A Randomized Trial of Radium-223 Dichloride and Cabozantinib in Patients with Advanced Renal Cell Carcinoma with Bone Metastases (RADICAL / Alliance A031801)
Rationale for Radium-223 + TKI

• 30% of patients with RCC have bone metastases
• Bone metastases are associated with worse morbidity and mortality
• Cabozantinib is a dual VEGF/cMET TKI with known activity in the bone
• Radium-223 is an alpha-emitting radiopharmaceutical which demonstrated improved overall survival in mCRPC
• Pilot study of radium-223 + TKI demonstrated safety, declines in bone turnover markers, and signal of efficacy

RCC=Renal cell carcinoma; TKI=Tyrosine kinase inhibitor; VEGF=Vascular endothelial growth factor; mCRPC=Metastatic castration resistant prostate cancer.
RADICAL Schema

Eligibility
- Any RCC histology
- ≥ 1 untreated bone metastases
- KPS ≥ 60%

Stratification
- Prior/concurrent osteoclast-targeted therapy use
- IMDC Risk Group
- Prior treatment
- Opioid use

1:1

Endpoints
- Primary
  SSE-free survival
- Secondary
  Safety, SSE-free survival in subsets, ORR, PFS, OS, MDA Bone Response

Cabozantinib
40-60 mg PO daily +
Radium-223
55 kBq/kg IV q28 days x 6 injections

Cabozantinib
60 mg qd PO

N=210 (non-clear cell cap at 20%)
90% power, α=0.025 (one-sided)
Detect improvement of 6-month SSE-FS from 65% to 78%

Imaging, QOL, biomarker assessment every 8 weeks
Acknowledgements

• Toni Choueiri (Co-Chair)
• Tareq Al Baghdadi (Community Co-Chair)
• Ron Chen (QOL Co-Chair)
• Young Kwok (Radiation Oncology Co-Chair)
• Atish Choudhury (Correlative Co-Chair)
• Heather Jacene (Imaging Co-Chair)
• Suzanne Cole (ECOG Champion)
• Mamta Parikh (SWOG Champion)
• Brain Baumann (NRG Champion)

• Michael Morris (Disease Committee Chair)
• Misha Beltran (Correlative Committee Chair)
• Pamela Atherton (Primary Statistician)
• Tyler Zemla (QOL Statistician)
• Gabriela Perez-Burbano (Staff Statistician)
• Shiva Baghaie (Protocol Coordinator)
• Janet Koball (Data Manager)