

Features and benefits of ^{223}Ra radiopharmaceuticals for treatment of cancer

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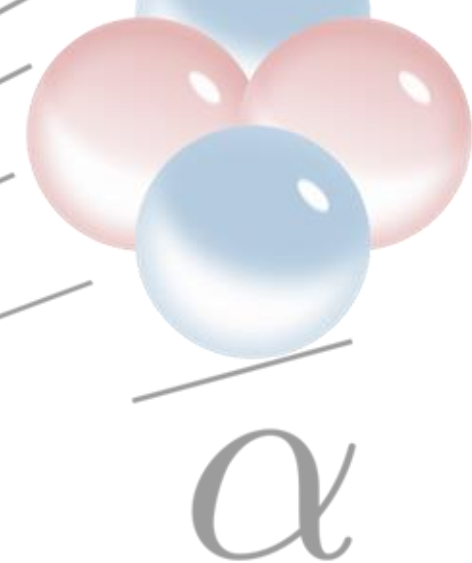
First international student symposium at Faculty of medical sciences 20th April 2016

What is Radium 223?

^{227}Ac
 β
21.8 y

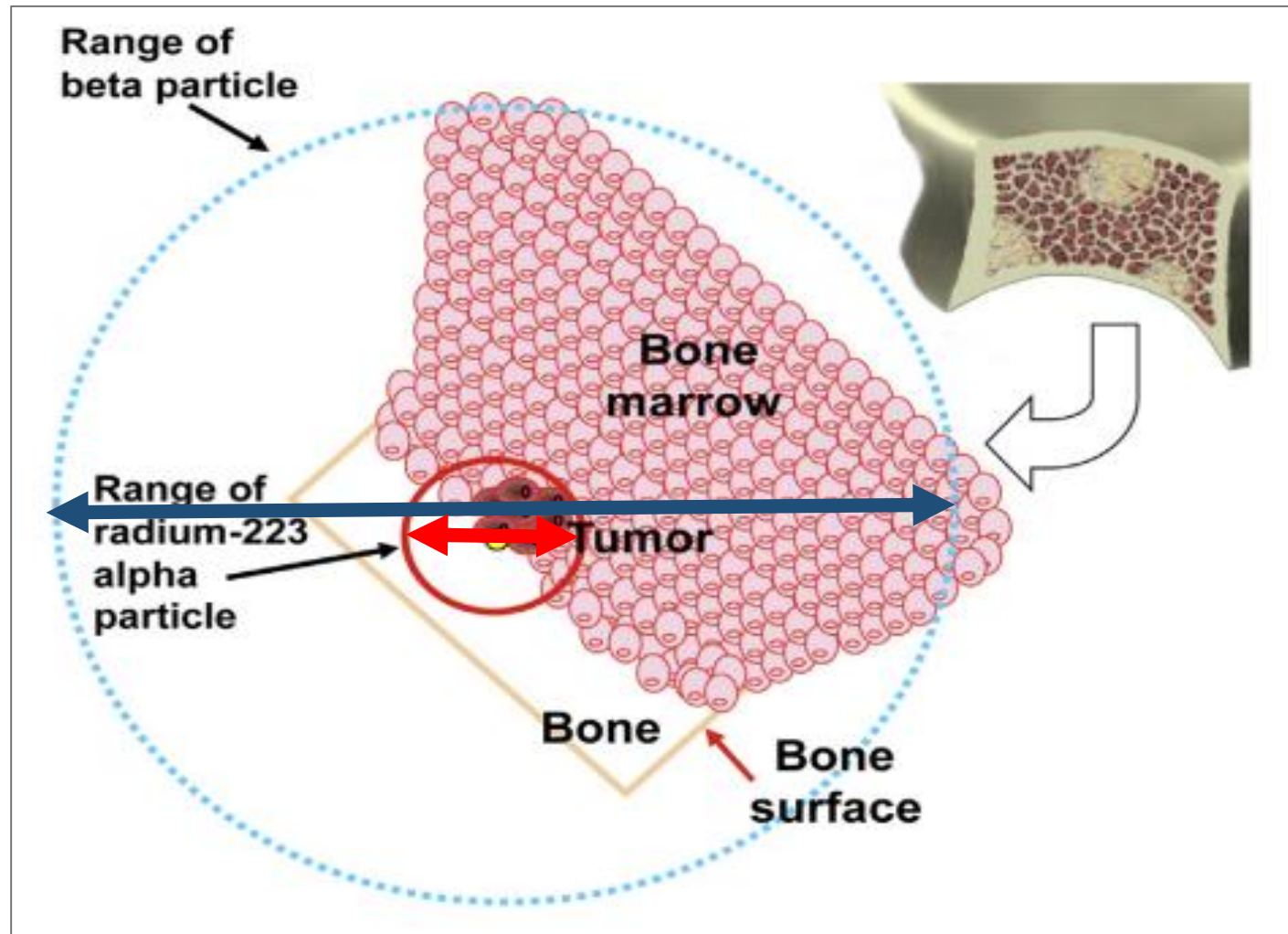
^{227}Th
 α
18.7 d

^{223}Ra
 α
11.4 d



Energy	α -energy 5,78 MeV
$t_{1/2}$	11,4 d
Parent nuclide	^{227}Ac
Radiopharmaceutical	$^{223}\text{RaCl}_2$
Usage	Prostate cancer Bone cancer

Mechanism of action of Radium-223





Clinical Trials

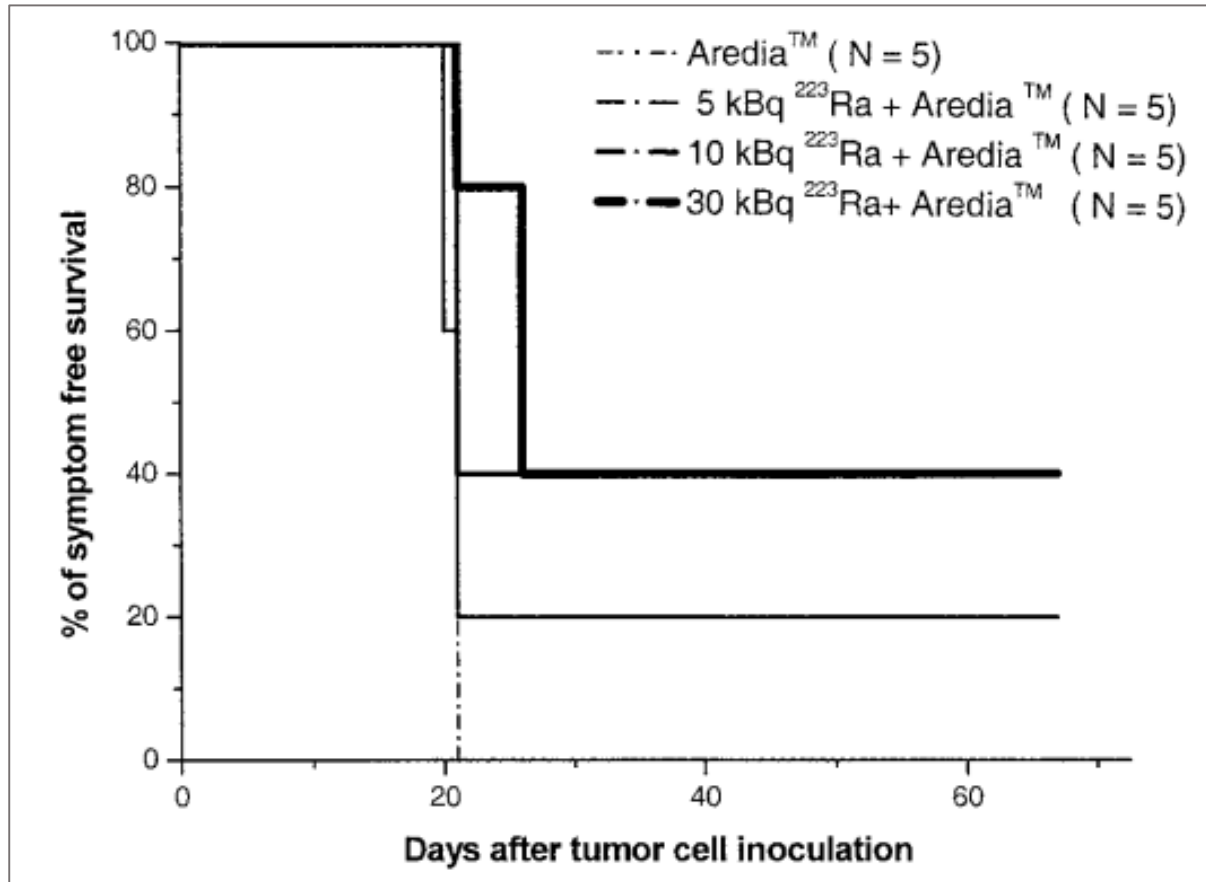
α

Biodistribution of radium-223 in Balb/C mice presented as % of injected dose per gram

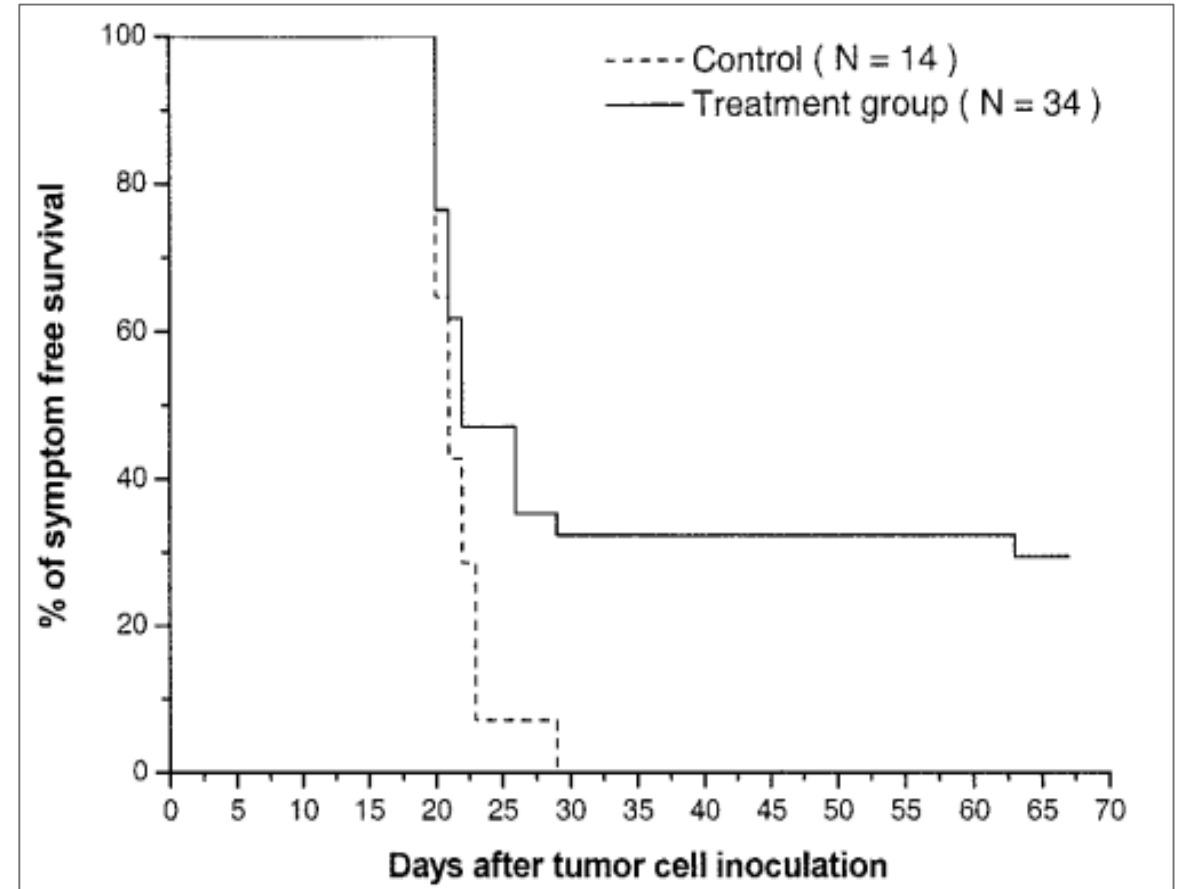
Tissue	6 hours	3 days
<u>femur</u>	25.86±1.99	34.55±7.87
blood	0.20±0.23	0.05±0.10
kidney	4.04±0.33	0.38±0.08
liver	0.89±0.18	0.22±0.32
lung	0.59±0.56	0.06±0.07
muscle	0.72±0.39	0.30±0.16
heart	0.10±0.10	0.06±0.07
brain	0.04±0.01	0.12±0.12
<u>spleen</u>	4.06±1.4	1.46±0,54
small intestine	0.79±0.26	0.04±0.03
large intestine	2.30±0.60	0.13±0.02

Henriksen, G, Larsen RH. The preparation and use of radium-223 to target calcified tissues for pain palliation, bone cancer therapy, and bone surface conditioning. Patent No. EP1140212 A2. 2001.

Antitumor Effect of ^{223}Ra in rats

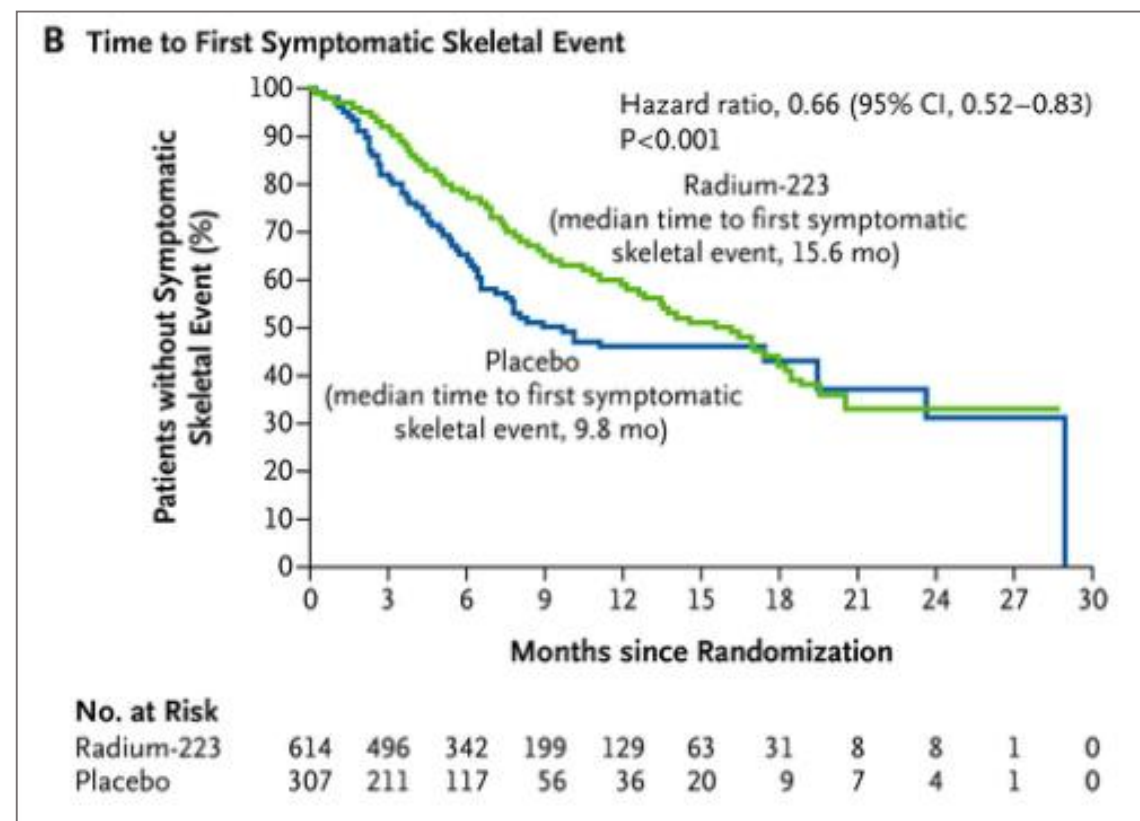
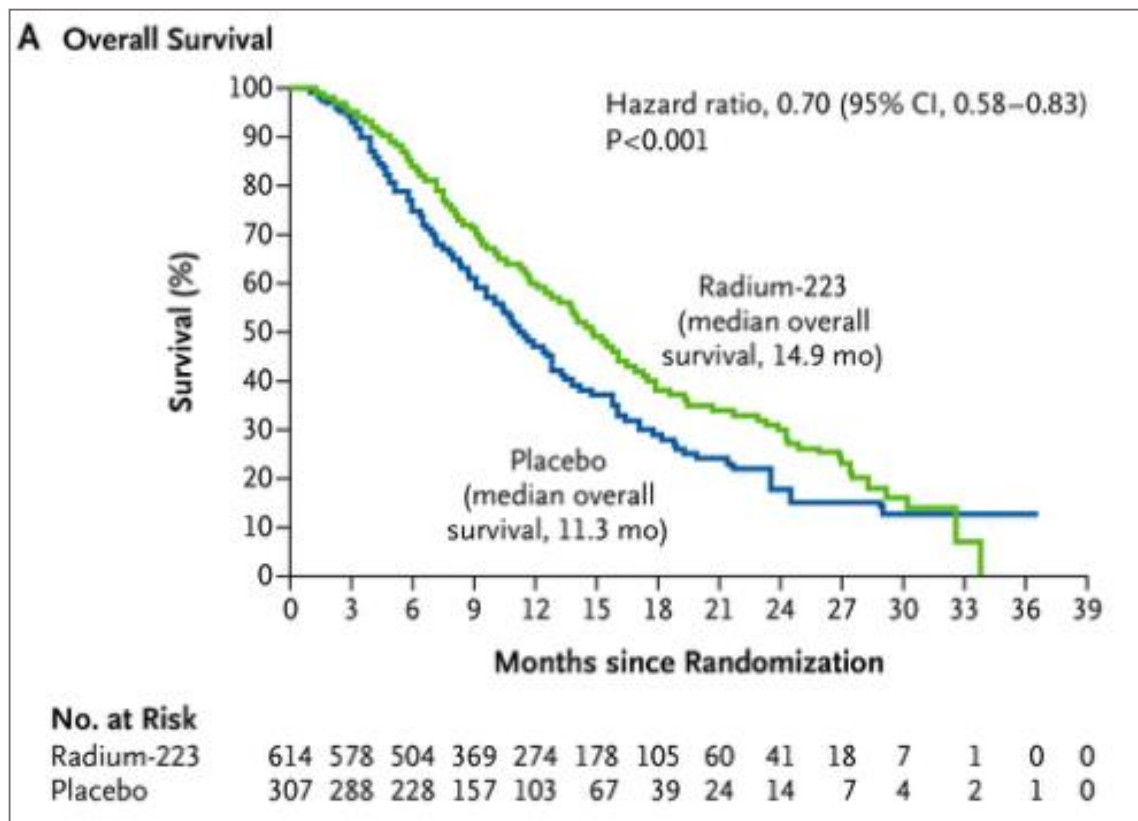


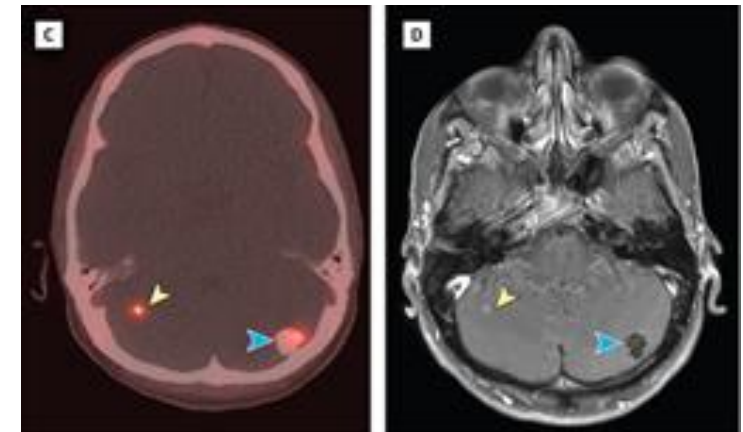
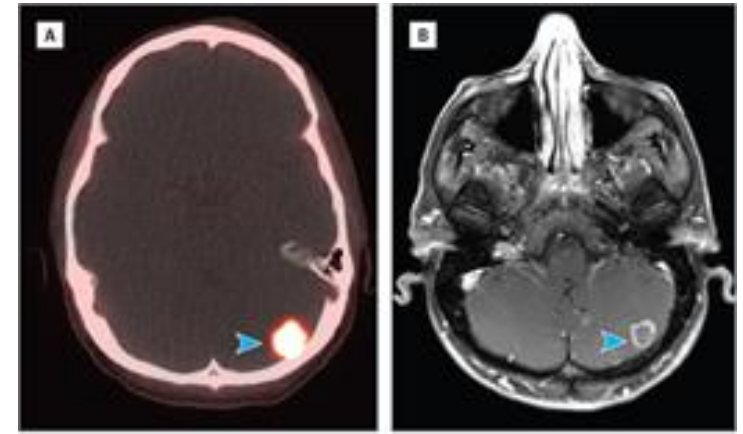
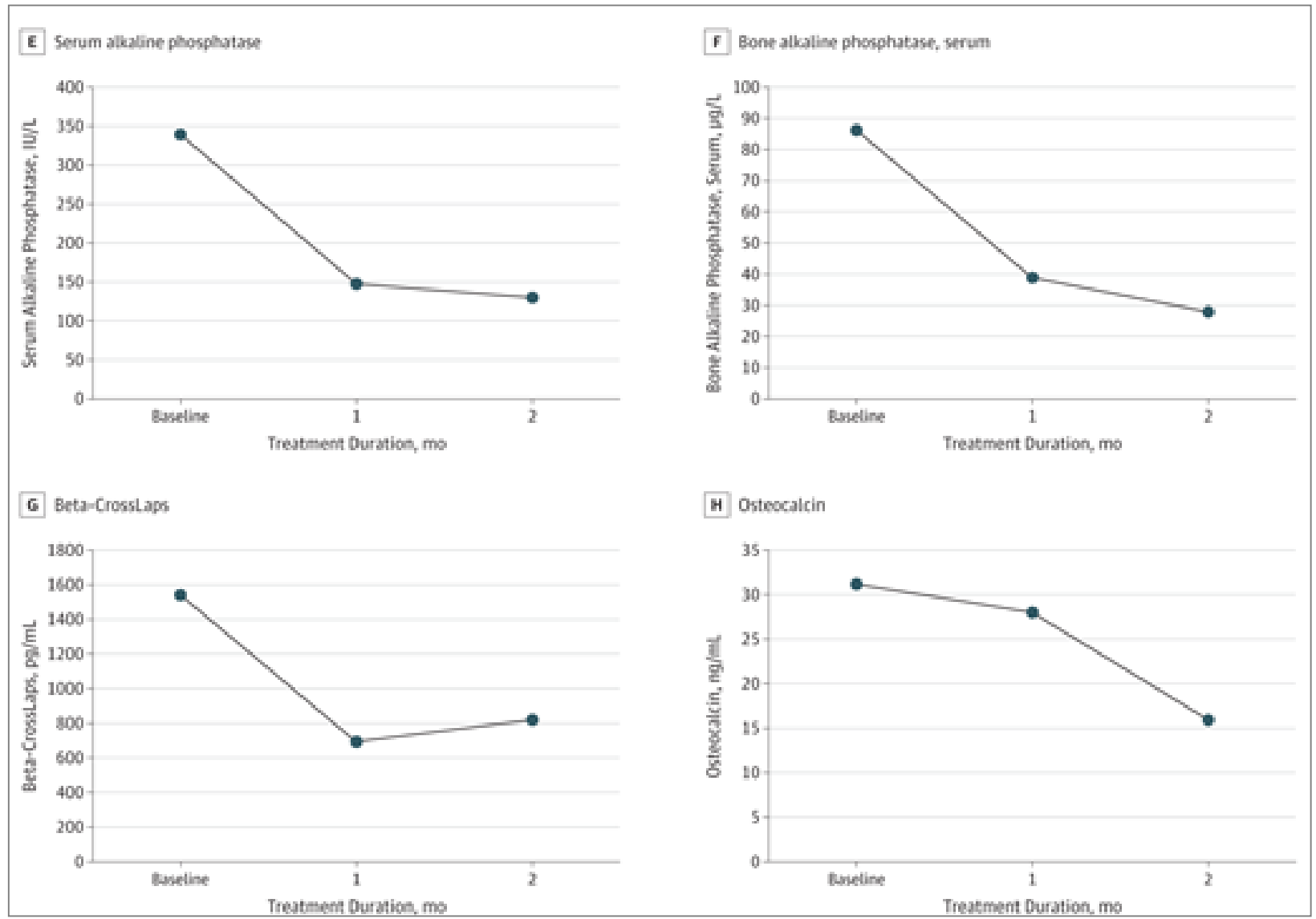
Effect of ^{223}Ra in prolonging symptom-free survival of rats.



Survival of ^{223}Ra -treated animals versus controls.

Kaplan–Meier Estimates of Overall Survival and the Time to the First Symptomatic Skeletal Event.





Subbiah, V et al. Alpha Emitter Radium 223 in High-Risk Osteosarcoma: First Clinical Evidence of Response and Blood-Brain Barrier Penetration. JAMA Oncol. 2015.1(2):253-255.

Limitations of Radium 223 radiopharmaceuticals

- **Bone marrow suppression**
- **Anemia, lymphocytopenia, leukopenia, thrombocytopenia and neutropenia**
- **Nausea, diarrhea, vomiting**
- **Swelling of the legs, ankles, or feet**
- **Dehydration, injection site reactions (redness, pain, swelling)**
- **Kidney impairment**



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From reality to dreams



**Characteristics and known
data about ^{223}Ra in trials**



**Ideal ^{223}Ra
radiopharmaceutical agent**

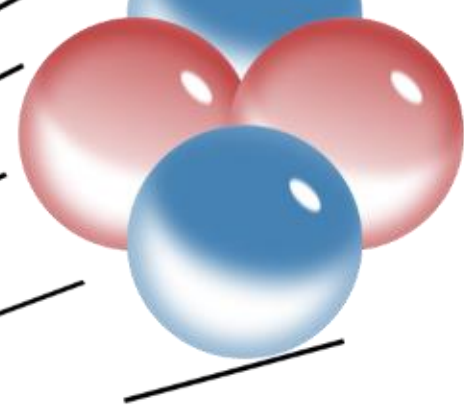
Conclusion

- For urologists dedicated to CRPC patient care, radium- 223 is an important therapeutic option for treating patients with symptomatic bone metastases
- Ra-223 is the first radiopharmaceutical to both prolong survival and provide pain relief, as well as reduce skeletal morbidity in patients with CRPC and bone metastases compared with placebo and best supportive care alone
- The safety profile has been established, specifically demonstrating a low incidence of myelosuppression ($\geq 3\%$)
- Can pass through blood-brain barrier



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Thank you!!!



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