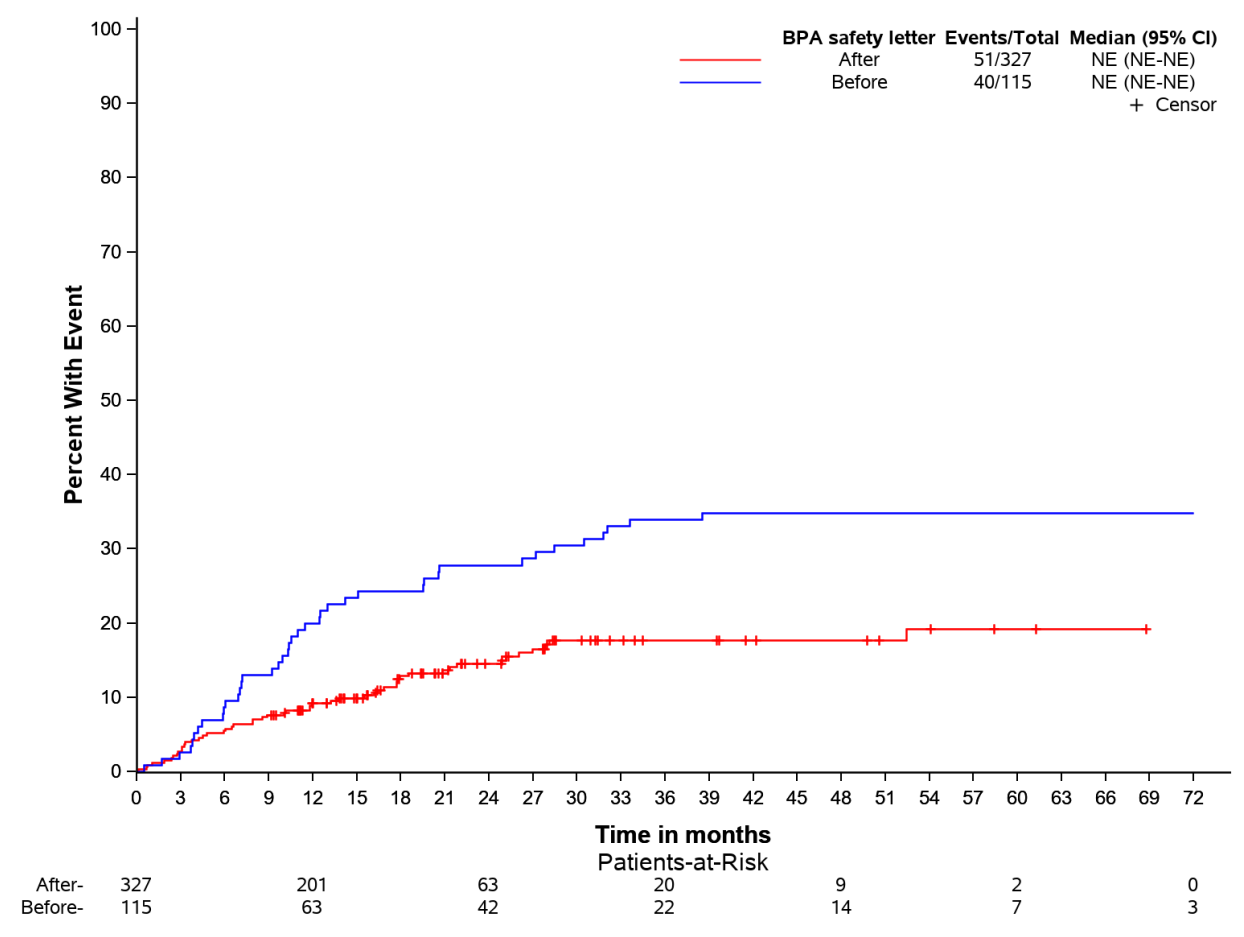


Arm	Median
Enza + Ra223	**42.3** mo
Enza	**35.0** mo
HR (95%CI)	**0.69** (0.52-0.90)
p-value (log-rank)	**0.0031**

Patients-at-Risk (No. Cumulative Events)

Enza-	224 (0)	206 (15)	107 (64)	58 (90)	30 (112)	14 (123)	1 (129)
Enza+Ra223-	222 (0)	194 (21)	114 (53)	71 (73)	43 (90)	23 (101)	12 (105)

Fracture rate before and after Urgent Safety Letter (USL)



Fracture incidence

Prior USL		After USL	
36.5% (42/115)		**12.5% (41/327)**	
Enza+Rad223	Enza	Enza+Rad223	Enza
53.6% (30/56)	20.3% (12/59)	14.2% (23/162)	10.9% (18/165)

Prior USL: BPA allowed but no recommendation given.
After USL: BPA mandatory at time of randomization (ie. before treatment start)

Objective

The objective of the present analysis was to determine long term efficacy of the treatment in the subgroup of patients who were treated with or without BPA prior to the Urgent Safety Letter (USL)

Materials and Methods

- A total of 119 patients were enrolled prior to the USL.
- Of those, 115 received protocol treatment (either Enzalutamide or Ra223) and are included in this analysis.
  - 59 (51%) received either no BPA or only after a fracture
  - 56 (49%) received BPA prior and/or during study treatment.
- Efficacy outcomes included rPFS and overall survival (OS).

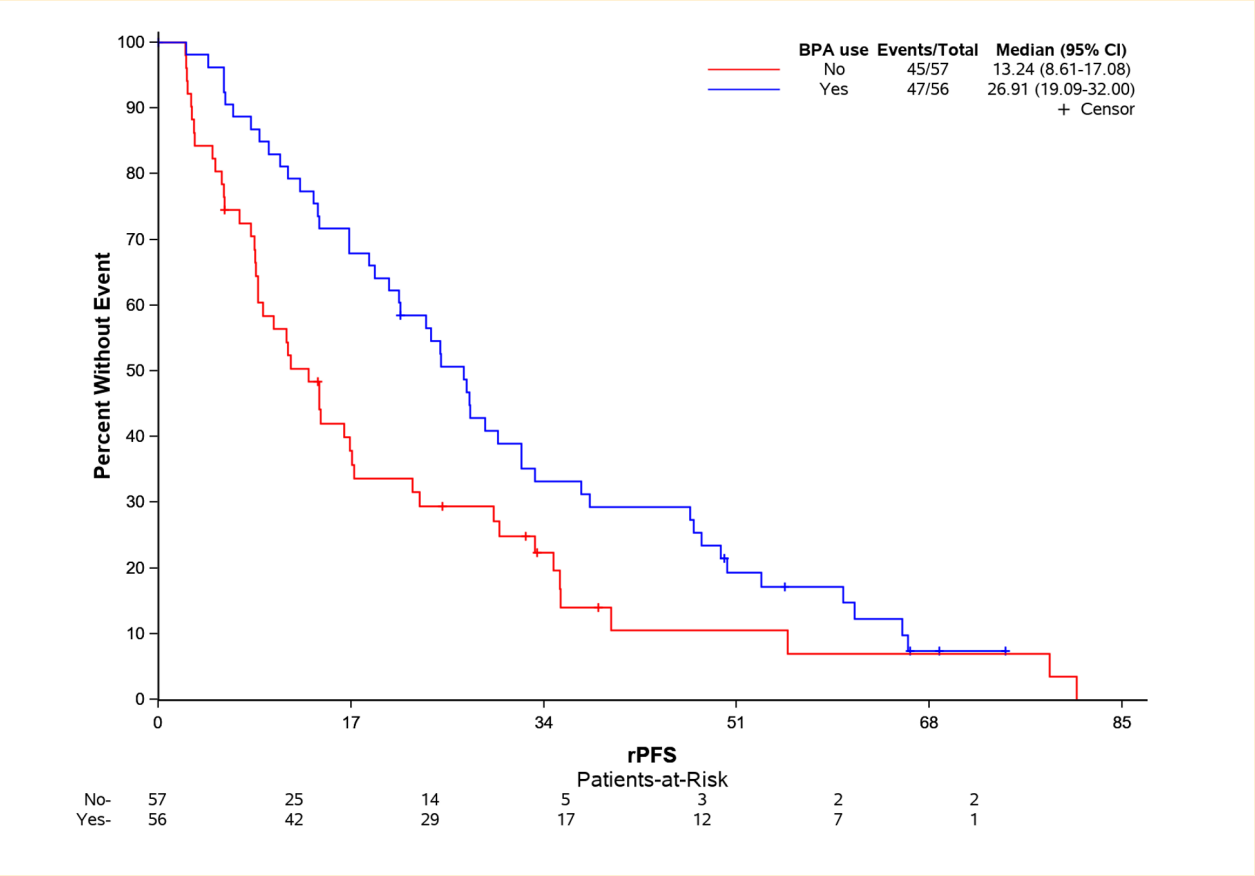
Baseline Demographics

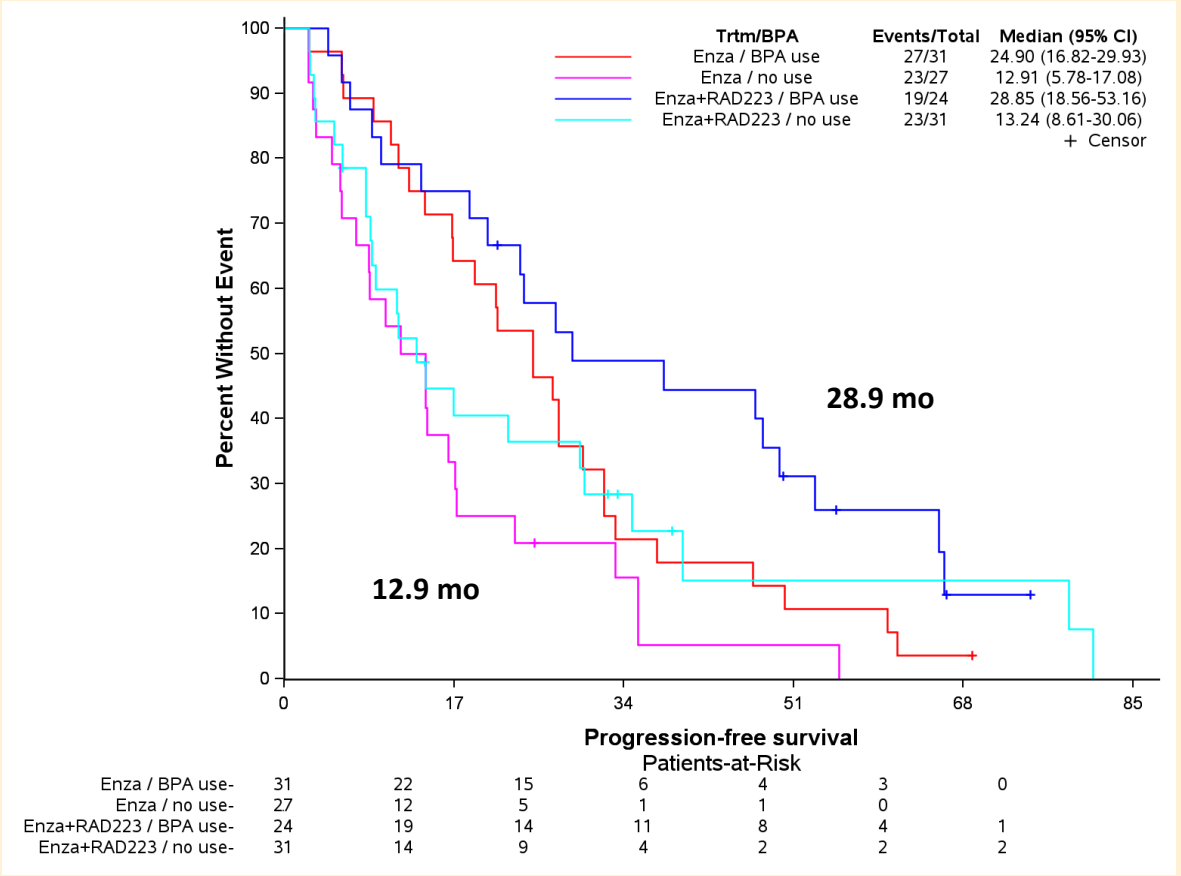
		No BPA use		Any BPA use	
		Enza+RAD223 (N=31)	Enza (N=28)	Enza+ RAD223 (N=25)	Enza (N=31)
Age	Median	72.0	74.0	69.0	74.0
	Range	53.0 - 88.0	57.0 - 88.0	50.0 - 83.0	48.0 - 84.0
WHO Performance status	0	18 (58.1)	17 (60.7)	18 (72.0)	24 (77.4)
	1	13 (41.9)	10 (35.7)	6 (24.0)	7 (22.6)
Charlson Comorbidity Index	0	17 (54.8)	13 (46.4)	18 (72.0)	17 (54.8)
	1	10 (32.3)	9 (32.1)	4 (16.0)	9 (29.0)
	2	3 (9.7)	3 (10.7)	2 (8.0)	4 (12.9)
	3	1 (3.2)	3 (10.7)	1 (4.0)	1 (3.2)
Extra-skeletal disease at baseline	Yes	14 (45.2)	13 (46.4)	8 (32.0)	8 (25.8)
Gleason score ≥ 8	≥ 8	19 (61.3)	21 (75.0)	10 (40.0)	21 (67.7)
Prior docetaxel	Yes	6 (19.4)	3 (10.7)	2 (8.0)	5 (16.1)

Results: rPFS based on use of BPA

rPFS longer by 14 mo

(HR=0.60 95%CI=0.39-0.93)



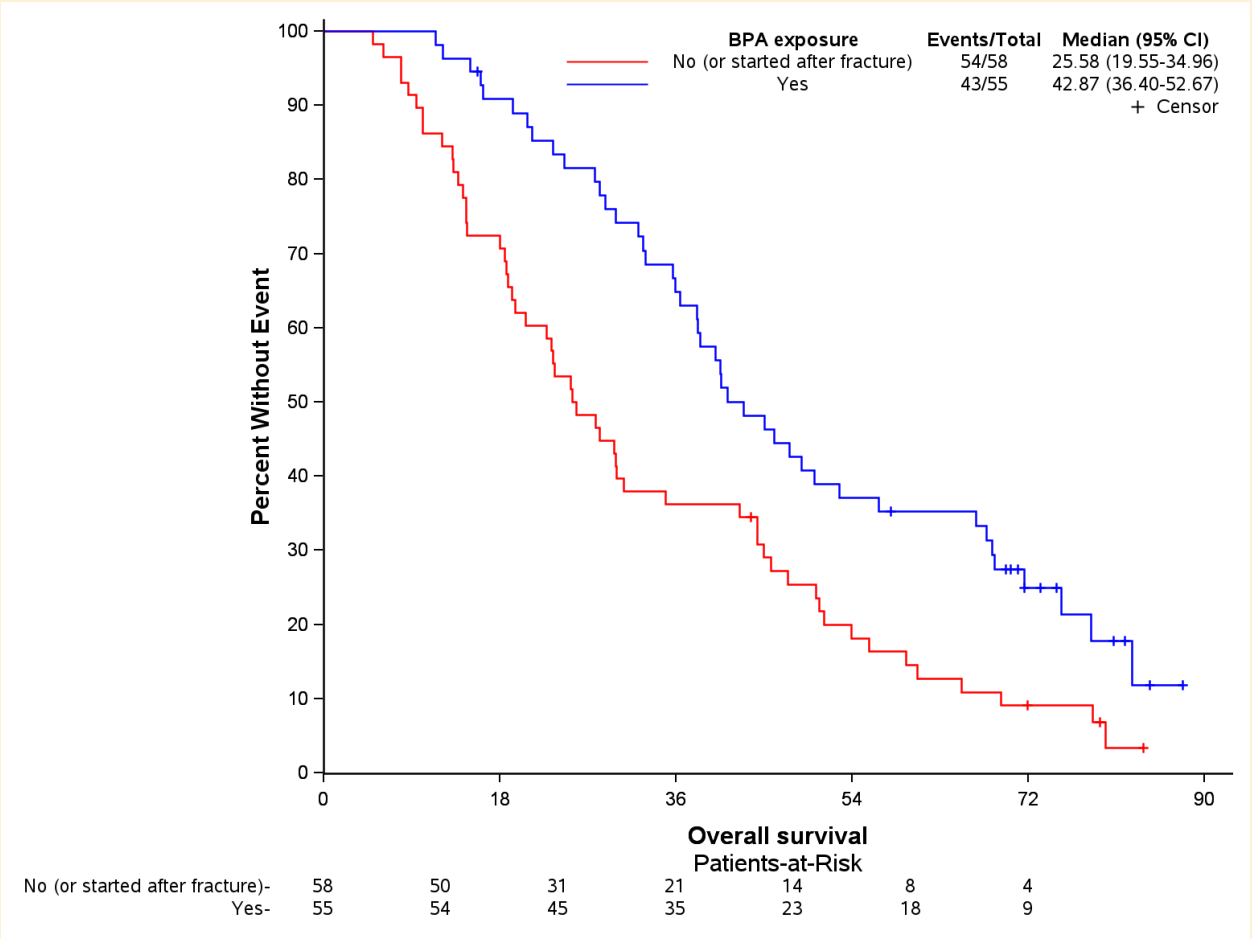


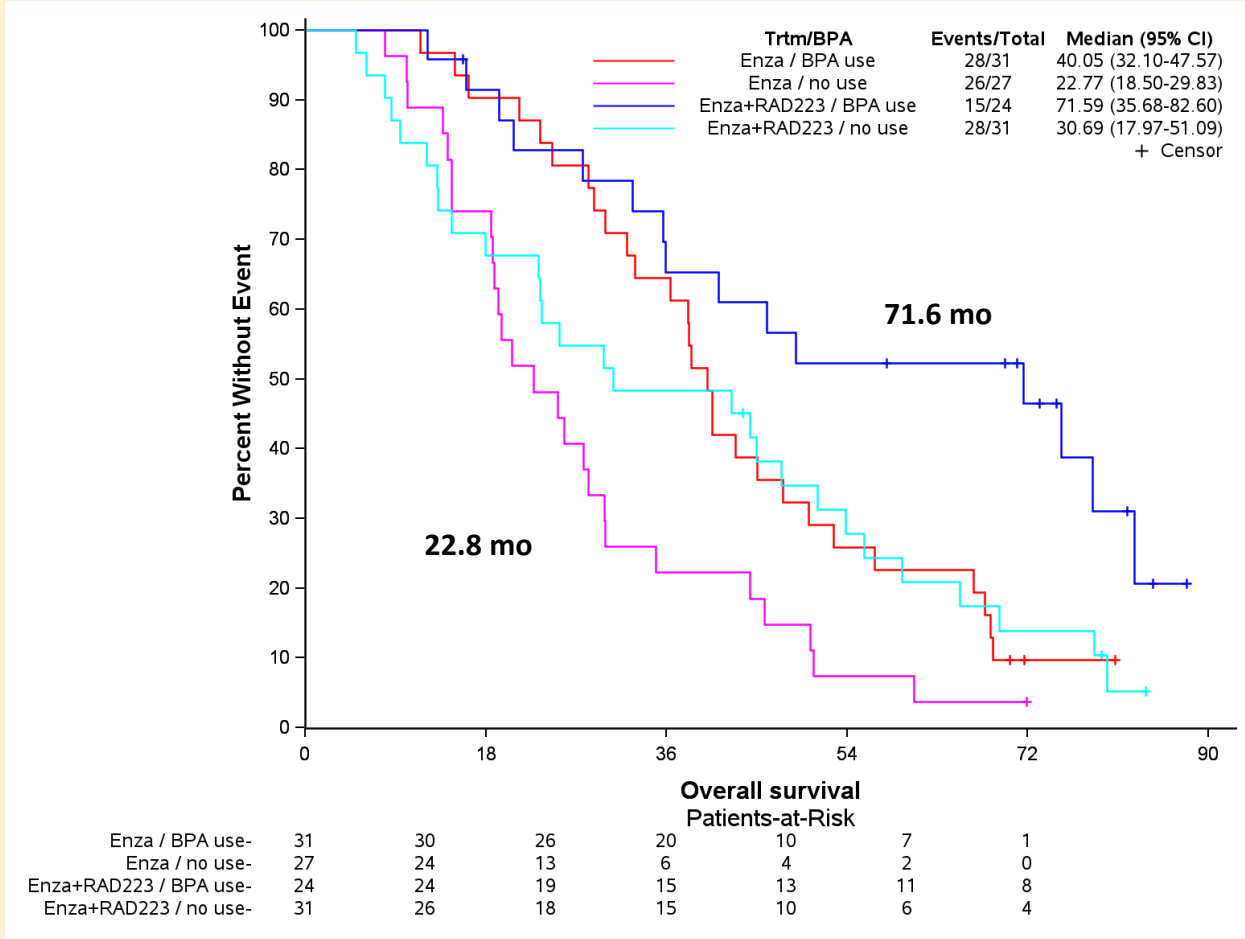
confidence intervals overlap and small samples require caution in interpretation

RESULTS: Overall Survival

Median OS longer by 17 mo

(HR=0.56 95%CI=0.37-0.86)





confidence intervals overlap and small samples require caution in interpretation

Safety

	No BPA	Any BPA
	N=59	N=56
Fracture rate	29 (49.2%)	13 (23.2%)
Nbr of fractures		
None	30 (50.8%)	43 (76.8%)
1	21 (35.6%)	9 (16.1%)
2 or more	8 (13.5%)	4 (7.1%)

	No BPA (N=59)		Any BPA (N=56)	
CTCAE SOC	**Grade ≥3 N (%)**	**Any grade N (%)**	**Grade ≥3 N (%)**	**Any grade N (%)**
PATIENTS' WORST GRADE	**45 (76.3)**	**57 (96.6)**	**39 (69.6)**	**56 (100.0)**
VASCULAR DISORDERS	24 (40.7)	40 (67.8)	29 (51.8)	46 (82.1)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	6 (10.2)	43 (72.9)	9 (16.1)	37 (66.1)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	6 (10.2)	41 (69.5)	1 (1.8)	42 (75)
INVESTIGATIONS	6 (10.2)	35 (59.3)	1 (1.8)	31 (55.4)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	6 (10.2)	25 (42.4)		9 (16.1)
NERVOUS SYSTEM DISORDERS	6 (10.2)	22 (37.3)	7 (12.5)	21 (37.5)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	6 (10.2)	9 (15.3)	1 (1.8)	4 (7.1)
GASTROINTESTINAL DISORDERS	5 (8.5)	28 (47.5)	3 (5.4)	25 (44.6)
INFECTIONS AND INFESTATIONS	5 (8.5)	23 (39)	3 (5.4)	21 (37.5)
RENAL AND URINARY DISORDERS	5 (8.5)	17 (28.8)	1 (1.8)	7 (12.5)

Conclusion

- In the overall population rPFS was significantly improved with the addition of radium-223 to enzalutamide
- BPA use led to a 14-month improvement in rPFS (HR=0.60 95%CI=0.39-0.93)
  - Similar advantage in both arms
  - ENZ-RAD with BPA had a median rPFS of 28.9 mo *vs.* 12.9 mo for ENZ arm without BPA.
- BPA use led to a 17-month improvement in OS (HR=0.56 95%CI=0.37-0.86)
  - Similar advantage in both arms
  - ENZA-RAD with BPA had a median OS of 71.6 mo vs 22.8 mo for ENZ without BPA
- These exploratory findings suggest that BPA in combination with life prolonging therapeutic options in mCRPC is safe and may provide additional therapeutic benefit