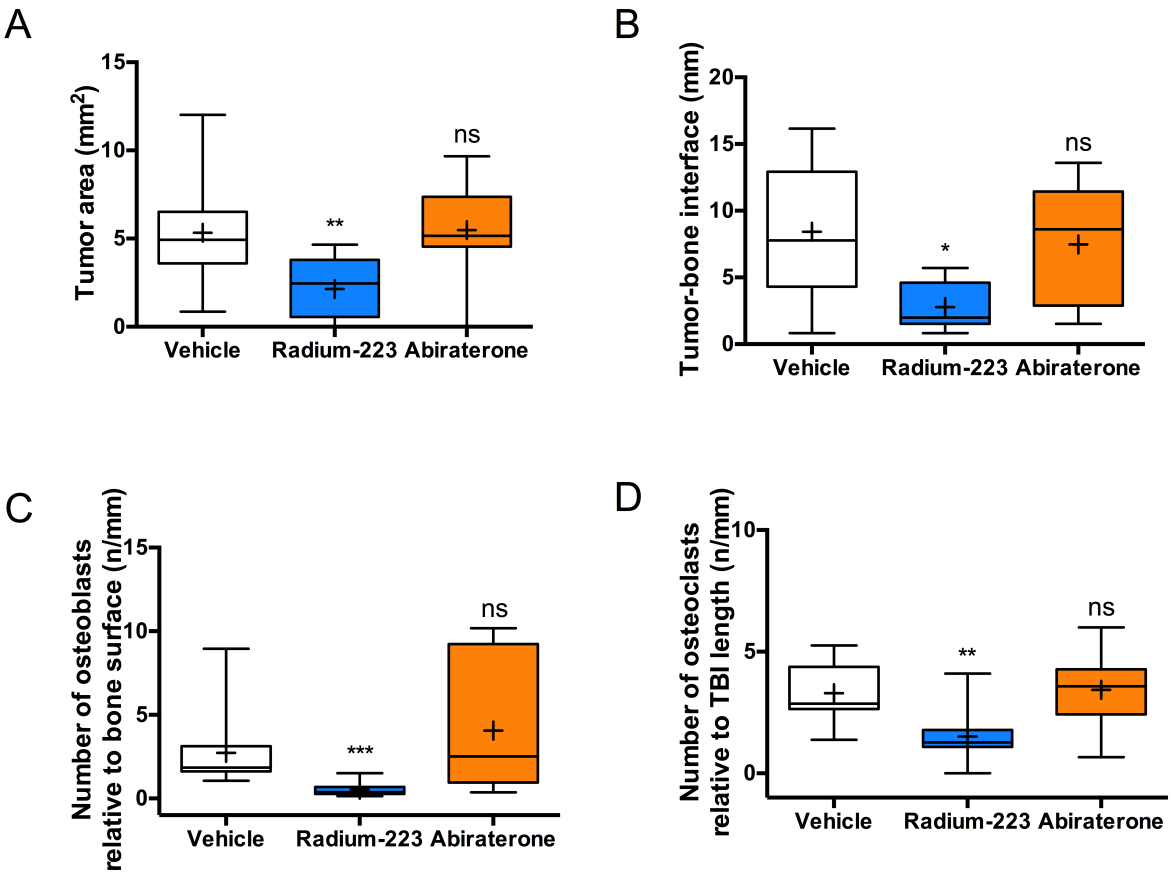
Supplementary data



Supplementary Figure S1. Radium-223 is efficacious in an abiraterone-resistant LuCaP 58 prostate cancer PDX model. A, Tumor area in mice bearing LuCaP 58 tumors (n = 11, p = 0.00427 for radium-223, p = 0.60632 for abiraterone). **B,** The length of tumor-bone interface in mice bearing LuCaP 58 tumors (n = 8-10, p = 0.01554 for radium-223, p = 0.63053 for abiraterone). **C,** The number of osteoblasts relative to bone surface in mice bearing LuCaP 58 tumors (n = 11, p = 0.00306 for radium-223, p = 0.85343 for abiraterone). **D,** The number of osteoclasts relative to TBI in mice bearing LuCaP 58 tumors (n = 8-10, p = 0.00001 for radium-223, p = 0.79694 for abiraterone). In box plots, horizontal lines show 5th, 25th, 50th, 75th and 95th centiles and crosses indicate mean values. ns = not significant,* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Supplementary Table S1. Characteristics of LNCaP and LuCaP 58 prostate cancer growth in bone models in mice – response to radium-223.

Parameter	**LNCaP 300 kBq/kg Q4W, i.v.**	**LuCaP 58 300 kBq/kg Q4W, i.v.**
Mouse strain	NOD.CB17-*Prkdc*^{scid}/NcrCrl	SCID
Tumor-induced bone morphology	Osteoblastic/mixed	Osteoblastic[a]/mixed
Biochemical markers		
PSA	* ↓	** ↓
PINP	*** ↓	** ↓
Histology		
Tumor area	* ↓	NS
Total tissue area	*** ↓	** ↓
Tumor-bone interface	*** ↓	*** ↓
Total bone area	*** ↓	NS
Relative trabecular bone area	NS	* ↓
Number of osteoblasts relative to bone surface	** ↓	** ↓
Number of osteoclasts relative to TBI length	* ↓	NS
Micro-CT		
Bone volume	** ↓	*** ↓
Radiography		
Lesion area	** ↓	* ↓

[a] Very strong osteoblastic component with ectopic bone growth

Q4W, every four weeks; i.v., intravenous administration; NS, not significant; TBI, tumor-bone interface

Asterisks indicate statistical significance (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$)

Arrows indicate the direction of the change

Supplementary Table S2. Responses of radium-223 and abiraterone in LuCaP 58 prostate cancer PDX model in mice.

Parameter	**Radium-223 300 kBq/kg Q4W, i.v.**	**Abiraterone 200 mg/kg QD, p.o.**
Biochemical markers		
PSA	NS	NS
PINP	** ↓	NS
Histology		
Tumor area	** ↓	NS
Total tissue area	* ↓	NS
Tumor-bone interface	* ↓	NS
Total bone area	NS	NS
Relative trabecular bone area	NS	NS
Number of osteoblasts relative to bone surface	*** ↓	NS
Number of osteoclasts relative to TBI length	** ↓	NS
Micro-CT		
Bone volume	* ↓	NS
Radiography		
Lesion area	* ↓	NS

Q4W, every four weeks; QD, once daily; i.v., intravenous administration; p.o., per os administration; NS, not significant; TBI, tumor-bone interface
Asterisks indicate statistical significance (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$)
Arrows indicate the direction of the change