Real-World Radium-223 Utilization Patterns and Survival in Older Men with Metastatic Castration-Resistant Prostate Cancer (mCRPC): A SEER Linked Medicare Database

Bo Zhou[1], Amit D. Raval[2], Yifan Zhang[1], Nethra Sambamoorthi[1], Matthew J. Korn[2], Niculae Constantinovici[3], Rana McKay[4], Usha Sambamoorthi[1]

[1]University of North Texas Health, Fort Worth, TX, USA

[2]Bayer HealthCare Pharmaceuticals, Whippany, NJ, USA

[3]Bayer Consumer Care, Basel, Switzerland

[4]Division of Hematology-Oncology, Department of Medicine, University of California, San Diego, La Jolla, CA, USA

Disclosure

- The research was funded from the following sources:
  - Bayer Healthcare Pharmaceuticals Inc.

- The following personal or financial relationships relevant to this presentation existed during the prior 12 months and/or during the conduct of the study:
  - Amit Raval, Matthew J. Korn, Niculae Constantinovici are employees and stockholders of Bayer
  - Bo Zhou, Nethra Sambamoorthi, and Usha Sambamoorthi received research funding from Bayer to conduct the study

Overview

To examine Radium-223 (Ra-223) treatment patterns, 5+ cycle completion, and associations with rwOS

Retrospective cohort analysis using Surveillance, Epidemiology, and End Results (SEER)-Medicare data from 2015 to 2020

- Nearly six in ten older men (59.4%) completed ≥5 cycles of Ra-223.
- Ra-223 was most commonly used as monotherapy (59.5%), followed by layered therapy (29.2%) and combination therapy (11.3%).
- Men receiving Ra-223 as first- or second-line therapy had better rwOS (median: 18.4 and 14.8 months) compared to those receiving it in later lines (median: 13.8 months)

Background

- Radium-223 (Ra-223) is the first and only approved alpha-emitting radiopharmaceutical for the treatment of men with castration-resistant prostate cancer and bone metastases with no visceral metastases since 2013.

- Change in the advanced prostate cancer treatment pattern:
  - Post 2013 for mCRPC: Androgen receptor pathway inhibitors (ARPIs), chemotherapy, immunotherapy, PARPIs, 177Lu
  - Post 2016 for earlier state: ARPI and chemotherapy

- RWE on the use of Ra-223 is limited to studies including selected centers or commercially insured populations with an evolving treatment landscape
- Medicare (public insurance provider for the older population (65+ years)), and potentially represents the vast population of prostate cancer

Methods

Design

Retrospective cohort study of New Initiator of Ra-223

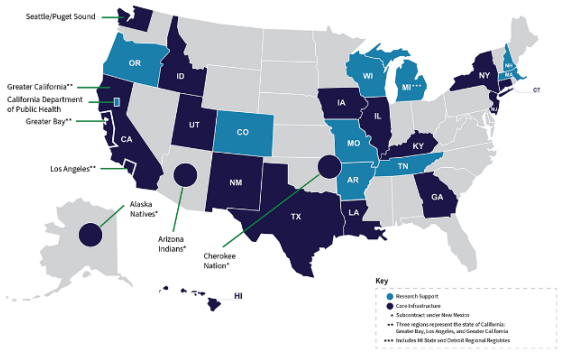
Data Sources

SEER registry: cancer incidence, diagnosis, initial treatment
Medicare: demographics, longitudinal treatment records

Outcomes

Treatment Patterns
- **Ra-223 Completion:** ≥5 cycles without ≥56-day gap
- Ra-223 as **mono, layered, or combination therapy**

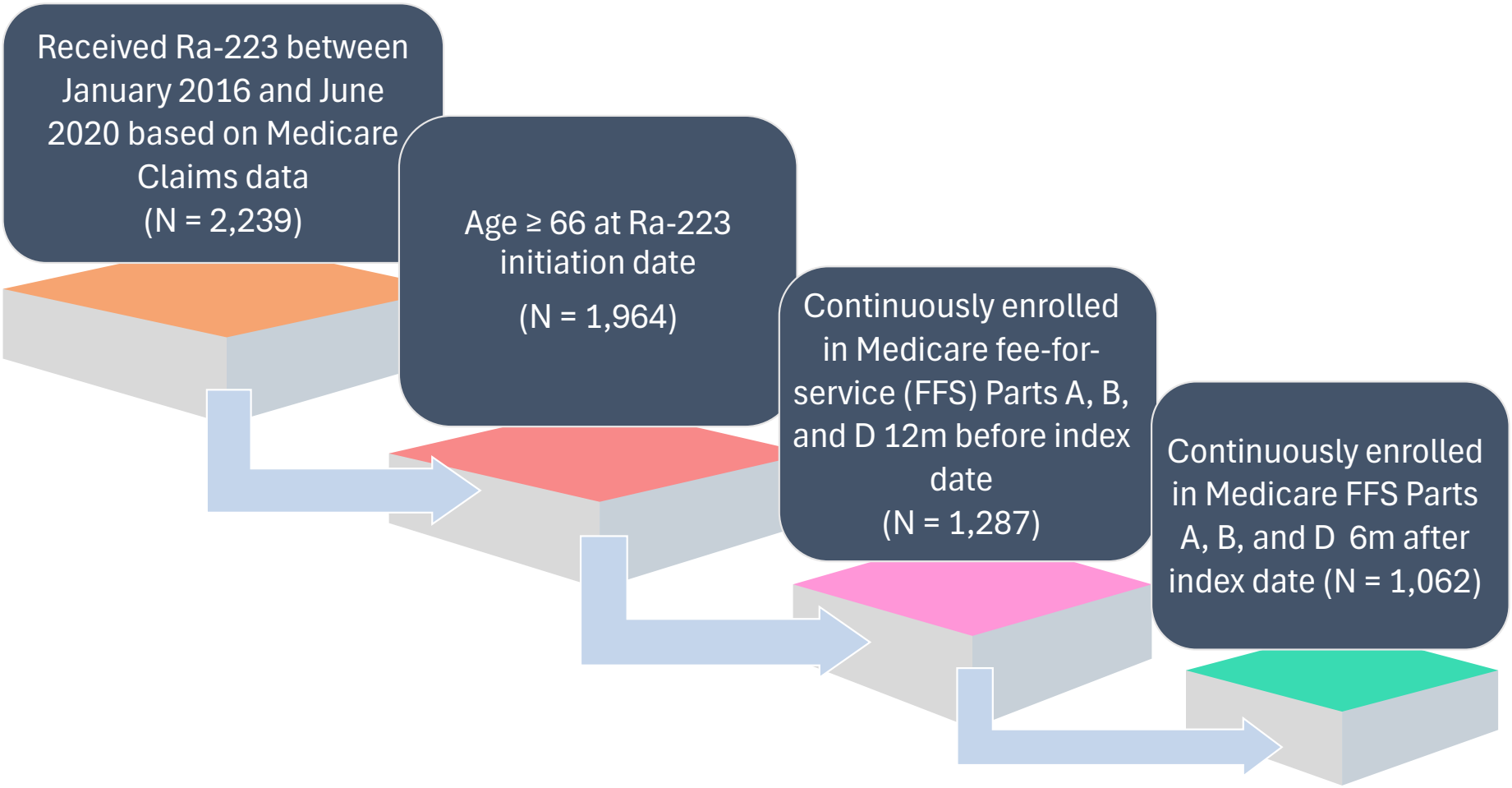
rwOS:
- Time from Ra-223 initiation to the death date



Statistical Analysis

Ra-223 Completion: multivariable logistic regression
Mono, layered, and combination therapy: multivariable multinomial regression
rwOS: Kaplan-Meier and multivariable Cox regression

Study Cohort Inclusion-Exclusion



Covariates/Measures

DEMOGRAPHICS

Age at Ra-223 Initiation

Race and Ethnicity

SOCIAL DETERMINANTS OF HEALTH

Dual Eligibility

Area-Level YOST Index

Marital Status at Diagnosis

Region

HEALTH STATUS

Claim-Based Frailty Index: the validated algorithm that allows quantification of frailty in a continuous spectrum based on deficit accumulation approach

MEDICATION USE

Opioid medications, Bone health agents

mCRPC medications: ARPI, Chemotherapy, Immunotherapy, PARPIs

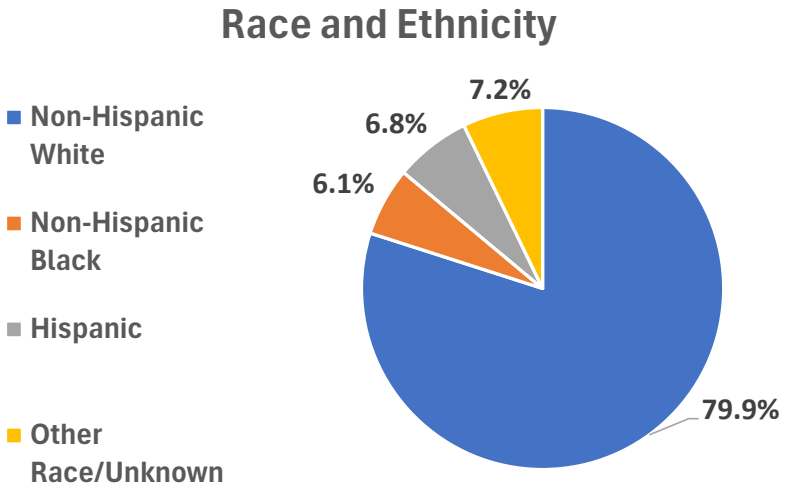
RA-223 RELATED

Line-of-Therapy (LOT)

Index Ra-223 Therapy: mono, combination, layered

Results – Baseline Demographic/SODH Characteristics

	Mean (SD)	Median [IQR]
Age at Ra-223 Initiation	75.6 (6.6)	75 [70 - 80]
Time from PC Diagnosis to Ra-223 Initiation, months	56.8 (33.5)	51.4 [28.3 - 83.1]
Follow-up time, months	15.9 (10.2)	12.7 [8.7 - 20.1]



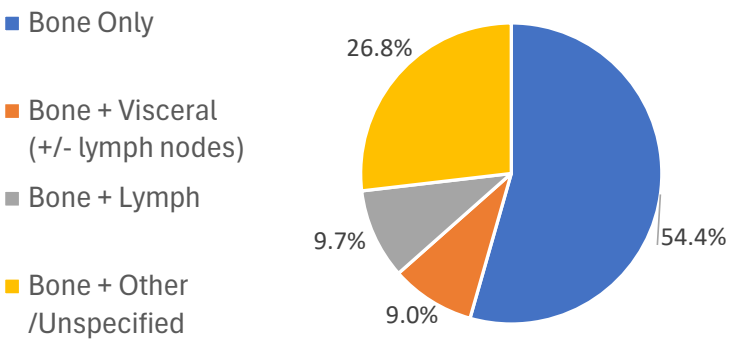
The study cohort was predominantly NHW. The majority were married (59.5%). 15.3% were dual (Medicare-Medicaid) eligible low-income individuals, 38.2% lived in the Northeast; 56.0% lived in areas with a higher socio-economic status (Quintiles 4 and 5), and most lived in urban areas (98.7%).

Results- Baseline Clinical Characteristics

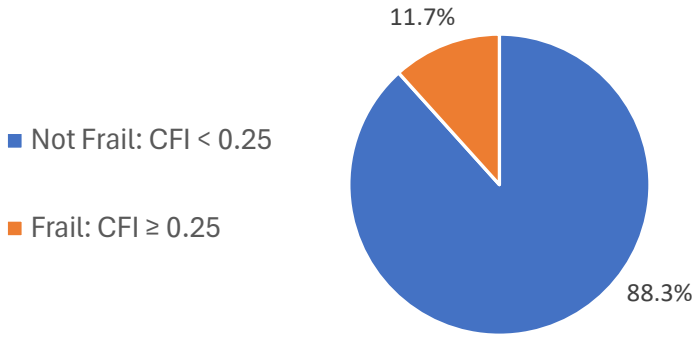
Clinical Characteristics	N	%
Chronic Conditions		
Hypertension	704	66.3
Hypercholesterolemia	610	57.4
Arthritis	415	39.1
Diabetes	345	32.5
Heart Failure	370	34.8
Coronary Artery Disease	352	33.1
Cardiac Arrhythmia	233	21.9

- **All had bone metastases, with a minor fraction with visceral metastases.**
- **Nearly 9 out of 10 had good performance status (CFI <0.25 proxy of performance status).**
- **Cardiometabolic conditions were the most common pre-existing chronic conditions.**

Claim-based Metastases Spread



Claim-Based Frailty Index (CFI)

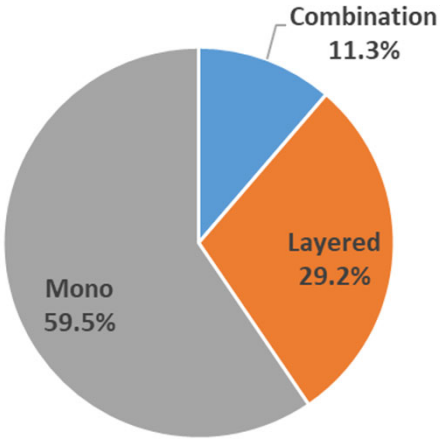


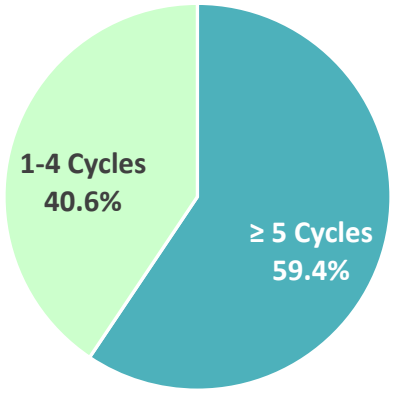
Results- Baseline Medication Usage

Baseline Medications	N	%
Androgen Receptor Pathways Inh.	718	67.6
Abiraterone	434	40.9
Enzalutamide	467	44.0
Chemotherapy	218	20.5
Docetaxel	185	17.4
Cabazitaxel	59	5.6
Immunotherapy	108	10.2
Sipuleucel-T	107	10.1
Prior Lines of Therapies		
None	224	21.1
One	468	44.1
Two+	370	34.8
Opioid Use	614	57.8
Bone Health Agent Use	793	74.7

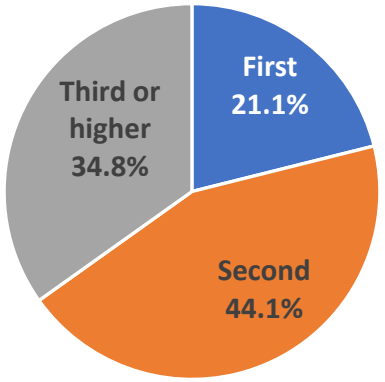
- **Nearly 2/3rd received prior ARPI.**
  - **Shift in the management with ARPI use post Ra-223 approval.**
- **Nearly 1/5th received prior chemotherapy.**
- **Approximately 8 in 10 received Ra-223 2L+ mCRPC.**
- **Nearly 3/4th had bone health agent use.**
  - **Consistent with the guideline for bone metastases.**

Ra-223 Utilization Patterns

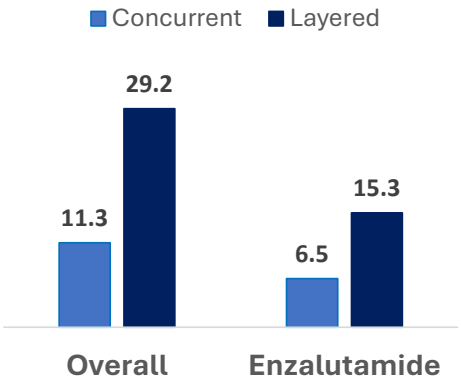




Ra-223 Completion



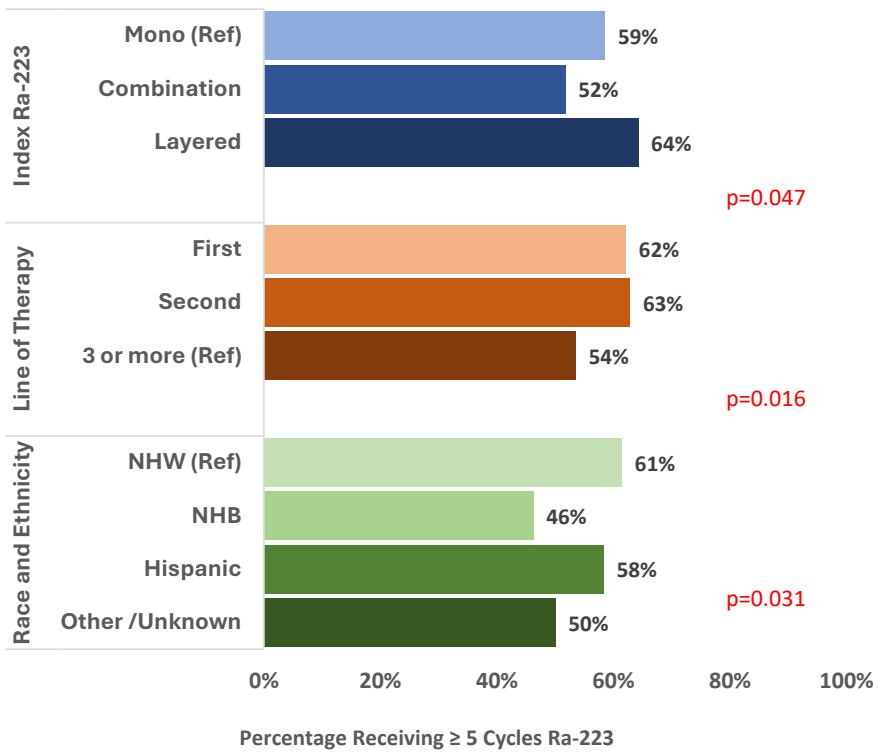
Ra-223 Line of Therapy



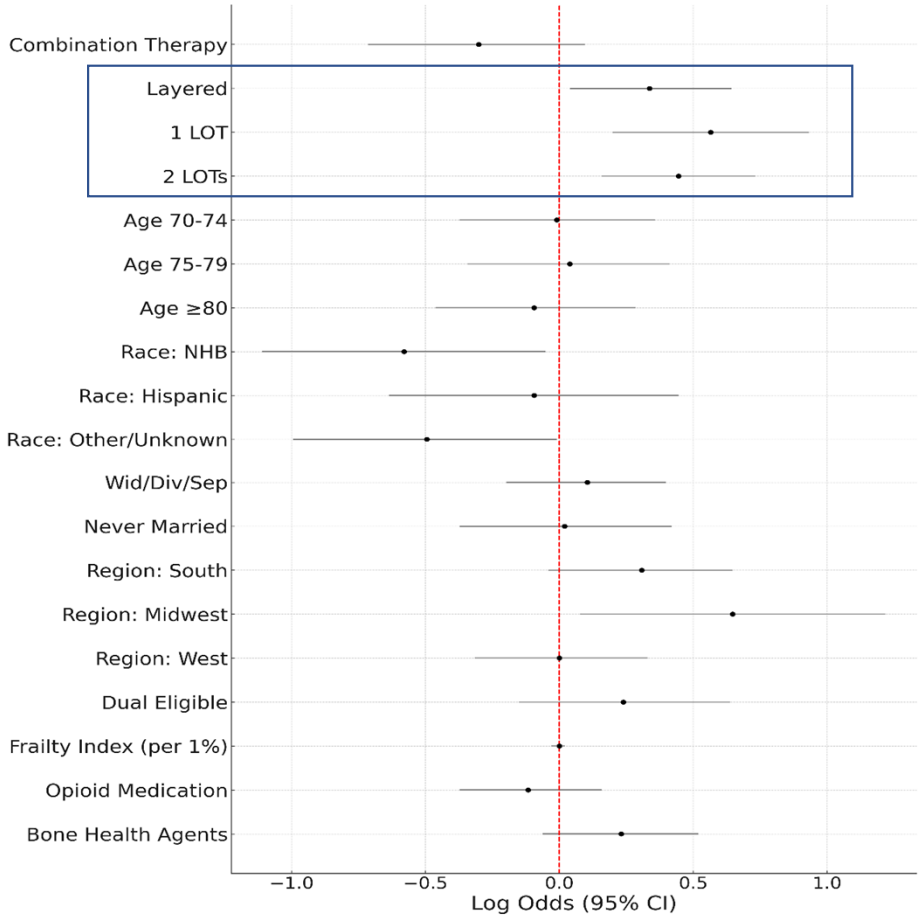
Ra-223 Index Therapy

Nearly 1/3 had 5+ Ra-223 cycle completion; only 40% utilized Ra-223 combination therapy mainly with enzalutamide.

Factors Associated with Ra-223 Completion

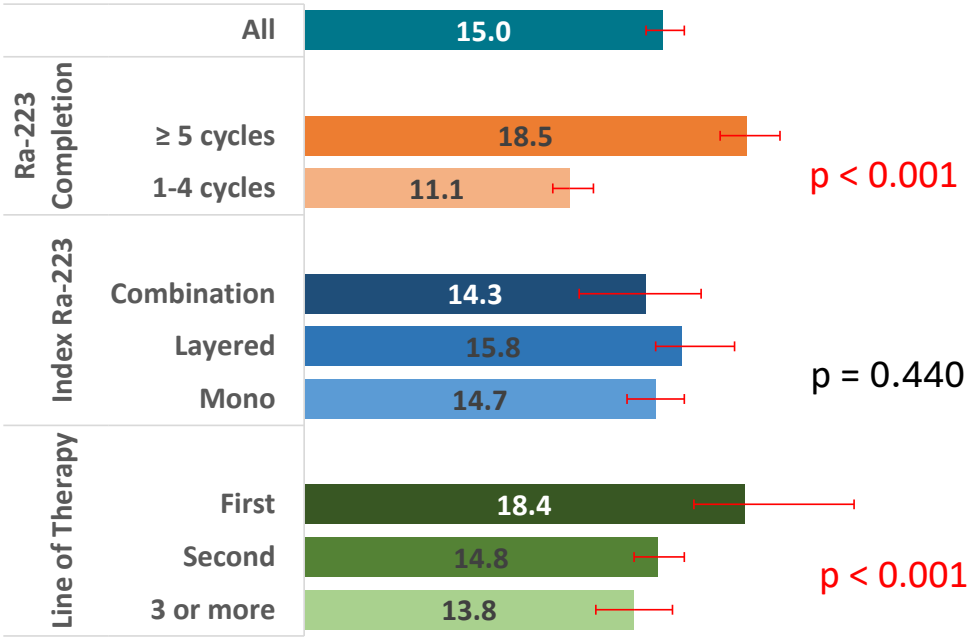


Ra-223 Completion Rate by Index Therapy, LOT, Race and Ethnicity



Real-World Overall Survival (in Months)

KM- Median rwOS Estimates by Ra-223 Use



Key Findings from Multivariable Cox-Regression Analysis

Model 1. Hazard Ratios with 95% CI: Cox-Regression	
5 + Cycle vs. 1- 4 cycle	0.51 (0.44, 0.59)
First vs. 3 or more LOT	0.56 (0.45, 0.68)
Second vs. 3 or more LOT	0.82 (0.69, 0.96)

Hazard Ratios with 95% CI: Cox-Regression	
Combination vs. Mono Therapy	1.01 (0.80, 1.28)
Layered vs. Mono Therapy	0.75 (0.63, 0.88)
First vs. 3 or more LOT	0.48 (0.38, 0.59)
Second vs. 3 or more LOT	0.75 (0.64, 0.88)

Notes: Adjusted for age at Ra-223 initiation, race and ethnicity, marital status at PC diagnosis, dual eligibility, region, socioeconomic status (YOST quintile), any opioid medication use, and any bone health agents use in pre-period

In a heavily pre-treated APRI population, Ra-223 survival estimates are consistent with the ALSYMPCA
Significantly prolonged survival with earlier use and completion of 5+ cycles of Ra-223

Strengths and Limitations

- Strengths
  - First and only Nationwide, population-based data (SEER-Medicare) on Ra-223-treated population in Post ARPI-era
  - Comprehensive demographic, clinical, and social information to gauge the association between completion and survival outcomes
- Limitations
  - Limited generalizability beyond fee-for-service Medicare
  - Did not capture more recently approved therapies post-2020 with limited information on PARPI and 177Lu use
  - Potential challenges in claims-based metastasis data

Conclusion

Early initiation of Ra-223 significantly improves completion and survival outcomes.

Completion of Ra-223 was associated with prolonged survival benefits irrespective of the line of therapy.

Identifying patients who can complete a full course of Ra-223 therapy is crucial for maximizing treatment benefits.

UNT Health FORT WORTH

BAYER

Thank you!

bo.zhou@unthsc.edu