Fig.S1

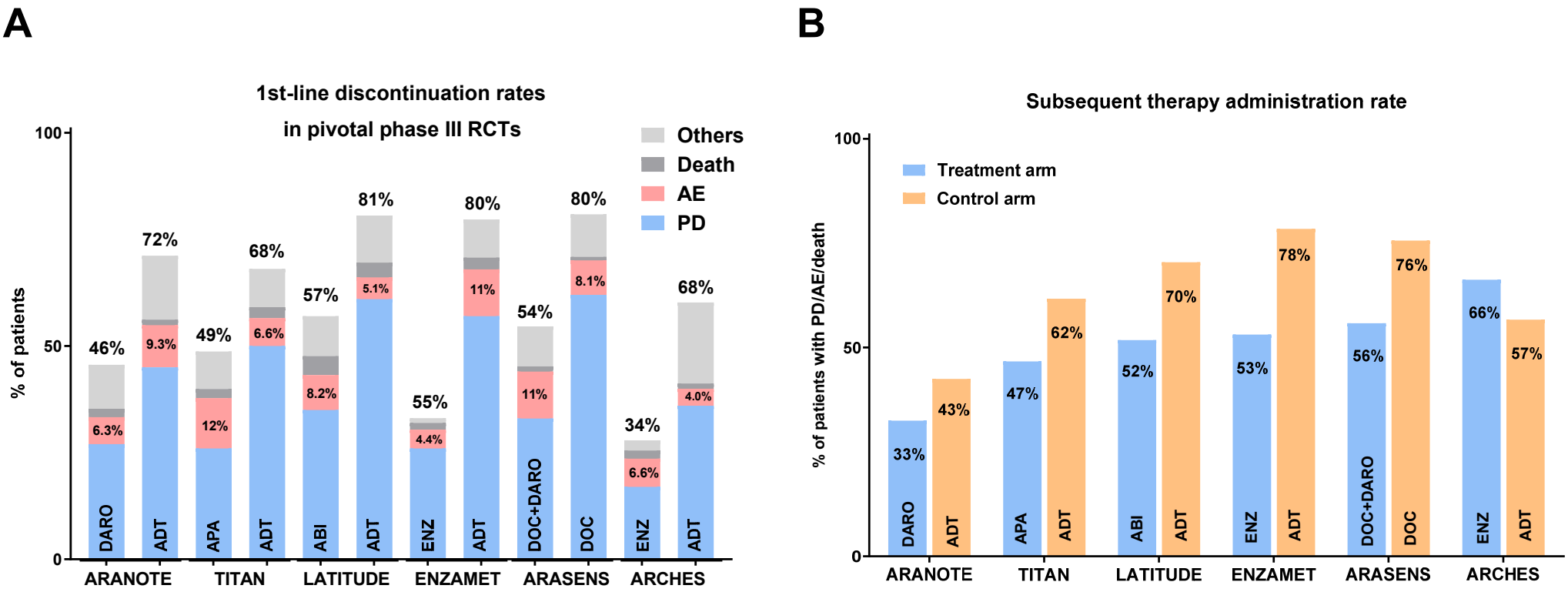

A
1st-line discontinuation rates
in pivotal phase III RCTs
Others
Death
AE
PD
% of patients
100
50
0
46%
6.3%
DARO
72%
9.3%
ADT
49%
12%
APA
68%
6.6%
ADT
57%
8.2%
ABI
81%
5.1%
ADT
55%
4.4%
ENZ
80%
11%
ADT
54%
11%
DOC+DARO
80%
8.1%
DOC
34%
6.6%
ENZ
68%
4.0%
ADT
ARANOTE
TITAN
LATITUDE
ENZAMET
ARASENS
ARCHES
B
Subsequent therapy administration rate
Treatment arm
Control arm
% of patients with PD/AE/death
100
50
0
33%
DARO
43%
ADT
47%
APA
62%
ADT
52%
ABI
70%
ADT
53%
ENZ
78%
ADT
56%
DOC+DARO
76%
DOC
66%
ENZ
57%
ADT
ARANOTE
TITAN
LATITUDE
ENZAMET
ARASENS
ARCHES

Figure S1. Pivotal phase III RCT-reported first-line discontinuation and subsequent therapy administration rates.

(A) First-line discontinuation rates reported in pivotal phase III RCTs for mHSPC, with discontinuation events categorized as PD, AE, death, or other reasons based on published trial reports. The definitions of subsequent therapy were based on those reported in each trial and may not be identical across studies.

(B) Subsequent therapy administration rates reported in the same RCTs, shown separately for treatment and control arms. Rates were extracted from published sources using the study definition based on patients with PD/AE/death. These published trial data are presented for contextual purposes only and should not be interpreted as direct benchmarks for the present real-world cohort.

Table S1. Exploratory analysis of factors associated with AE-related treatment transitions among patients receiving ARSI-based upfront intensification.

Variable	No AE-related transition (n=460)	AE-related transition (n=54)	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Age, years, median (IQR)	73 (69–78)	73 (70–78)	1.00 (0.96–1.04)	0.87		
Age ≥80 years, n (%)	81 (17.6)	12 (22.2)	1.34 (0.67–2.65)	0.41		
ECOG PS ≥1, n (%)	120 (26.1)	13 (24.1)	0.90 (0.47–1.73)	0.75		
CHAARTED high-volume disease, n (%)	334 (72.6)	38 (70.4)	0.90 (0.48–1.66)	0.73		
Diagnostic PSA, ng/mL, median (IQR)	265 (53.0–920)	168 (59.5–770)	0.98 (0.85–1.13)	0.77		
Baseline hemoglobin,	13.3 (11.8–14.5)	13.6 (11.9–14.8)	1.04 (0.91–1.19)	0.59		

g/dL, median (IQR)						
Initial ARPI dose reduction, n (%)	143 (31.1)	13 (24.1)	0.70 (0.37–1.35)	0.29		
ARSI regimen						
ENZ	114/121 (94.2%)	7/121 (5.8%)	Reference	—	Reference	—
ABI	193/222 (86.9%)	29/222 (13.1%)	2.45 (1.04–5.77)	0.04	2.40 (0.99–5.81)	0.053
APA	153/171 (89.5%)	18/171 (10.5%)	1.92 (0.77–4.74)	0.16	2.51 (0.91–6.93)	0.075

AE-related treatment transition was defined as treatment discontinuation because of AEs or switching to another ARPI without PD. PSA was log-transformed for logistic regression analysis. The multivariable model included age, ECOG performance status, baseline hemoglobin, initial ARPI dose reduction, and ARSI regimen. These analyses were exploratory because of the limited number of events. The OR for diagnostic PSA was calculated per 1-unit increase in log-transformed PSA. In the multivariable model adjusted for age, ECOG PS, baseline hemoglobin, and initial dose reduction, the adjusted ORs were 2.40 (95% CI, 0.99–5.81) for ABI and 2.51 (95% CI, 0.91–6.93) for APA, with ENZ as the reference.