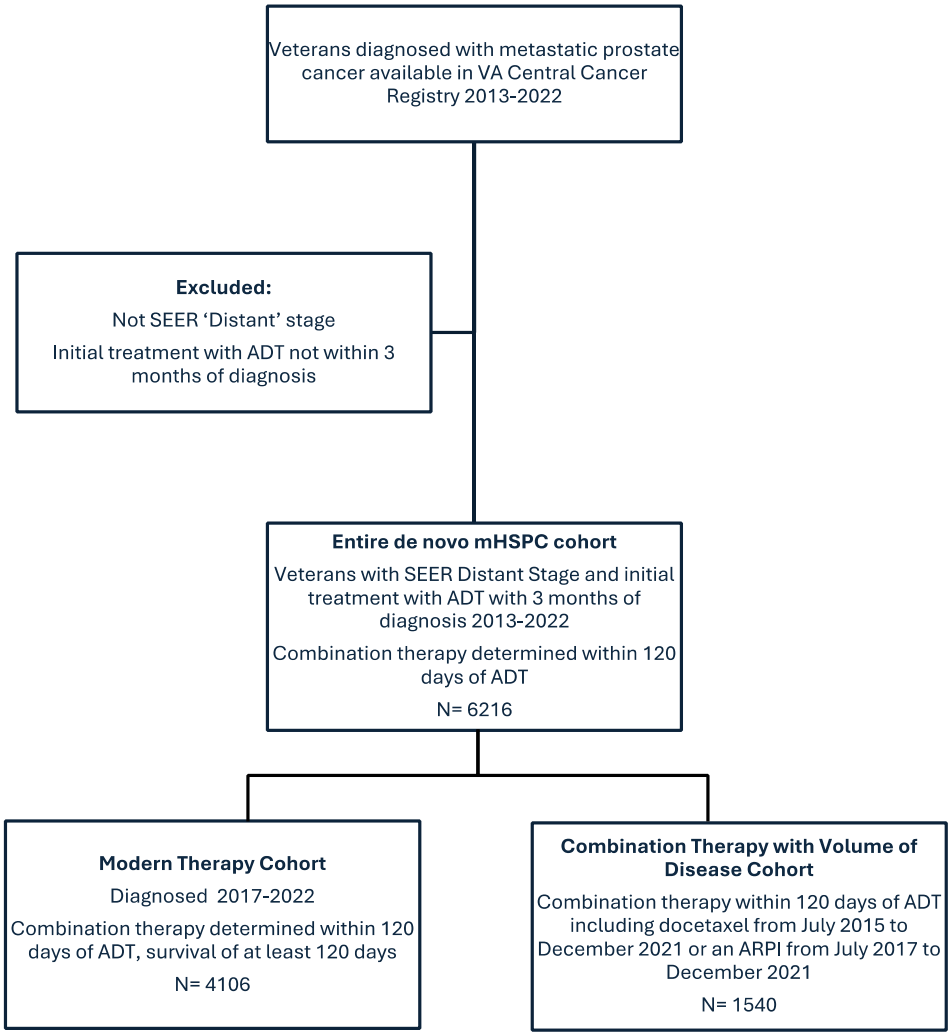
Supplementary Online Content

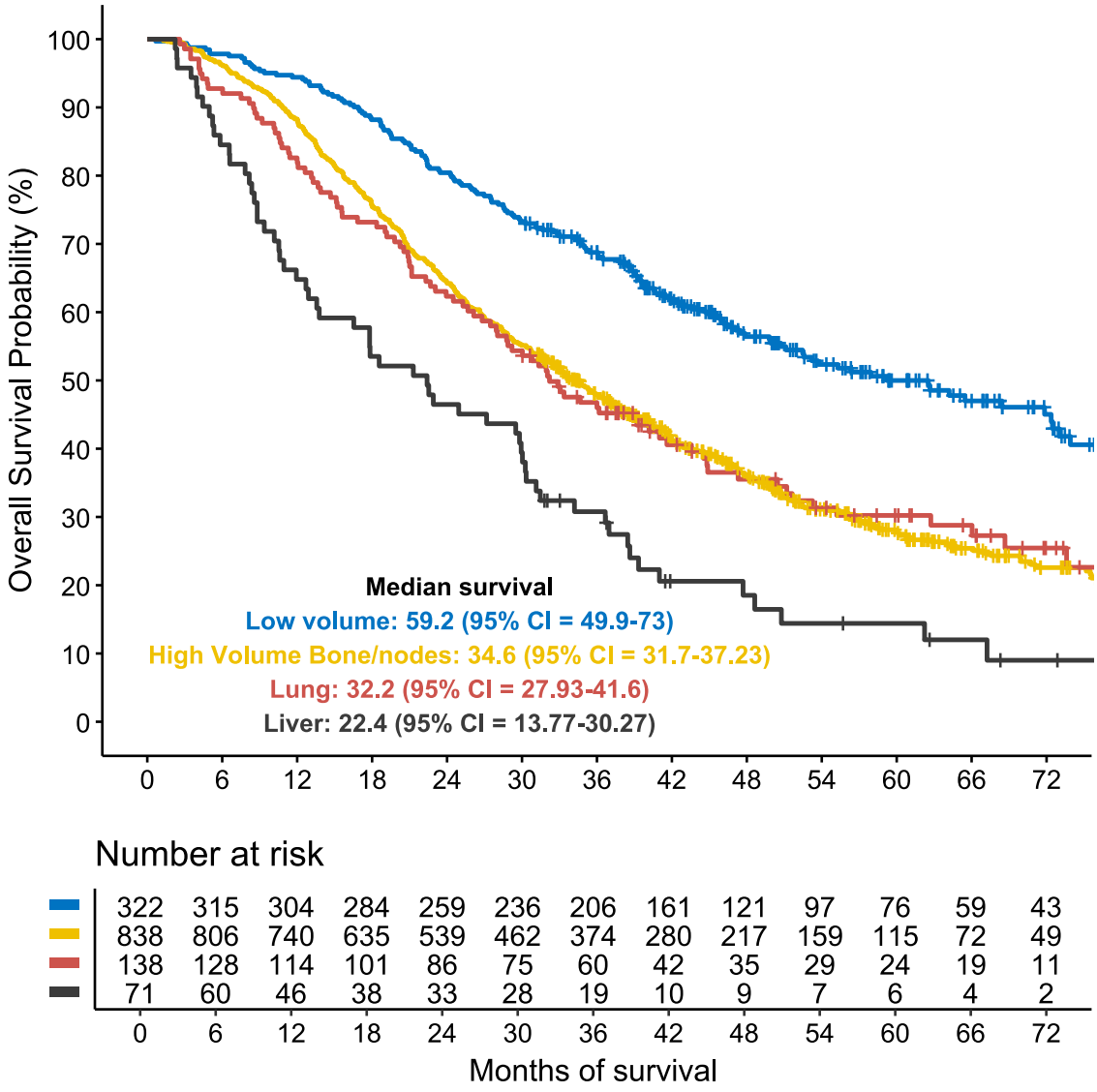
Schoen MW, Doherty J, Eaton D, et al. Treatment patterns and survival among veterans with de novo metastatic hormone-sensitive prostate cancer. *JAMA Netw Open.* 2025;8(5):e259433. doi:10.1001/jamanetworkopen.2025.9433

This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. CONSORT Diagram Cohort Selection and Inclusion. Three analytic cohorts were created. The entire de novo mHSPC cohort included all Veterans in the VA Central Cancer Registry diagnosed with prostate cancer and SEER 'distant' stage disease from 2013-2022. These patients had to then have their initial treatment with ADT occur withing 3 months of diagnosis. The modern therapy cohort included only patient treated 2017 to 2022, therefore after ARPIs started to be available for mHSPC. The combination therapy cohort with volume of disease included patients treated with combination therapy including docetaxel from July 2015 to December 2021 or with an ARPI from July 2017 to December 2021.



eFigure 2. Overall Survival by Site of Disease in Patients Treated With Combination Therapy. Low volume survival median survival was 59.2 months (95% CI, 49.9-73). High volume survival with cancer in the bones or lymph nodes but not lung or liver was 34.6 months (95% CI 31.7-37.2). In patients with lung nodules but not liver, median survival was 32.2 months (95% CI 27.9-41.6) and in patients with liver involvement, median survival was 22.4 months (95% CI 13.8-30.27).



eTable 1. Cox Proportional Hazard Model to Examine the Association of Combination Therapy With Survival Including Age, Charlson Comorbidity Index, Race, Baseline PSA and BMI in 4106 Veterans With mHSPC Diagnosed 2017-2022

Variable	aHR#	95% CI	p
Combination therapy vs. ADT monotherapy	0.89	0.82-0.97	0.007
Age: <70	Ref		
70-80	1.10	0.99-1.22	0.067
80+	1.45	1.29-1.62	<0.001
Charlson Index Categories: 0	Ref		
1	1.17	1.03-1.35	0.017
2-3	1.40	1.24-1.59	<0.001
4+	2.30	2.02-2.61	<0.001
Race: Non-Black	Ref		
Black	0.89	0.81-0.98	0.021
PSA Category: 0-4 ng/mL	1.44	1.01-2.05	0.042
4-10 ng/mL	Ref		
10-20 ng/mL	1.07	0.82-1.40	0.61
20-50 ng/mL	1.32	1.04-1.68	0.021
50-100 ng/mL	1.70	1.34-2.16	<0.001
100-200 ng/mL	1.80	1.42-2.29	<0.001
200+ ng/mL	1.97	1.57-2.47	<0.001
unknown	1.87	1.41-2.47	<0.001
BMI Category: < 25	1.12	1.01-1.23	0.026
25 ≤ BMI < 30	Ref		
BMI ≥ 30	0.88	0.79-0.97	0.017

eTable 2. Cox Proportional Hazard Model in 1174 Patients With High Volume Disease to Examine the Association of ARPI vs Docetaxel Therapy With Survival Including Age, Charlson Comorbidity Index, Baseline PSA and BMI

Variable	aHR#	95% CI	p
ARPI vs. docetaxel combination	0.89	0.76-1.05	0.168
Age (per 1 year increase)	1.02	1.01-1.03	<0.001
Charlson Index (per 1 point increase)	1.13	1.09-1.18	<0.001
PSA Category: 0-4 ng/mL	0.88	0.44-1.76	0.71
4-10 ng/mL	Ref		
10-20 ng/mL	1.21	0.76-1.94	0.42
20-50 ng/mL	1.41	0.93-2.12	0.10
50-100 ng/mL	1.98	1.31-2.98	<.001
100-200 ng/mL	1.72	1.14-2.61	0.01
200+ ng/mL	1.76	1.20-2.58	0.004
unknown	1.24	0.68-2.23	0.48
BMI Category: <25	1.03	0.86-1.23	0.79
25 ≤ BMI <30	Ref		
BMI ≥30	1.01	0.85-1.21	0.90

eTable 3. Baseline Characteristics of the Propensity Matched Cohort of Patients Treated With Combination Therapy and Had High Volume of Disease

Demographic clinical characteristics	Total (n=742)		Mean difference	
	ARPI n=345	Docetaxel n=397	Cohen's d	95% Confidence Interval
age (mean years)	68.6	67.1	0.19	0.046 - 0.335
Charlson Comorbidity index (mean)	1.9	1.8	0.09	-0.051 – 0.237
BMI (mean)	28.2	28.7	-0.085	-0.236 – 0.065
PSA closest to start of therapy (mean, ng/ml)	441.7	561.4	-0.093	-0.238 – 0.052

eTable 4. Additional Life Prolonging Therapy Based on Initial Therapy

Subsequent Treatment	Initial Treatment		
	ADT monotherapy n=3839 No (%)	**ADT with ARPI n=1719 No (%)**	**ADT with docetaxel n=658 No (%)**
Abiraterone	1692 (44.1)	92 (5.4)	367 (55.8)
Enzalutamide	1151 (30.0)	332 (19.3)	269 (40.9)
Apalutamide	43 (1.1)	58 (3.4)	6 (0.9)
Darolutamide	69 (1.8)	33 (1.9)	47 (7.1)
Docetaxel	299 (7.8)	193 (11.2)	-
Cabazitaxel	132 (3.4)	70 (4.1)	134 (20.4)
Sipuleucel-T	<11 (-)	<11 (-)	<11 (-)
Radium-223	89 (2.3)	44 (2.6)	45 (6.8)
Olaparib	50 (1.3)	45 (2.6)	26 (4.0)

eTable 5. Additional Life Prolonging Therapy Based on Initial Therapy in Patients Who Developed Castration Resistance

Subsequent Treatment	Initial Treatment		
	ADT monotherapy n=1373 No (%)	**ADT with ARPI n=563 No (%)**	**ADT with docetaxel n=407 No (%)**
Abiraterone	686 (49.9)	50 (8.9)	243 (55.8)
Enzalutamide	458 (33.3)	223 (39.6)	113 (40.9)
Apalutamide	<11 (-)	12 (2.1)	<11 (-)
Darolutamide	16 (1.7)	32 (56.8)	13 (7.1)
Docetaxel	250 (18.2)	159 (28.2)	-
Cabazitaxel	118 (8.6)	64 (11.4)	121 (29.7)
Sipuleucel-T	<11 (-)	<11 (-)	<11 (-)
Radium-223	70 (5.1)	34 (6.0)	42 (10.3)
Olaparib	31 (2.3)	36 (6.4)	25 (6.1)