Original Article

Real-world effectiveness of rezvilutamide plus androgen deprivation therapy in patients with low-volume, metastatic hormone-sensitive prostate cancer: a retrospective multicenter study

Shaoxi Niu[1#], Dan Xia[2#], Baojun Wang[1], Xiaotian Wang[3], Qifu Zhang[4], Jiangping Wang[5], Xin Jin[5], Lijun Mao[6], Yashi Ruan[5], Hui Wang[7], Fanghu Sun[7], Zheng Cai[8], Yifan Chen[9], Tao Zeng[10], Xuebao Xiang[11], Ziyang Qiang[12], Jun Zhang[12], Yugang Liu[13], Peijie Chen[14], Jun Li[15], Xu Zhang[1], Liping Wang[16], Zhou Ying[16], Du Wang[16], Chaoyu Lin[16], Ting He[16]

[1]Department of Urology, Chinese PLA General Hospital, Beijing, China; [2]Department of Urology, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China; [3]Department of Urology, Shengjing Hospital of China Medical University, Shenyang, China; [4]Department of Urology, Jilin Cancer Hospital, Changchun, China; [5]Department of Urology, The Affiliated Taizhou People's Hospital of Nanjing Medical University, Taizhou, China; [6]Department of Urology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, China; [7]Department of Urology, The First People's Hospital of Lianyungang, Lianyungang, China; [8]Department of Urology, Suzhou Municipal Hospital, Suzhou, China; [9]Department of Urology, Shanghai Tenth People's Hospital, Shanghai, China; [10]Department of Urology, The Second Affiliated Hospital of Nanchang University, Nanchang, China; [11]Department of Urology, Affiliated Hospital of Guilin Medical University, Guilin, China; [12]Department of Urology, Qinghai University Affiliated Hospital, Qinghai, China; [13]Department of Urology, The First Hospital of Yulin, Yulin, China; [14]Department of Urology, Zhongshan Hospital Xiamen University, Xiamen, China; [15]Department of Urology, Yunnan Cancer Hospital, Kunming, China; [16]Department of Medical Affairs, Jiangsu Hengrui Pharmaceuticals Co., Ltd., Shanghai, China

Contributions: (I) Conception and design: S Niu, B Wang; (II) Administrative support: D Xia, X Zhang; (III) Provision of study materials or patients: S Niu, B Wang, X Wang, Q Zhang, J Wang, X Jin, L Mao, Y Ruan, H Wang, F Sun, Z Cai, Y Chen, T Zeng, X Xiang, Z Qiang, J Zhang, Y Liu, P Chen, J Li; (IV) Collection and assembly of data: L Wang, Z Ying; (V) Data analysis and interpretation: D Wang, C Lin, T He; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Baojun Wang, PhD. Department of Urology, Chinese PLA General Hospital, Yongding Road 69th, Haidian District, Beijing 100039, China. Email: baojun40009@126.com.

Background: The CHART study established the combination of rezvilutamide and androgen deprivation therapy (ADT) as a standard treatment for patients with high-volume metastatic hormone-sensitive prostate cancer (mHSPC). However, the therapeutic outcomes of this regimen in patients with low-volume mHSPC remain insufficiently defined. This study thus aimed to assess the real-world effectiveness of rezvilutamide combined with ADT in the treatment of low-volume mHSPC.

Methods: This multicenter, noninterventional, observational study was conducted in China and included adult patients diagnosed with low-volume mHSPC who were treated with rezvilutamide in combination with ADT as determined by the investigator. The study assessed prostate-specific antigen (PSA) responses at multiple time points (3, 6, 9, and 12 months), including a PSA decline ≥50% (PSA50), a PSA decline ≥90% (PSA90), and a PSA level <0.2 ng/mL (undetectable PSA). Subgroup analyses of PSA responses were conducted according to baseline characteristics, including age, Eastern Cooperative Oncology Group performance status (ECOG PS), and Gleason score.

Results: Between August 29, 2023 and December 31, 2024, a total of 257 patients were enrolled in the study. The median age was 73 years [interquartile range (IQR), 68–77 years], and the median baseline PSA level was 38 ng/mL (IQR, 7–100 ng/mL). PSA responses were observed as early as 3 months after initiating rezvilutamide treatment, with 88% [176/199; 95% exact confidence interval (CI): 83–93%] achieving PSA50, 75% (149/199; 95% exact CI: 68–81%) achieving PSA90, and 54% (108/199; 95% exact CI: 47–61%)

achieving undetectable PSA levels. These responses further improved at subsequent time points (6, 9, and 12 months). By 12 months, 100% (12/12; 95% exact CI: 74–100%) achieved PSA50, 92% (11/12; 95% exact CI: 62–100%) achieved PSA90, and 83% (10/12; 95% exact CI: 52–98%) had undetectable PSA levels.

Conclusions: This study is the first to evaluate the effectiveness of rezvilutamide in patients with low-volume mHSPC. In a real-world clinical setting, the combination of rezvilutamide and ADT demonstrated favorable PSA response in this patient population. These findings provide additional treatment options for patients with low-volume mHSPC and support the need for further large-scale research on rezvilutamide in this subgroup.

Keywords: Rezvilutamide; low-volume; hormone-sensitive; castration-sensitive; metastatic prostate cancer

Submitted Mar 28, 2025. Accepted for publication Apr 09, 2025. Published online Apr 17, 2025.
doi: 10.21037/tau-2025-239
View this article at: https://dx.doi.org/10.21037/tau-2025-239

Introduction

Prostate cancer is one of the most commonly diagnosed malignancies in men, ranking as the second most frequently diagnosed cancer worldwide and the sixth most common in China (1,2). Although the incidence of prostate cancer in China remains lower than that observed in Western countries, it is anticipated to rise steadily over time, with projections indicating an increase from the 2018–2022 period to 2028–2032 (1,3). Among patients with metastatic hormone-sensitive prostate cancer (mHSPC), those with low-volume disease account for approximately 23–66% of cases (4-8).

Androgen deprivation therapy (ADT) remains the cornerstone of treatment for mHSPC. However, ADT alone is insufficient for sustained disease control and long-term survival, as the majority of patients ultimately progress to castration-resistant disease (9). Data from pivotal phase III clinical trials involving the overall mHSPC population—including the ARCHES (6), ENZAMET (10), ARASENS (11), ARANOTE (12), and TITAN (13) trials—have demonstrated that combining ADT with second-generation androgen receptor (AR) inhibitors, with or without docetaxel, provide significant survival benefits. Consequently, ADT-based combination therapies have become the standard of care for mHSPC (14). However, determining the optimal treatment strategy for mHSPC remains complex due to the availability of multiple effective therapies and the clinical heterogeneity among patients (15). A meta-analysis showed that, within the overall mHSPC population, the triplet regimen of ADT + AR inhibitor + docetaxel provides the greatest benefit. In patients with high-volume disease, both triplet therapy and the combination of ADT with rezvilutamide—a novel AR inhibitor developed in China—appear to offer the most clinical benefit. In contrast, patients with low-volume mHSPC are more likely to benefit from

Highlight box

Key findings

- This study evaluated the real-world effectiveness of rezvilutamide combined with androgen deprivation therapy (ADT) in patients with low-volume metastatic hormone-sensitive prostate cancer (mHSPC).
- Prostate-specific antigen (PSA) response was observed as early as 3 months after treatment initiation, with 88% of patients achieving a PSA decline ≥50% (PSA50), a PSA decline ≥90% (PSA90), and 54% demonstrating undetectable PSA levels.
- These responses were sustained and improved over time, with PSA50, PSA90, and undetectable PSA rates reaching 100%, 92%, and 83%, respectively, by 12 months.

What is known and what is new?

- The CHART study established rezvilutamide plus ADT as a standard treatment for high-volume mHSPC, but its efficacy in low-volume mHSPC has not been determined.
- This study provides the first real-world evidence supporting the effectiveness of rezvilutamide plus ADT in low-volume mHSPC, demonstrating robust and sustained PSA responses.

What is the implication, and what should change now?

- These findings highlight the potential role of rezvilutamide plus ADT in treating patients with low-volume mHSPC. The results provide additional therapeutic options for this patient group and establish a foundation for future large-scale studies evaluating rezvilutamide in low-volume mHSPC.
- Further prospective trials are warranted to validate these results and assess the long-term survival outcomes.

the doublet regimen of ADT plus an AR inhibitor (16). However, some studies included in this meta-analysis, including the CHART trial, did not provide data specifically for the low-volume subgroup.

The phase III CHART study (17) reported that rezvilutamide, in combination with ADT, significantly improved radiographic progression-free survival (rPFS) and overall survival (OS) compared to bicalutamide combined with ADT in patients with high-volume mHSPC. Additionally, this treatment demonstrated a favorable safety and tolerability profile. Based on these findings, rezvilutamide was approved by the National Medical Products Administration (NMPA) in China for the treatment of high-volume mHSPC. However, large-scale data on the use of rezvilutamide in patients with low-volume disease remain limited (18). In real-world clinical practice in China, many patients with low-volume mHSPC have been treated with rezvilutamide plus ADT, as this regimen is covered by the national health insurance. Therefore, the aim of this study was to collect and analyze data on the effectiveness of rezvilutamide in combination with ADT for the treatment of patients with low-volume mHSPC under real-world conditions. A secondary aim of the study was to assess the influence of baseline characteristics on treatment outcomes across various subgroups of patients with low-volume mHSPC. We present this article in accordance with the STROBE reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-2025-239/rc).

Methods

Study design

Between August 29, 2023 and December 31, 2024, we conducted a retrospective, multicenter, real-world observational study across 21 offline centers and 1 online center in China. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and its subsequent amendments, and the study protocol, along with any amendments, was approved by the Ethics Committee of the Chinese PLA General Hospital (No. S2022-623-03). Written informed consent was obtained from all participants prior to their inclusion in the study. All participating hospitals/institutions were informed and agreed with the study.

Study population

The study enrolled patients aged ≥18 years who were diagnosed with low-volume mHSPC and received a treatment regimen containing rezvilutamide, as determined at the investigator's discretion. Individuals participating in other clinical trials involving rezvilutamide at the time or those deemed unsuitable for inclusion based on the investigator's assessment were excluded from the study.

Data collection

Patient data were collected primarily through medical records and/or patient interviews. Baseline characteristics included age, time from diagnosis to the first dose of rezvilutamide, Eastern Cooperative Oncology Group performance status (ECOG PS), prostate-specific antigen (PSA) levels, Gleason score, treatment regimen, and previous therapies. PSA response rates at 3, 6, 9, and 12 months following the initiation of rezvilutamide treatment were also recorded, including rates of PSA decline from baseline ≥50% (PSA50), PSA decline from baseline ≥90% (PSA90) and undetectable PSA levels. PSA levels were confirmed by a repeat assessment conducted at least 3 weeks after the first assessment. The undetectable PSA rate was defined as the proportion of patients with detectable PSA levels (≥0.2 ng/mL) at baseline that became undetectable (<0.2 ng/mL) during the study.

Statistical analysis

Descriptive analyses were used to summarize patients' baseline characteristics and PSA responses. The analysis population included all enrolled patients who received at least one dose of rezvilutamide. Categorical variables are reported as the number of patients (N) and percentage (%), while continuous variables are expressed as the median and interquartile range (IQR). The 95% confidence intervals (CIs) for PSA response rates were calculated using the Clopper-Pearson method. Rates for PSA responses, including PSA50, PSA90, and undetectable PSA, were assessed at 3, 6, 9, and 12 months following the initiation of rezvilutamide treatment. To further characterize the rates of PSA responses across different populations, a predefined subgroup analysis was conducted. Subgroups were stratified according to baseline characteristics, which included age (<75 *vs.* ≥75 years), ECOG PS (0–1 *vs.* ≥2), and Gleason score (<8 *vs.* ≥8). All statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA).

Table 1 Baseline characteristics of the enrolled patients

Characteristic	Low-volume mHSPC (N=257)
Age (years), median [IQR]	73 [68–77]
Age group, n [%]	
<75 years	159 [62]
≥75 years	98 [38]
Time from diagnosis to first dose of drug (days)	
Median [IQR]	12 [5–41]
Data missing, n [%]	63 [25]
ECOG performance status, n [%]	
<2 (0/1)	214 [83]
≥2 (2/3/4)	33 [13]
Data missing	10 [4]
PSA (ng/mL), median [IQR]	38 [7–100]
Gleason score, n [%]	
<8	40 [16]
≥8	103 [40]
Data missing, n [%]	114 [44]
Therapeutic regimen, n [%]	
Rezvilutamide + ADT	252 [98]
Rezvilutamide + ADT + chemotherapy	2 [1]
Rezvilutamide + ADT + others	3 [1]
Prior treatment, n [%]	
Yes*	52 [20]
Previous surgery	41 [16]
Previous radiotherapy	1 [0]
Previous ADT therapy	17 [7]
Previous antiandrogenic therapy	3 [1]
No	85 [33]
Data missing, n [%]	120 [47]

*, patients who have received at least one prior treatment. ADT, androgen deprivation therapy; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; mHSPC, metastatic hormone-sensitive prostate cancer; PSA, prostate-specific antigen.

Results

Baseline characteristics

Between August 29, 2023 and December 31, 2024, a total of 257 patients with low-volume mHSPC were enrolled from 21 offline centers and 1 online center across China. The median age was 73 years (IQR, 68–77 years), with 98 patients (38%) aged ≥75 years. The median time from diagnosis to the first dose of rezvilutamide was 12 days (IQR, 5–41 days). All patients initiated treatment with rezvilutamide at a dose of 240 mg. During the course of treatment, dose adjustments were made for 2 patients due to tolerability issues: one was adjusted to 160 mg and the other to 80 mg. The use of ADT in this study adhered to local guidelines. A total of 33 (13%) patients had an ECOG PS of ≥2. The median baseline PSA level was 38 ng/mL (IQR, 7–100 ng/mL), and 103 patients (40%) had a Gleason score of ≥8. The majority (n=252, 98%) of patients received rezvilutamide in combination with ADT, while 2 (1%) patients were treated with rezvilutamide plus ADT and chemotherapy, and 3 (1%) received rezvilutamide plus ADT with other therapies. Prior to the initiation of rezvilutamide plus ADT, 52 (20%) individuals had previously received at least one anti-tumor treatment, including 41 (16%) who underwent surgery, 1 who received radiotherapy, 17 (7%) who underwent ADT, and 3 (1%) who received antiandrogen therapy. Additionally, 85 patients (33%) had not received any antineoplastic therapy, and data were missing for 120 patients (47%). The detailed baseline characteristics of the enrolled patients are presented in *Table 1*.

PSA response

At 3 months, 88% (176/199; 95% exact CI: 83–93%) of patients achieved a PSA50 response, which increased to 91% (64/70; 95% exact CI: 82–97%) at 6 months, 97% (32/33; 95% exact CI: 84–100%) at 9 months, and 100% (12/12; 95% exact CI: 74–100%) at 12 months. Similarly, the proportion of patients achieving PSA90 was 75% (149/199; 95% exact CI: 68–81%) at 3 months, rising progressively to 89% (62/70; 95% exact CI: 79–95%) at 6 months, 91% (30/33; 95% exact CI: 76–98%) at 9 months, and 92% (11/12; 95% exact CI: 62–100%) at 12 months.

Table 2 PSA responses

Response	3 months (N=199)	6 months (N=70)	9 months (N=33)	12 months (N=12)
PSA50	176 (88, 83–93)	64 (91, 82–97)	32 (97, 84–100)	12 (100, 74–100)
PSA90	149 (75, 68–81)	62 (89, 79–95)	30 (91, 76–98)	11 (92, 62–100)
Undetectable PSA	108 (54, 47–61)	48 (69, 56–79)	24 (73, 54–87)	10 (83, 52–98)

Data are presented as n (%, 95% exact CI). CI, confidence interval; PSA, prostate-specific antigen; PSA50, PSA decline ≥50%; PSA90, PSA decline 90%.

An undetectable PSA level was observed in 54% (108/199; 95% exact CI: 47–61%) of patients at 3 months, with a consistent increase over time to 69% (48/70; 95% exact CI: 56–79%) at 6 months, 73% (24/33; 95% exact CI: 54–87%) at 9 months, and 83% (10/12; 95% exact CI: 52–98%) at 12 months. The detailed results are presented in *Table 2*.

Subgroup analysis

In patients aged <75 years, the proportions achieving PSA50, PSA90, and an undetectable PSA response at 3 months were 89% (109/123), 79% (97/123), and 59% (72/123), respectively. These response rates were consistently higher than those observed in the ≥75-year subgroup, where response rates for PSA50, PSA90, and undetectable PSA were 88% (67/76), 68% (52/76), and 47% (36/76), respectively. However, at 6 and 9 months, the rates of PSA response—including PSA50, PSA90, and undetectable PSA—were higher in the ≥75-year subgroup as compared to the <75-year subgroup. By 12 months, the PSA50 response rate reached 100% in both age groups, while the <75-year subgroup demonstrated higher PSA90 and undetectable PSA rates as compared to the ≥75-year subgroup. Notably, the sample sizes in both groups were small at the 12 months, with fewer than 10 patients in each group (*Table 3*).

At 3 months, the PSA50, PSA90, and undetectable PSA rates in the ECOG PS 0–1 subgroup were 90% (148/165), 77% (127/165), and 55% (90/165), respectively, all of which were higher than those observed in the ECOG PS ≥2 subgroup, where the corresponding rates were 76% (19/25), 56% (14/25), and 48% (12/25). However, at 6, 9 and 12 months, the sample size in the ECOG PS ≥2 subgroup was limited (n=4, n=3 and n=1, respectively), and the differences in PSA response rates between the two subgroups deviated from the patterns observed at 3 months.

At 3, 6, and 9 months, the rates of PSA50 and undetectable PSA response in the Gleason score <8 subgroup were comparable to or higher than those in the Gleason score ≥8 subgroup. A similar pattern was observed for PSA90 at 6 and 9 months. However, at 3 months, the rate of PSA90 response was lower in the Gleason score <8 subgroup (22/32, 69%) as compared to the Gleason score ≥8 subgroup (68/85, 80%). At 12 months, no analyzable samples were available in the Gleason score <8 subgroup, while the rates for PSA50, PSA90, and undetectable PSA response all reached 100% (5/5) in the Gleason score ≥8 subgroup. Notably, the sample size in the Gleason score <8 subgroup was limited at 6 and 9 months (n=7 and n=4, respectively).

Discussion

This nationwide, multicenter observational study evaluated the real-world efficacy of rezvilutamide in combination with ADT for the treatment of low-volume mHSPC. To the best of our knowledge, this is the first study to investigate the outcomes of rezvilutamide specifically in this patient population. Our findings revealed that undetectable PSA (PSA <0.2 ng/mL) was achieved as early as 3 months after the initiation of rezvilutamide treatment and was sustained to 6, 9, and 12 months. These results underscore the potential clinical value of rezvilutamide combined with ADT in achieving rapid, profound, and durable PSA reductions in patients with low-volume mHSPC.

Over the past two decades, significant advances have been made in the treatment of mHSPC (19). Multiple phase III randomized controlled trials have confirmed that combining ADT with AR inhibitors, with or without docetaxel, can significantly prolong OS (6,10-13). Previous studies have shown differences in the extent of benefit from triple and double regimens in mHSPC patients with varying tumor burdens (11,16). A meta-analysis that included data from the CHART study found that, in patients with high-volume mHSPC, both triplet therapy and the combination of ADT with rezvilutamide provided the greatest benefit.

Table 3 PSA responses across subgroups over time

Variables	3 months			6 months			9 months			12 months		
	PSA50	PSA90	Undetectable PSA	PSA50	PSA90	Undetectable PSA	PSA50	PSA90	Undetectable PSA	PSA50	PSA90	Undetectable PSA
Age												
<75 years	109/123 [89]	97/123 [79]	72/123 [59]	35/39 [90]	33/39 [85]	25/39 [64]	19/20 [95]	18/20 [90]	14/20 [70]	8/8 [100]	8/8 [100]	7/8 [88]
≥75 years	67/76 [88]	52/76 [68]	36/76 [47]	29/31 [94]	29/31 [94]	23/31 [74]	13/13 [100]	12/13 [92]	10/13 [77]	4/4 [100]	3/4 [75]	3/4 [75]
ECOG PS												
0–1	148/165 [90]	127/165 [77]	90/165 [55]	54/58 [93]	52/58 [90]	39/58 [67]	25/26 [96]	23/26 [88]	18/26 [69]	7/7 [100]	6/7 [86]	5/7 [71]
≥2	19/25 [76]	14/25 [56]	12/25 [48]	4/6 [67]	4/6 [67]	4/6 [67]	3/3 [100]	3/3 [100]	2/3 [67]	1/1 [100]	1/1 [100]	1/1 [100]
Gleason score												
<8	30/32 [94]	22/32 [69]	18/32 [56]	7/7 [100]	7/7 [100]	7/7 [100]	4/4 [100]	4/4 [100]	3/4 [75]	0	0	0
≥8	78/85 [92]	68/85 [80]	46/85 [54]	33/35 [94]	32/35 [91]	25/35 [71]	17/17 [100]	16/17 [94]	11/17 [65]	5/5 [100]	5/5 [100]	5/5 [100]

Data are presented as n/N [%]. ECOG PS, Eastern Cooperative Oncology Group performance status; PSA, prostate-specific antigen; PSA50, PSA decline ≥50%; PSA90, PSA decline 90%.

In contrast, patients with low-volume mHSPC were more likely to benefit from the doublet regimen of ADT plus an AR-targeted agent (16). Consistent with this, the National Comprehensive Cancer Network (NCCN) guidelines recommend combining ADT with an AR-targeted therapy as the preferred treatment option for patients with low-volume mHSPC (14).

In the phase III CHART registration trial of rezvilutamide, 654 patients with high-volume mHSPC were enrolled. As of February 28, 2022, rezvilutamide combined with ADT significantly improved rPFS [hazard ratio (HR) =0.44; 95% CI: 0.33–0.58] and OS (HR =0.58, 95% CI: 0.44–0.77) compared with bicalutamide plus ADT, with an acceptable safety profile (17). A *post hoc* analysis presented at the 2023 European Society for Medical Oncology (ESMO) conference (20) further evaluated the association between PSA response and survival outcomes. At 3 months, 38.34% (125/326) of patients in the rezvilutamide plus ADT group achieved undetectable PSA (≤0.2 ng/mL) compared to 17.68% (58/328) in the bicalutamide plus ADT group. This proportion increased at subsequent time points, reaching 52.15% (170/326) at 6 months and 61.66% (201/326) at 12 months in the rezvilutamide group, compared to 27.44% (90/328) and 32.93% (108/328) in the bicalutamide group, respectively. Notably, patients in the rezvilutamide group who achieved undetectable PSA at 6 months experienced significantly prolonged rPFS and OS, highlighting the clinical relevance of PSA response as a prognostic indicator. These findings suggest that rezvilutamide combined with ADT significantly improves PSA response rates in patients with high-volume mHSPC, with undetectable PSA closely associated with survival benefit. However, data on rezvilutamide in the treatment of low-volume mHSPC remain scarce. One case report described a 68-year-old male with low-volume mHSPC who demonstrated PSA reduction and radiographic improvement following treatment with rezvilutamide plus ADT. The patient experienced only mild treatment-related adverse events, indicating a favorable therapeutic response (18).

To address the lack of evidence regarding rezvilutamide in low-volume mHSPC, this study analyzed PSA responses in patients treated with rezvilutamide plus ADT. We found that 54% of patients achieved undetectable PSA levels at 3 months, with this proportion progressively increasing over time to 69%, 73%, and 83% at 6, 9, and 12 months, respectively. Although comparisons with previous trials should be made cautiously due to variations in patient characteristics such as age, performance status, disease

stage, and prior treatment, the rate of undetectable PSA observed in this study was comparable to those reported in earlier studies, including the ARASENS (4) and ARANOTE (21) trials. According to the ARASENS trial's *post hoc* analysis, patients with low-volume mHSPC treated with darolutamide + ADT + docetaxel demonstrated rates of undetectable PSA of 45%, 67%, 76%, and 78% at 12, 24, 36, and 52 weeks, respectively—outperforming the placebo + ADT + docetaxel group (4). Similarly, in the ARANOTE trial's *post hoc* analysis, the rate of undetectable PSA among patients with low-volume mHSPC receiving darolutamide + ADT reached 72%, 78%, and 79% at 24, 36, and 48 weeks, respectively, which were consistently higher than those in the placebo + ADT group (21).

Notably, consistent with the findings from the ARASENS (4) and ARANOTE (21) trials, patients with low-volume mHSPC in these studies exhibited higher rates of undetectable PSA as compared to their high-volume counterparts. Specifically, the rates of undetectable PSA in this study's low-volume population exceeded those reported in the CHART study's high-volume population. Moreover, the rates of PSA90 and PSA50 response were markedly high, surpassing 85% at all evaluated time points, except for PSA90 at 3 months (75%). These results align with the PSA kinetics analysis from the ARASENS trial (4), which similarly reported increasing rates of PSA90 and PSA50 response with prolonged treatment, underscoring the importance of sustained therapy in achieving deeper and more durable PSA reductions.

PSA response is widely recognized as a critical biomarker in the management of prostate cancer, playing a key role in prognostic assessment, treatment efficacy evaluation, and therapeutic decision-making (22). Changes in PSA levels are also frequently used as primary endpoints in clinical studies (23-25). Evidence from the ARASENS *post hoc* analysis demonstrated that achieving deep PSA responses was significantly associated with prolonged OS, delayed progression to castration-resistant prostate cancer (CRPC), and extended PSA progression-free intervals in both high-volume and low-volume mHSPC patients (4). Similar associations between PSA response and improved clinical outcomes in mHSPC have been reported in other key trials, including CHAARTED (26), LATITUDE (27), TITAN (9), and CHART (20). Furthermore, real-world studies have consistently confirmed that PSA declines are predictive of better clinical outcomes in patients with mHSPC (7,28,29). Beyond the mHSPC setting, the prognostic value of PSA response extends to other contexts, such as nonmetastatic CRPC, in which PSA reduction has been shown to correlate with survival benefit (30). In our study, the rezvilutamide plus ADT regimen achieved high and sustained rates of PSA response, suggesting a potential positive impact on the long-term prognosis of patients with low-volume mHSPC. However, further research and robust clinical evidence are needed to validate these findings and establish their broader implications.

This study has several limitations that should be acknowledged. First, the retrospective nature of data collection and the inherent constraints of observational research might have introduced biases, potentially impacting the robustness of the findings. Additionally, this design inevitably resulted in a significant amount of missing data, which impacted the analysis and interpretation of the results. Second, the study population was limited to Chinese patients, which may limit the generalizability of the results to other ethnic groups and a broader population. Third, the relatively short follow-up period precluded the assessment of long-term survival outcomes, including rPFS and OS, leaving uncertainties regarding whether the observed PSA benefits translate into meaningful survival advantages. Fourth, due to the retrospective nature of the data collection, comprehensive safety data were difficult to obtain, and as such, this study focused primarily on effectiveness. According to safety data from the CHART study (17), the combination of rezvilutamide and ADT in treating high-volume mHSPC demonstrated manageable safety, with the most common grade 3 or higher treatment-related adverse events being weight gain, hypertriglyceridemia, and hypertension, with no treatment-related deaths reported. The safety of rezvilutamide in low-volume mHSPC patients requires further investigation. Finally, the small sample sizes of the subgroups at later stages may have affected the stability of the observed results and further restricted their generalizability. Future large-scale, prospective studies in a diversity of populations and extended follow-up periods are warranted to address these limitations.

Conclusions

This study demonstrated the feasibility and effectiveness of rezvilutamide combined with ADT in treating patients with low-volume mHSPC. The combination regimen achieved rapid, profound, and sustained PSA reductions—key indicators strongly associated with improved tumor control and survival outcomes—in the majority of patients.

These findings highlight the potential of this regimen as a promising therapeutic option for patients with low-volume mHSPC. The results contribute to expanding treatment options for this patient population and support the further development of large-scale studies evaluating rezvilutamide in this subgroup.

Acknowledgments

We would like to thank all the patients who participated in this study and their families. We also thank the following hospitals/institutions for their invaluable contributions to the study: Chinese PLA General Hospital, Peking, China; Shanghai General Hospital, Shanghai, China; Zaozhuang Municipal Hospital, Zaozhuang, China; Zhangjiagang Hospital of Traditional Chinese Medicine, Zhangjiagang, China; The Affiliated Hospital of Qingdao University, Qingdao, China; Cancer Hospital Chinese Academy of Medical Sciences, Peking, China; Anhui Provincial Hospital, Anhui, China; Tianjin Medical University Cancer Institute & Hospital, Tianjin, China; Peking University First Hospital, Peking, China; The First Hospital of China Medical University, Shenyang, China; Linyi People's Hospital, Linyi, China; Qilu Hospital of Shandong University Dezhou Hospital, Dezhou, China; Huangshan City People's Hospital, Huangshan, China; Weifang People's Hospital, Weifang, China; The First Affiliated Hospital of Kunming Medical University, Kunming, China; Changshu No. 2 People's Hospital, Changshu, China; The First People's Hospital of Zhangjiagang, Zhangjiagang, China; The First People's Hospital of Lianyungang, Lianyungang, China; Affiliated Hospital of Panzhihua University, Panzhihua, China; Yueyang Central Hospital, Yueyang, China; Anyang Tumor Hospital, Anyang, China; Yinchuan Medical Duoyun Internet Hospital Co., Ltd., Yinchuan, China.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-2025-239/rc

Data Sharing Statement: Available at https://tau.amegroups.com/article/view/10.21037/tau-2025-239/dss

Peer Review File: Available at https://tau.amegroups.com/article/view/10.21037/tau-2025-239/prf

Funding: This study was supported by Jiangsu Hengrui Pharmaceuticals Co., Ltd. Although the funders were engaged in statistical analysis and data interpretation, they were not involved in shaping the study's design, data collection, decisions concerning publication, or preparation of the manuscript.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-2025-239/coif). L.W., Z.Y., D.W., C.L., and T.H. are employees of Jiangsu Hengrui Pharmaceuticals Co., Ltd. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and its subsequent amendments, and was approved by the Ethics Committee of the Chinese PLA General Hospital (No. S2022-623-03). All participating hospitals/institutions were informed and agreed with this study. Informed consent was obtained from all patients.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2024;74:229-63.
2. Han B, Zheng R, Zeng H, et al. Cancer incidence and mortality in China, 2022. J Natl Cancer Cent 2024;4:47-53.
3. Li M, Hu M, Jiang L, et al. Trends in Cancer Incidence

and Potential Associated Factors in China. JAMA Netw Open 2024;7:e2440381.
4. Saad F, Hussain MHA, Tombal B, et al. Deep and Durable Prostate-specific Antigen Response to Darolutamide with Androgen Deprivation Therapy and Docetaxel, and Association with Clinical Outcomes for Patients with High- or Low-volume Metastatic Hormone-sensitive Prostate Cancer: Analyses of the Randomized Phase 3 ARASENS Study. Eur Urol 2024;86:329-39.
5. Kyriakopoulos CE, Chen YH, Carducci MA, et al. Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer: Long-Term Survival Analysis of the Randomized Phase III E3805 CHAARTED Trial. J Clin Oncol 2018;36:1080-7.
6. Armstrong AJ, Szmulewitz RZ, Petrylak DP, et al. ARCHES: A Randomized, Phase III Study of Androgen Deprivation Therapy With Enzalutamide or Placebo in Men With Metastatic Hormone-Sensitive Prostate Cancer. J Clin Oncol 2019;37:2974-86.
7. López-Abad A, Belmonte M, Ramírez Backhaus M, et al. Ultralow Prostate-Specific Antigen (PSA) Levels and Improved Oncological Outcomes in Metastatic Hormone-Sensitive Prostate Cancer (mHSPC) Patients Treated with Apalutamide: A Real-World Multicentre Study. J Clin Med 2024;13:6221.
8. Hassi Roman M, Mate K, De Pablos-Rodriguez P, et al. Prostate-specific Antigen at 3 Months as a Predictor of Radiologic Progression-free Survival in Metastatic Hormone-sensitive Prostate Cancer Treated with Apalutamide: Analysis of 633 Patients in a Real-world Database. Eur Urol Open Sci 2024;70:58-63.
9. Chowdhury S, Bjartell A, Agarwal N, et al. Deep, rapid, and durable prostate-specific antigen decline with apalutamide plus androgen deprivation therapy is associated with longer survival and improved clinical outcomes in TITAN patients with metastatic castration-sensitive prostate cancer. Ann Oncol 2023;34:477-85.
10. Davis ID, Martin AJ, Stockler MR, et al. Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer. N Engl J Med 2019;381:121-31.
11. Hussain M, Tombal B, Saad F, et al. Darolutamide Plus Androgen-Deprivation Therapy and Docetaxel in Metastatic Hormone-Sensitive Prostate Cancer by Disease Volume and Risk Subgroups in the Phase III ARASENS Trial. J Clin Oncol 2023;41:3595-607.
12. Saad F, Vjaters E, Shore N, et al. Darolutamide in Combination With Androgen-Deprivation Therapy in Patients With Metastatic Hormone-Sensitive Prostate Cancer From the Phase III ARANOTE Trial. J Clin Oncol 2024;42:4271-81.
13. Chi KN, Chowdhury S, Bjartell A, et al. Apalutamide in Patients With Metastatic Castration-Sensitive Prostate Cancer: Final Survival Analysis of the Randomized, Double-Blind, Phase III TITAN Study. J Clin Oncol 2021;39:2294-303.
14. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer. Version 1. 2025 ed: National Comprehensive Cancer Network; 2024.
15. Riaz IB, Naqvi SAA, He H, et al. First-line Systemic Treatment Options for Metastatic Castration-Sensitive Prostate Cancer: A Living Systematic Review and Network Meta-analysis. JAMA Oncol 2023;9:635-45.
16. Jian T, Zhan Y, Yu Y, et al. Combination therapy for high-volume versus low-volume metastatic hormone-sensitive prostate cancer: A systematic review and network meta-analysis. Front Pharmacol 2023;14:1148021.
17. Gu W, Han W, Luo H, et al. Rezvilutamide versus bicalutamide in combination with androgen-deprivation therapy in patients with high-volume, metastatic, hormone-sensitive prostate cancer (CHART): a randomised, open-label, phase 3 trial. Lancet Oncol 2022;23:1249-60.
18. Zhang C, Ren J, Kang Y, et al. Case report and literature review of rezvilutamide in the treatment of hormone-sensitive prostate cancer. Front Oncol 2024;14:1374039.
19. Hoeh B, Chun FKH, Mandel P. Disease volume and risk subgroup analyses for darolutamide plus androgen-deprivation therapy and docetaxel in the phase III ARASENS: should triplet therapy become standard of care in certain metastatic hormone-sensitive prostate cancer patients? Chin Clin Oncol 2024;13:14.
20. Chang K, Zhang X, Xie L, et al. 1788P - Association between deep prostate-specific antigen decline and survival in patients with high-volume metastatic hormone-sensitive prostate cancer treated with rezvilutamide in the CHART trial. Ann Oncol 2023;34:S954-S1000.
21. Saad F, Shore N, Vjaters E, et al. editors. The ARANOTE phase 3 trial of darolutamide plus androgen-deprivation therapy in patients with metastatic hormone-sensitive prostate cancer: efficacy and safety by disease volume. American Society of Clinical Oncology Genitourinary Cancers Symposium; 2025 February 13-15, 2025; San Francisco, CA, USA.
22. Scher HI, Morris MJ, Stadler WM, et al. Trial Design and Objectives for Castration-Resistant Prostate

Cancer: Updated Recommendations From the Prostate Cancer Clinical Trials Working Group 3. J Clin Oncol 2016;34:1402-18.
23. Aglan M, Kong Y, Connell B. Testosterone therapy in patients with locoregional prostate cancer treated with prior androgen deprivation therapy and radiation: a retrospective single center review. Transl Androl Urol 2025;14:250-7.
24. Leuva H, Teply BA. The COMBAT trial: use of bipolar androgen therapy to enhance immune checkpoint blockade in the management of metastatic castration-resistant prostate cancer. AME Clin Trials Rev 2024;2:105.
25. Giesen A, De Meerleer G, Joniau S, et al. The TRACE-II trial: will this draw the path for radioguided surgery and androgen deprivation therapy combination, or not? AME Clin Trials Rev 2024;2:68.
26. Harshman LC, Chen YH, Liu G, et al. Seven-Month Prostate-Specific Antigen Is Prognostic in Metastatic Hormone-Sensitive Prostate Cancer Treated With Androgen Deprivation With or Without Docetaxel. J Clin Oncol 2018;36:376-82.
27. Matsubara N, Chi KN, Özgüroğlu M, et al. Correlation of Prostate-specific Antigen Kinetics with Overall Survival and Radiological Progression-free Survival in Metastatic Castration-sensitive Prostate Cancer Treated with Abiraterone Acetate plus Prednisone or Placebos Added to Androgen Deprivation Therapy: Post Hoc Analysis of Phase 3 LATITUDE Study. Eur Urol 2020;77:494-500.
28. Elewaily MI, Campione M, Hassan MA, et al. Prognostic factors and treatment choice for stage IV, low-volume metastasis hormone-sensitive prostate cancer: cross-sectional study of real-world data. Ther Adv Urol 2024;16:17562872241297579.
29. López-Abad A, Ramírez Backhaus M, Server Gómez G, et al. Real-world prostate-specific antigen reduction and survival outcomes of metastatic hormone-sensitive prostate cancer patients treated with apalutamide: An observational, retrospective, and multicentre study. Prostate Int 2024;12:20-6.
30. Saad F, Small EJ, Feng FY, et al. Deep Prostate-specific Antigen Response following Addition of Apalutamide to Ongoing Androgen Deprivation Therapy and Long-term Clinical Benefit in SPARTAN. Eur Urol 2022;81:184-92.

(English Language Editor: J. Gray)

Cite this article as: Niu S, Xia D, Wang B, Wang X, Zhang Q, Wang J, Jin X, Mao L, Ruan Y, Wang H, Sun F, Cai Z, Chen Y, Zeng T, Xiang X, Qiang Z, Zhang J, Liu Y, Chen P, Li J, Zhang X, Wang L, Ying Z, Wang D, Lin C, He T. Real-world effectiveness of rezvilutamide plus androgen deprivation therapy in patients with low-volume, metastatic hormone-sensitive prostate cancer: a retrospective multicenter study. Transl Androl Urol 2025;14(4):1119-1128. doi: 10.21037/tau-2025-239