

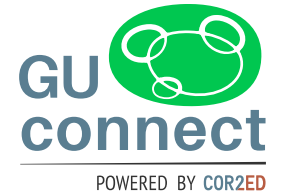
POWERED BY COR2ED



# **AN UPDATE ON THE TREATMENT OF PATIENTS WITH mCRPC WITH RA-223 PLUS AAP**

**Dr. Tia Higano**  
**University of Washington**  
**Seattle, USA**

# DISCLAIMER



Please note: The views expressed within this presentation are the personal opinions of the author. They do not necessarily represent the views of the author's academic institution or the rest of the GU CONNECT group.

This content is supported by an Independent Educational Grant from Bayer.

---

**ERA223: A PHASE 3 TRIAL OF  
Ra-223 IN COMBINATION WITH AAP  
FOR THE TREATMENT OF ASYMPTOMATIC  
OR MILDLY SYMPTOMATIC CHEMOTHERAPY-  
NAÏVE PATIENTS WITH BONE-  
PREDOMINANT mCRPC**

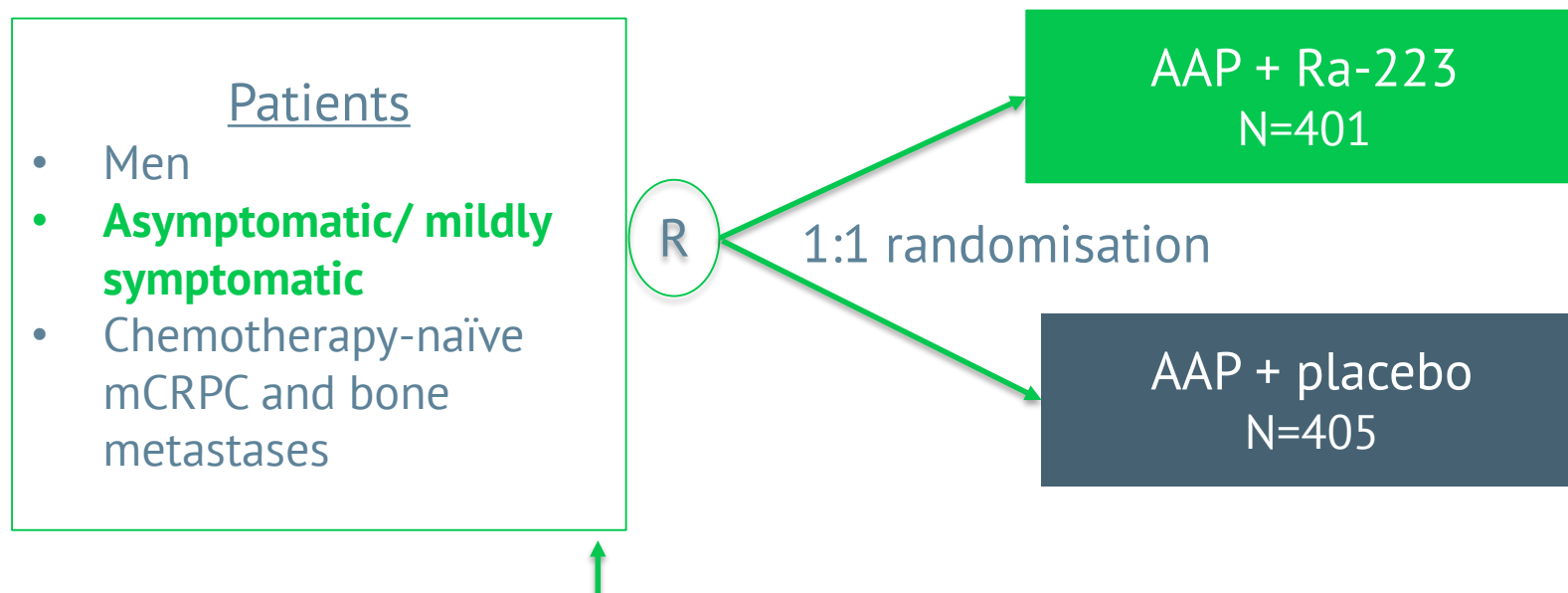
MR. Smith. Abstract LBA30

# ERA223 BACKGROUND

- AAP improves PFS and OS in men with mCRPC
- Ra-223 increases OS and decreases SSEs in men with mCRPC and bone metastases
- The results of ERA223, a study that evaluated concurrent treatment with AAP and Ra-223 are reported and commented upon

# ERA223 STUDY DESIGN

- Study name: ERA223
- Phase 3, double-blind, randomised
- Primary endpoint: **SSE-FS**



**Bone health agents** (bisphosphonates or denosumab) were **only allowed in patients receiving them at baseline**

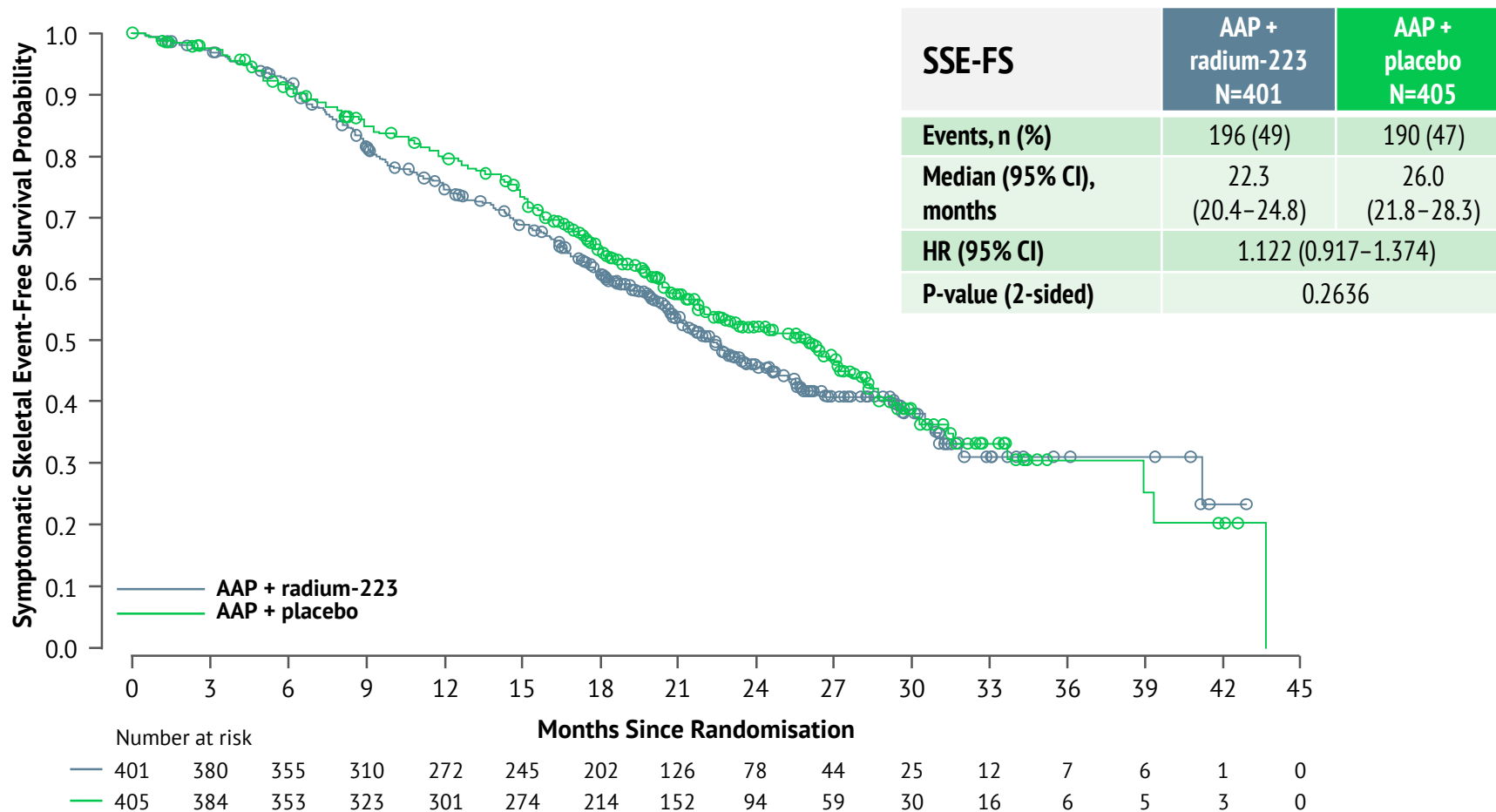
AAP, Abiraterone Acetate and Prednisone/Prednisolone; mCRPC, metastatic Castration-Resistant Prostate Cancer;

R, Randomisation; Ra-223, Radium-223; SSE-FS, Symptomatic Skeletal Events-Free Survival

Smith MR. ESMO 2018, Abstract LBA30

# ERA223 PRIMARY ENDPOINT

## SSE-FS (ITT)

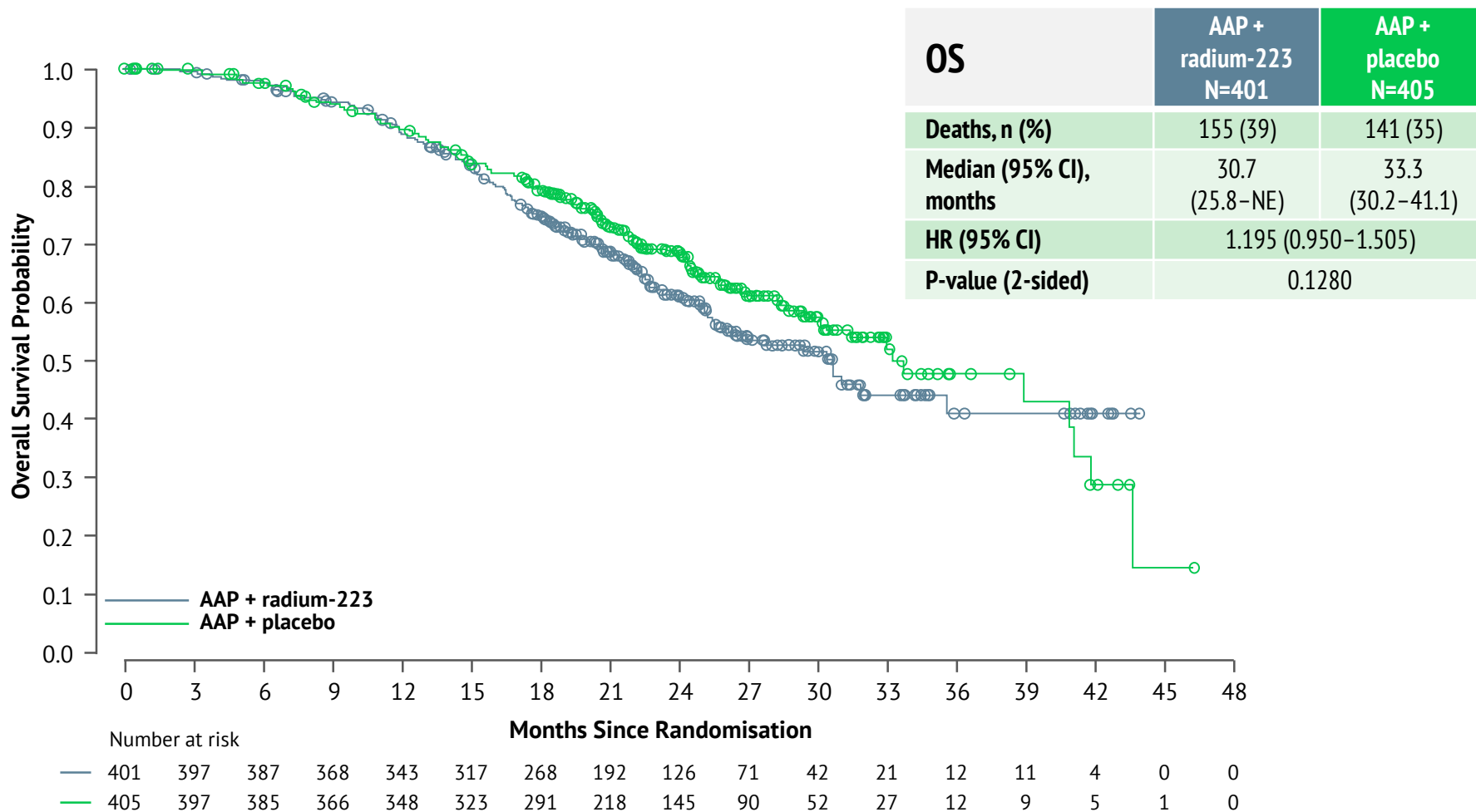


AAP, Abiraterone Acetate and Prednisone/Prednisolone; CI, Confidence Interval.; HR, Hazard's Ratio; ITT, intention-to-treat; mCRPC, metastatic Castration-Resistant Prostate Cancer; Ra-223, Radium-223; SSE-FS, Symptomatic Skeletal Events-Free Survival

Smith MR. ESMO 2018, Abstract LBA30 and presentation

# ERA223 SECONDARY ENDPOINT

## OS (ITT)



AAP, Abiraterone Acetate and Prednisone/Prednisolone; CI, Confidence interval; HR, Hazard's Ratio; ; ITT, Intention-To-Treat; mCRPC, metastatic Castration-Resistant Prostate Cancer; NE, Not Evaluable; OS, Overall Survival; Ra-223, Radium-223

Smith MR. ESMO 2018, Abstract LBA30 and presentation



# ERA223 MOST FREQUENT ADVERSE EVENTS

TEAEs in ≥15% of patients in either group, n (%)	AAP + radium-223 N=392			AAP + placebo N=394		
	All	Grade 3	Grade 4	All	Grade 3	Grade 4
Back pain	133 (34)	23 (6)	0	121 (31)*	16 (4)	0
Fatigue	89 (23)	4 (1)	0	79 (20)	6 (2)	0
Arthralgia	80 (20)	4 (1)	0	75 (19)	5 (1)	0
Fracture†	103 (26)	35 (9)	1 (0.3)	38 (10)*	12 (3)	0
Hypertension	59 (15)	43 (11)	0	78 (20)	51 (13)	1 (0.3)
ALT increased	69 (18)	29 (7)	5 (1)	59 (15)	28 (7)	0
Constipation	56 (14)	1 (0.3)	0	72 (18)	0	0
Diarrhoea	65 (17)	4 (1)	0	60 (15)	7 (2)	0
Nausea	66 (17)	1 (0.3)	0	59 (15)	1 (0.3)	0
AST increased	61 (16)	18 (5)	1 (0.3)	53 (14)	16 (4)	0
Peripheral oedema	51 (13)	2 (0.5)	0	61 (16)	0	0
Anaemia	57 (15)	24 (6)	0	46 (12)	11 (3)	0

No grade 5 TEAEs reported in ≥10% of patients; \*Grade of severity missing for one patient; †Compound term for events of femoral neck, femur, humerus, lumbar vertebral, osteoporotic, pathological, radius, rib, spinal compression, stress, thoracic vertebral, tooth, traumatic and ulna fracture.

AAP, Abiraterone Acetate and Prednisone/Prednisolone; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; mCRPC, metastatic Castration-Resistant Prostate Cancer; Ra-223, Radium-223; TEAEs, Treatment-Emergent Adverse Events

# ERA223 FREQUENCY OF FRACTURES

<b>Frequency of fractures and use of BHAs</b>	<b>AAP + Ra-223 N=401, % patients</b>	<b>AAP + PBO N=405, % patients</b>
Use of BHAs at baseline	39%	42%
Fractures (all patients)	29%	11%
Fractures in patients receiving BHAs	15%	7%
Fractures in patients not receiving BHAs	37%	15%

AAP, Abiraterone Acetate and Prednisone/Prednisolone; BHAs, Bone health agents; mCRPC, metastatic Castration-Resistant Prostate Cancer; PBO, placebo; Ra-223, Radium-223

# ERA223 DISCUSSION

- The results of the comparison of AAP + Ra-223 versus AAP + placebo showing the combination therapy **did not improve SSE-FS or OS compared with monotherapy** were unexpected, given both AAP and Ra-223 have been shown to improve OS in mCRPC<sup>1</sup>
- In addition, there were **more bone fractures with combination treatment compared with monotherapy**
- When interpreting these results it is important to consider that **this trial studied Ra-223 concomitant with Abiraterone in the ‘first-line setting’ of mCRPC patients which is not where it has been used or studied previously**, for example in the ALSYMPCA trial<sup>2</sup>
- **BHAs were used in less than half the patients despite them being recommended** because of improvement in skeletal related events

# ERA223 CONCLUSIONS

- In mCRPC with bone metastases **BHAs should be used to prevent fractures**, both clinical and sub-clinical fractures
- **Radium-223 should be used as recommended** and not in combination with Abiraterone for treatment of mCRPC

REACH GU CONNECT VIA TWITTER,  
LINKEDIN, VIMEO AND EMAIL  
OR VISIT THE GROUP'S WEBSITE

<http://www.guconnect.info>



Follow us on Twitter  
[@guconnectinfo](https://twitter.com/guconnectinfo)



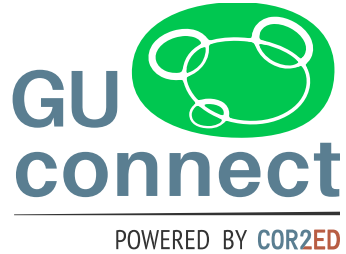
Join the  
[GU CONNECT](#)  
group on LinkedIn



Watch us on the  
Vimeo Channel  
[GU CONNECT](#)



Email  
[elaine.wills@cor2ed.com](mailto:elaine.wills@cor2ed.com)



GU CONNECT  
Bodenackerstrasse 17  
4103 Bottmingen  
SWITZERLAND

Dr. Antoine Lacombe  
Pharm D, MBA  
Phone: +41 79 529 42 79  
[antoine.lacombe@cor2ed.com](mailto:antoine.lacombe@cor2ed.com)

Dr. Froukje Sosef  
MD  
Phone: +31 6 2324 3636  
[froukje.sosef@cor2ed.com](mailto:froukje.sosef@cor2ed.com)

