ERLEADA® (apalutamide)
Publication Summary: Lowentritt et al 2025 – Real-World OS Comparison with Abiraterone Acetate in Patients with mCSPC

REAL-WORLD STUDY

Lowentritt et al (2025)[1] conducted a real-world study to compare overall survival (OS) by 24 months in androgen receptor pathway inhibitor (ARPI)-naïve patients with metastatic castration-sensitive prostate cancer (mCSPC) who were newly initiated on ARPIs, ERLEADA (n=1879) or abiraterone acetate (n=2073).

Study Design/Methods

- Real-world, retrospective, head-to-head, causal longitudinal study
- A weighted Kaplan-Meier analysis was used to compare OS between the ERLEADA and abiraterone acetate cohorts at 24 months postindex (primary) and using all available follow-up data (exploratory outcome, nominal) using weighted Cox proportional hazards model.
    - HR <1 indicates a lower death rate for the ERLEADA cohort compared with the abiraterone acetate cohort.
- Clinical and demographic data from Precision Point Specialty (PPS) Analytics collected as part of routine clinical care from community-based urology practices in the United States (US) were linked with administrative claims data from the Komodo Research Database (KRD) obtained from September 17, 2018 to December 31, 2023. Mortality data from KRD was used to inform the OS analysis and both databases were linked by Datavent.
    - PPS: includes prostate-specific antigen (PSA) results and prostate cancer-specific medication details
    - KRD: includes over 320 million US patients across commercial, Medicaid, and Medicare insurers, with information on insurance eligibility, diagnoses, procedures, and prescription information. Mortality data are obtained from multiple third-party sources, capturing >90% of all deaths in oncology settings between 2018-2023 identified by the US Centers for Disease Control (CDC).
- Patients were assigned to mutually exclusive treatment cohorts based on the first dispensation in PPS or paid pharmacy claim in the KRD. Index dates were set as the date of treatment initation for ERLEADA or abiraterone acetate on or after September 17, 2019.
- **Select inclusion criteria**: ARPI-naïve patients with mCSPC; diagnosis code or clinical indicator for bone, nodal, or visceral metastasis without castration resistance prior to or on the index date.
- **Select exclusion criteria**: initiated ≥2 different ARPIs on the index date; diagnosis for another primary cancer during the baseline period; prescription in PPS for non-index ARPI; use of estrogens, immunotherapy, poly(ADP-ribose) polymerase inhibitors, radiopharmaceuticals, or etoposide; used cabazitaxel or carboplatin after docetaxel.
- Concomitant use of androgen deprivation therapy (ADT) was not required for inclusion in either cohort and concomitant use of prednisone was not required for inclusion in the abiraterone acetate cohort.
- Baseline patient characteristics were evaluated 12 months pre-index date and the observation period spanned from the index date until the latter of open insurance claim activity in the KRD or clinical activity in PPS, both no later than December 31, 2023.
- To account for differences in baseline characteristics between the ERLEADA and abiraterone acetate cohorts, inverse probability of treatment weighting (IPTW) based on propensity score was used.
    - Each patient was attributed an inverse probability of treatment weight, defined as 1/(propensity score) for the ERLEADA cohort and 1/(1-propensity score) for the abiraterone acetate cohort.

- Patients were not censored if they discontinued index ARPI, switched to another ARPI, initiated therapy with another advanced prostate cancer treatment, or progressed to castration resistance.
- Treatment patterns were assessed from the index date up to 24 months.
- **Primary outcome:** OS by 24 months postindex ARPI initiation
- This study was not designed to assess differences in safety between cohorts.

Results

Patient Characteristics

- Baseline patient characteristics were well-balanced between weighted cohorts, with standardized differences <10%.
- Patient demographics and baseline characteristics in the weighted population are included in Table: Select Demographics and Baseline Disease Characteristics.

Select Demographics and Baseline Disease Characteristics[1]

Characteristic	Weighted Population[a]		
	ERLEADA (n=1879)	Abiraterone Acetate (n=2073)	Standardized difference, %
Mean age, years (SD)	72.1 (9.3)	71.9 (9.1)	2.5
Race, n (%)			
White	1159 (61.7)	1295 (62.5)	1.6
Black or African American	359 (19.1)	374 (18.0)	2.8
Hispanic or Latino	141 (7.5)	152 (7.3)	0.6
Other	85 (4.5)	100 (4.8)	1.3
Unknown	134 (7.1)	152 (7.3)	0.7
Geographic region, n (%)			
South	900 (47.9)	923 (44.5)	6.8
Midwest	515 (27.4)	602 (29.0)	3.6
Northeast	247 (13.1)	296 (14.3)	3.3
West	217 (11.5)	253 (12.2)	2.0
Index year, n (%)			
2019-2020	414 (22.0)	473 (22.8)	1.8
2021	444 (23.6)	484 (23.3)	0.8
2022	514 (27.4)	555 (26.8)	1.3
2023	506 (27.0)	562 (27.1)	0.4
Mean time between metastasis and index date, months (SD)	9.7 (17.6)	10.2 (17.1)	2.5
Mean time between PC diagnosis and index date, months (SD)	37.4 (45.5)	35.5 (47.7)	0.3
Metastasis type,[b] n (%)			
Bone	1249 (66.5)	1373 (66.2)	0.6
Nodal	994 (52.9)	1097 (52.9)	0.1
Visceral	396 (21.1)	477 (23.0)	4.7
Metastasis in multiple sites	477 (25.4)	492 (23.7)	3.9
Mean Quan-CCI (SD)	8.5 (3.0)	8.5 (2.9)	0.7
Comorbidities, n, %			
Any malignancy, including lymphoma and leukemia, except malignant neoplasm of skin	1865 (99.3)	2048 (98.8)	4.9
Metastatic solid tumor	1589 (84.6)	1783 (86.0)	4.0
Diabetes without chronic complication	452 (24.1)	442 (21.3)	6.6
Renal disease	277 (14.7)	304 (14.7)	0.2
Peripheral vascular disease	269 (14.3)	307 (14.8)	1.4
Diabetes with chronic complication	237 (12.6)	196 (9.5)	10.0
Chronic pulmonary disease	232 (12.4)	262 (12.6)	0.8

Characteristic	Weighted Population[a]		
	ERLEADA (n=1879)	Abiraterone Acetate (n=2073)	Standardized difference, %
Congestive heart failure	197 (10.5)	192 (9.2)	4.2
Mild liver disease	177 (9.4)	197 (9.5)	0.3
Cerebrovascular disease	122 (6.5)	192 (9.3)	10.2
Myocardial infarction	81 (4.3)	92 (4.4)	0.7
Dementia	41 (2.2)	41 (2.0)	1.4
Rheumatic disease	34 (1.8)	30 (1.5)	2.7
Peptic ulcer disease	18 (1.0)	22 (1.1)	1.1
Hemiplegia or paraplegia	10 (0.5)	21 (1.0)	5.4
Moderate or severe liver disease	5 (0.2)	10 (0.5)	4.0
AIDS/HIV	0	0	0.0
De novo PC,[c] n (%)	1100 (58.5)	1223 (59.0)	1.0
Concurrent use of ADT with index ARPI,[d] n (%)	1443 (76.8)	1535 (74.0)	6.4
Mean duration of ADT episode overlapping with index date, months (SD)	4.5 (8.0)	5.0 (8.3)	6.4
Prior use of first-generation ARPI,[e] n (%)	343 (18.2)	396 (19.1)	2.2
Prior use of chemotherapy,[f] n (%)	51 (2.7)	72 (3.5)	4.6
Most recent PSA level, ng/mL, n (%)			
≤0.2	288 (15.3)	298 (14.4)	2.7
>0.2 to ≤2	286 (15.2)	296 (14.3)	2.7
>2 to ≤5	186 (9.9)	194 (9.3)	1.9
>5 to ≤10	168 (9.0)	172 (8.3)	2.3
>10	533 (28.4)	577 (27.8)	1.3
Unknown	417 (22.2)	537 (25.9)	8.7
Initial Gleason score,[g] n (%)			
≤6	94 (5.0)	97 (4.7)	1.6
7	355 (18.9)	383 (18.5)	1.1
8	276 (14.7)	311 (15.0)	0.9
9	408 (21.7)	446 (21.5)	0.6
10	60 (3.2)	65 (3.2)	0.3
Unknown	685 (36.5)	771 (37.2)	1.5

Abbreviations: ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; CCI, Charlson Comorbidity Index; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation.
[a]The number of patients reported in this weighted population represents the sum of weights for the corresponding nonweighted patients, rounded to the nearest integer. The proportions displayed were calculated before rounding and may be slightly different than if they were calculated based on rounded numbers.
[b]Types of metastases were defined at any time prior to (and including) the index date. The types of metastases were not mutually exclusive.
[c]*De novo* PC was defined as ≤180 days between the first PC diagnosis and date of metastasis.
[d]Concurrent ADT use was defined as an episode of continuous ADT use overlapping with the index date (using a 60-day gap to define discontinuation).
[e]Prior use of first-generation ARPI was defined as any prescription for bicalutamide, nilutamide, or flutamide in the 12 months preceding the index date.
[f]Prior chemotherapy use was defined as administration in the 12 months preceding the index date.
[g]The Gleason score was evaluated at any time prior to and including the index date.

OS

- Results are reported in Table: OS Results.
  - By 24 months postindex, patients initiated on ERLEADA had a statistically significant 26% reduction in the risk of death when compared with patients initiated on abiraterone acetate.
  - When evaluating OS using all available follow-up at 48 months postindex, results were consistent with OS at 24 months postindex.
  - Results were consistent in a sensitivity analysis assessing OS among patients with a claim for ADT 180 days before or 180 days after the index date.

OS Results[1]

	ERLEADA (n=1879)	Abiraterone Acetate (n=2073)	HR (95% CI)	*P*-Value
24 months postindex				
Median OS	NR	NR	0.74 (0.59-0.93)	0.010
Patients surviving, %	88.7	85.8		
48 months postindex				
Median OS	NR	NR	0.72 (0.59-0.88)	<0.001*
Patients surviving, %	77.3	69.4		
Sensitivity analysis				
Median OS	NR	NR	0.78 (0.62-0.98)	0.035*

Abbreviations: CI, confidence interval; HR, hazard ratio; NR, not reached; OS, overall survival.
*This endpoint was not adjusted for multiple comparisons. Therefore, the p-value displayed is nominal, and statistical significance has not been established.

Treatment Patterns

- Results are summarized in Table: Treatment Patterns by 24 Months Postindex.

Treatment Patterns by 24 Months Postindex[1]

	Weighted Population[a]	
	ERLEADA (n=1879)	Abiraterone Acetate (n=2073)
Mean (median) follow-up duration, months	16.8 (19.5)	16.3 (19.0)
Mean (median) duration of continuous index ARPI use, months	9.3 (6.6)	10.7 (8.9)
Proportion of patients that discontinued index ARPI,[b] n (%)	1045 (55.6)	929 (44.8)
Proportion of patients with no additional treatment after discontinuation, n (%)	692 (36.8)	636 (30.7)
Proportion of patients who received different advanced PC medication after discontinuation of index ARPI, n (%)	353 (18.8)	294 (14.2)
Median time to first advanced PC medication after discontinuation of index ARPI, months	4.9	3.3
First advanced PC medication received after discontinuation of index ARPI, n (%)		
Non-index ARPI	170 (9.0)	144 (6.9)
Enzalutamide	78 (4.2)	93 (4.5)
Abiraterone acetate	70 (3.7)	-
Darolutamide	22 (1.2)	14 (0.7)
Apalutamide	-	37 (1.8)
Immunotherapies	38 (2.0)	18 (0.9)
Chemotherapies	69 (3.7)	77 (3.7)
Estrogens	56 (3.0)	19 (0.9)
Radiotherapies	12 (0.6)	26 (1.3)
PARP inhibitors	9 (0.5)	10 (0.5)

Abbreviations: ARPI, androgen receptor pathway inhibitor; PARP, poly(ADP-ribose) polymerase; PC, prostate cancer.
[a]The number of patients reported in this weighted population represents the sum of weights for the corresponding nonweighted patients, rounded to the nearest integer. The proportions displayed were calculated before rounding and may be slightly different than if they were calculated based on rounded numbers.
[b]Used a >90-day gap in days of supply to define discontinuation.

Safety results were not reported.

REFERENCES

1. Lowentritt B, Bilen MA, Khilfeh I, et al. Overall survival in patients with metastatic castration-sensitive prostate cancer treated with apalutamide versus abiraterone acetate: a head-to-head analysis of real-world patients in the USA [published online ahead of print May 9, 2025]. *J. Comp. Eff. Res*. 2025. doi:10.57264/cer-2025-0023.