



Enzalutamide alleviates anxiety and depression as well as improves quality of life compared to bicalutamide in metastatic castration-resistant prostate cancer patients: a cohort study

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Background: This study aimed to evaluate the efficacy of enzalutamide compared with bicalutamide on anxiety, depression and quality of life (QoL) in metastatic castration-resistant prostate cancer (mCRPC) patients.

Methods: Totally 134 mCRPC patients were consecutively enrolled and baseline data were documented, among whom 53 patients received enzalutamide as Enzalutamide group, while 81 patients received bicalutamide as Bicalutamide group. Anxiety and depression were assessed by Hospital Anxiety and Depression Scale (HADS) as well as Zung Self-Rating Anxiety/Depression Scale (SAS/SDS), and QoL was assessed by Functional Assessment of Cancer Therapy (FACT)-General/Prostate (FACT-G/FACT-P) questionnaires at W0 (baseline), W12, W24, W36, W48 and W60.

Results: No difference of HADS-anxiety (HADS-A), SAS, HADS-depression (HADS-D), SDS, FACT-G or FACT-P score at baseline was observed between Enzalutamide group and Bicalutamide group. Both HADS-A score and SAS score were decreased at W48 and W60 in Enzalutamide group compared to Bicalutamide group. HADS-D score was reduced at W60 and SDS score was attenuated at W48 and W60 in Enzalutamide group compared to Bicalutamide group. As to QoL assessments, FACT-G score disclosed no difference at each visit between Enzalutamide group and Bicalutamide group, while FACT-P score was decreased at W60 in Enzalutamide group compared to Bicalutamide group. In addition, the reduction of HADS-A, SAS, HADS-D, SDS, FACT-G and FACT-P scores from W0 to W60 were all higher in Enzalutamide group compared to Bicalutamide group.

Conclusions: In conclusion, enzalutamide presents with better efficacy on alleviating anxiety and depression, as well as improving QoL in mCRPC patients compared to bicalutamide.

Keywords: Anxiety; bicalutamide; depression; enzalutamide; metastatic castration-resistant prostate cancer (mCRPC); quality of life (QoL)

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Introduction

Prostate cancer is the second most frequently diagnosed cancer and the fifth leading cause of cancer death in men all around the world, with approximately 1,600,000 newly diagnosed cases and 366,000 prostate cancer-related deaths each year (1-6). Metastatic castration-resistant prostate cancer (mCRPC), the advanced stage of prostate cancer, happens in about 10–20% prostate cancer patients within 5 years after initial diagnosis (5,7-9). Recently, improved survival in mCRPC patients has been achieved partly owing to the application of common therapeutic agents (such as bicalutamide), whereas there are still a large portion of patients complicated with psychological disorders including anxiety and depression due to the fast disease progression, intolerable clinical symptoms or other severe complications, which directly decrease their quality of life (QoL) and indirectly cause poor prognosis (10-13). Therefore, exploring additional and convincing treatment agents that not only delay disease progression but also alleviate psychological disorders is pivotal for improving QoL and prognosis in mCRPC patients.

Enzalutamide, a second-generation nonsteroidal antiandrogen (NSAA) approved by United States food and drug administration (FDA) in 2012 for the mCRPC treatment, suppresses proliferation of LNCaP/AR human prostate cancer cells through inhibiting translocation of androgen receptor (AR) to cell nucleus (14,15). In clinical practices, enzalutamide presents with better efficacy in delaying prostate specific antigen (PSA) progression and improving median progression-free survival (PFS) as well as overall survival (OS) compared with bicalutamide in mCRPC patients. However, limited information related to its efficacy on psychological disorders (especially on anxiety and depression) in mCRPC patients is discovered (5,14,16-18). Therefore, the objective of the current study was to evaluate the effect of enzalutamide on anxiety, depression and QoL in treating mCRPC patients compared with bicalutamide.

Methods

Patients

One hundred and thirty-four mCRPC patients underwent enzalutamide or bicalutamide treatment between 2015/6/30 and 2016/12/30 at The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and

Technology were consecutively enrolled in this prospective cohort study. Patients were included according to the following inclusion criteria: (I) diagnosed as prostate cancer by pathological findings; (II) documented metastases; (III) testosterone concentration equal or below 50 ng/dL; (IV) disease progression by androgen deprivation therapy (ADT) treatment. Disease progression was defined by the presence of at least one of the following criteria: (I) PSA progression: the increment of PSA values ≥ 2 ng/mL at an interval ≥ 1 week between determinations; if PSA values ≥ 2 and < 5 ng/mL, then PSA doubling time ≤ 10 months; (II) soft tissue disease progression: defined by Response Evaluation Criteria for Solid Tumors (RECIST) (version 1.1 criteria); (III) bone disease progression: defined by at least two new lesions on bone scan; (IV) about to receive enzalutamide or bicalutamide treatment. While patients with the following conditions were excluded: (I) life expectancy less than 60 weeks; (II) cognitive impairment or other mental diseases that affects the evaluation of anxiety, depression or QoL; (III) unable to be followed up regularly as the protocol; (IV) secondary prostate cancer patients. This study was approved by the Ethics Review Board of The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology with the ethical approval ID of No. 2015-2, and all patients provided written informed consents.

Baseline data collection

Comprehensive baseline data of all patients were documented including: (I) demographic features: age, body mass index (BMI), smoke and drink; (II) tumor features: disease duration, disease localization, prostate-specific antigen (PSA) level and Gleason score at diagnosis; (III) previous treatments for prostate cancer; (IV) common complications: hypertension, hyperlipidemia, diabetes, chronic kidney disease (CKD); (V) education status.

Treatments

Patients received enzalutamide or bicalutamide treatment and were correspondingly categorized into Enzalutamide group (N=53) and Bicalutamide group (N=81). In Enzalutamide group, patients received 160 mg enzalutamide capsule orally per day, while in Bicalutamide group, patients received 50 mg bicalutamide tablet orally per day. Patients in both groups received combined ADT treatment.

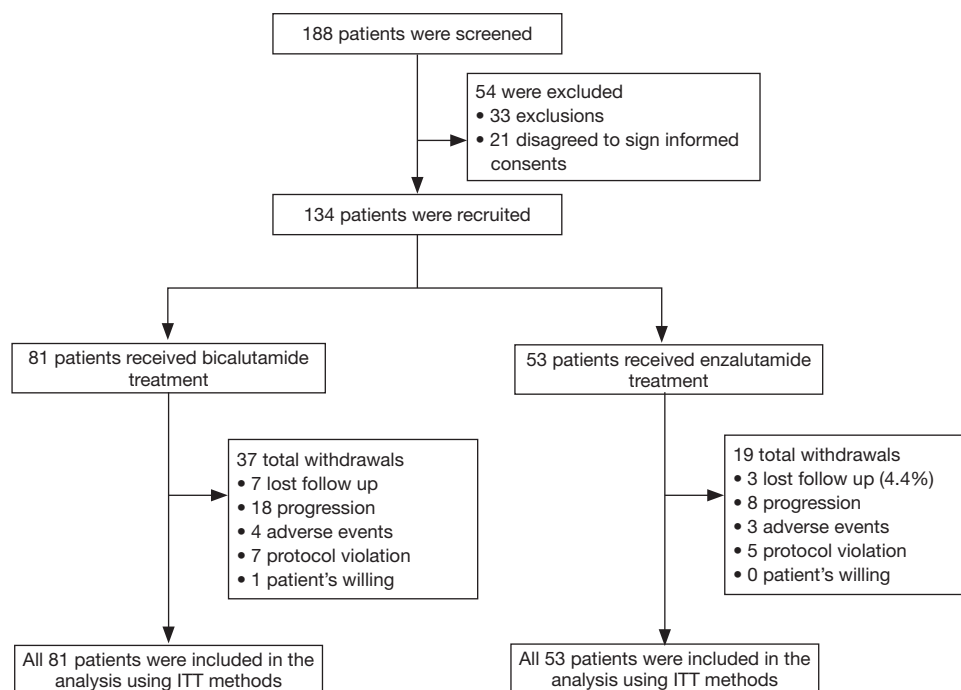


Figure 1 Study flow.

Assessments of anxiety, depression and QoL

Hospital Anxiety and Depression Scale (HADS) and Zung Self-Rating Anxiety/Depression Scale (SAS/SDS) were used for measurement of anxiety and depression, and Functional Assessment of Cancer Therapy-General (FACT-G) as well as Functional Assessment of Cancer Therapy-Prostate (FACT-P) scores were used for measurement of QoL at W0 (baseline), W12, W24, W36, W48 and W60. Anxiety assessed by HADS was defined as HADS-anxiety (HADS-A) score ≥ 8 points while anxiety assessed by SAS was defined as SAS score ≥ 50 points; Similarly, depression assessed by HADS was defined as HADS-depression (HADS-D) score ≥ 8 points while depression assessed by SDS was defined as SDS score ≥ 50 points.

Statistics

Statistical analysis was performed using SPSS 21.0 software (IBM, USA) and graphs were made using GraphPad 6.01 software (GraphPad Int, USA). Intent-to-treat (ITT) method was used for statistical analysis and patients who withdrew during the study were analyzed

based on the data at last follow-up visit. Data were presented as mean \pm standard deviation, median (range) or count (percentage). Comparison was determined by *t* test, Wilcoxon rank sum test or Chi-square test. $P < 0.05$ was considered as significant.

Results

Study flow

As depicted in *Figure 1*, 188 mCRPC patients were screened for eligibility, among whom 33 patients didn't meet inclusion criteria and 21 patients disagreed to sign informed consents. Subsequently, 134 patients remained, among whom 53 patients received enzalutamide and assigned into Enzalutamide group, while 81 patients received bicalutamide and assigned into Bicalutamide group. In Enzalutamide group, 19 patients withdrew, including that: 3 patients lost follow up, 8 patients progressed, 3 patients were intolerant to adverse events and 5 patients violated protocol. In Bicalutamide group, 37 patients withdrew, including that: 7 patients lost follow up, 18 patients progressed, 4 patients were intolerant to adverse

events, 7 patients violated protocol and 1 patient decided to quit. This study adopted ITT method that patients who withdrew during the study were analyzed based on the data at last visit. Therefore, all 53 patients in Enzalutamide group and 81 patients in Bicalutamide group were included in the analysis.

Baseline characteristics of mCRPC patients in Enzalutamide group and Bicalutamide group

There was no difference of demographic characteristics between Enzalutamide group and Bicalutamide group, including age, BMI, smoke and drink (all $P>0.05$, *Table 1*). The mean age in Enzalutamide group and Bicalutamide group was 65.94 ± 9.19 and 65.85 ± 9.61 years, respectively. For tumor features, disease duration was longer in Enzalutamide group compared with Bicalutamide group ($P=0.028$), while no difference in disease localization, PSA level or Gleason score at diagnosis was observed between two groups (all $P>0.05$). Furthermore, the percentage of patients with previous treatment history of antiandrogen ($P=0.044$) or radiation therapy ($P=0.031$) was greater in Enzalutamide group than that in Bicalutamide group. There was no difference in other baseline characteristics between two groups (all $P>0.05$, *Table 1*).

Baseline anxiety, depression as well as QoL status in Enzalutamide group and Bicalutamide group

Comparison of baseline anxiety, depression as well as QoL status between Enzalutamide group and Bicalutamide group was performed, which revealed that no difference was observed in anxiety status (assessed by HADS-A and SAS), depression status (assessed by HADS-D and SDS) or QoL status (assessed by FACT-G and FACT-P) between Enzalutamide group and Bicalutamide group at W0 (baseline) (all $P>0.05$, *Table 2*), which indicated that these assessments were comparable between two groups.

Comparison of anxiety assessed by HADS-A between Enzalutamide group and Bicalutamide group

No difference of HADS-A score was found between two groups at W12, W24, W36, W48 or W60 (all $P>0.05$, *Figure 2A*). However, the reduction of HADS-A score (W60–W0) was increased in Enzalutamide group compared to Bicalutamide group ($P=0.028$, *Figure 2B*). Meanwhile, percentage of anxiety patients was numerically decreased in

Enzalutamide group compared to Bicalutamide group, but no statistical significance ($P=0.055$, *Figure 2C*).

Comparison of anxiety assessed by SAS between Enzalutamide group and Bicalutamide group

SAS score was decreased in Enzalutamide group compared with Bicalutamide group at W60 ($P<0.05$), while the score was of no difference between two groups at W12, W24, W36 or W48 (all $P>0.05$, *Figure 3A*). Decrement of SAS score (W60–W0) in Enzalutamide group was greater compared with Bicalutamide group ($P=0.041$, *Figure 3B*), whereas percentage of anxiety patients between two groups was similar ($P=0.182$, *Figure 3C*).

Comparison of depression assessed by HADS-D between Enzalutamide group and Bicalutamide group

HADS-D score was of no difference between Enzalutamide group and Bicalutamide group at each visit (all $P>0.05$, *Figure 4A*), whereas HADS-D score reduction (W60–W0) in Enzalutamide group was larger than that in Bicalutamide group ($P=0.009$, *Figure 4B*). As to percentage of depression patients, no difference was found between two groups ($P=0.251$, *Figure 4C*).

Comparison of depression assessed by SDS between Enzalutamide group and Bicalutamide group

At W60 ($P<0.05$), SDS score was reduced in Enzalutamide group compared to Bicalutamide group, while it was similar between two groups at W12, W24, W36 and W48 (all $P>0.05$, *Figure 5A*). What's more, Enzalutamide group presented with more SDS score reduction (W60–W0) compared with Bicalutamide group ($P=0.033$, *Figure 5B*). Additionally, percentage of depression patients between two groups was similar ($P=0.238$, *Figure 5C*).

Comparison of QoL assessed by FACT-G and FACT-P between Enzalutamide group and Bicalutamide group

FACT-G score between Enzalutamide group and Bicalutamide group was similar at each visit (all $P>0.05$, *Figure 6A*), whereas the decrement of FACT-G score (W60–W0) in Enzalutamide group was larger compared with Bicalutamide group ($P=0.009$, *Figure 6B*). As for FACT-P score, it was also similar between two groups at each visit (all $P>0.05$, *Figure 6C*). However, it was reduced more

Table 1 Baseline characteristics of mCRPC patients

Parameters	Bicalutamide (N=81)	Enzalutamide (N=53)	P value
Demographic features			
Age (years)	65.85±9.61	65.94±9.19	0.956
BMI (kg/m ²)	25.93±2.74	26.32±2.82	0.424
Smoke (n/%)	35 (43.2)	27 (50.9)	0.380
Drink (n/%)	32 (39.5)	16 (30.2)	0.271
Tumor features			
Disease duration (years)	3 (0–19)	6 (0–21)	0.028
Disease localization (n/%)			0.256
Bone only	43 (53.1)	27 (50.9)	
Soft tissue only	21 (25.9)	9 (17.0)	
Both bone and soft tissue	17 (21.0)	17 (32.1)	
PSA level (ug/L)	18 [2–4,226]	34 [2–4,192]	0.226
Gleason score at diagnosis (n/%)			0.306
≥8	37 (45.7)	29 (54.7)	
≤7	44 (54.3)	24 (45.3)	
Previous treatments (n/%)			
Antiandrogen use	36 (44.4)	33 (62.3)	0.044
Radiation therapy	22 (27.2)	24 (45.3)	0.031
Prostatectomy	19 (23.5)	15 (28.3)	0.529
Orchiectomy	10 (12.3)	4 (7.5)	0.375
TURP	4 (4.9)	2 (3.8)	0.750
Cryoablation	2 (2.5)	1 (1.9)	0.824
Pelvic lymph node dissection	4 (4.9)	3 (5.7)	0.854
Common complications (n/%)			
Hypertension	41 (50.6)	24 (45.3)	0.546
Hyperlipidemia	32 (39.5)	13 (24.5)	0.073
Diabetes	12 (14.8)	6 (11.3)	0.562
CKD	9 (11.1)	3 (5.7)	0.280
Education status (n/%)			
Highest education			0.599
Primary school or less	40 (49.4)	20 (37.7)	
High school	22 (27.2)	19 (35.8)	
Undergraduate	15 (18.5)	11 (20.8)	
Graduate or above	4 (4.9)	3 (5.7)	

Data were presented as mean ± standard deviation, median (range) or count (percentage). Comparison was determined by *t* test, Wilcoxon rank sum test or Chi-square test. mCRPC, metastatic castration-resistant prostate cancer; BMI, body mass index; PSA, prostate-specific antigen; TURP, transurethral resection of the prostate; CKD, chronic kidney disease.

Table 2 Baseline anxiety, depression and QoL status of mCRPC patients

Parameters	Bicalutamide (N=81)	Enzalutamide (N=53)	P value
Anxiety status			
HADS-A score (n/%)	6.49±3.96	6.77±3.52	0.677
Anxiety patients (HADS-A ≥8)	30 (37.0)	17 (32.1)	0.556
SAS score (n/%)	49.43±10.82	49.00±10.92	0.822
Anxiety patients (SAS ≥50)	38 (46.9)	22 (41.5)	0.538
Depression status			
HADS-D score (n/%)	6.42±4.02	7.23±3.23	0.223
Depression patients (HADS-D ≥8)	30 (37.0)	25 (47.2)	0.244
SDS score (n/%)	47.83±11.79	49.04±11.40	0.557
Depression patients (SDS ≥50)	34 (42.0)	24 (45.3)	0.706
QoL status			
FACT-G score	82.7±14.2	85.1±14.9	0.350
FACT-P score	112.8±19.3	118.4±20.6	0.112

Data were presented as mean ± standard deviation or count (percentage). Comparison was determined by *t* test or Chi-square test. QoL, quality of life; mCRPC, metastatic castration-resistant prostate cancer; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, Hospital Anxiety and Depression Scale-Depression; SAS, Zung Self-Rating Anxiety Scale; SDS, Zung Self-Rating Depression Scale; FACT-G, Functional Assessment of Cancer Therapy-General; FACT-P, Functional Assessment of Cancer Therapy-Prostate.

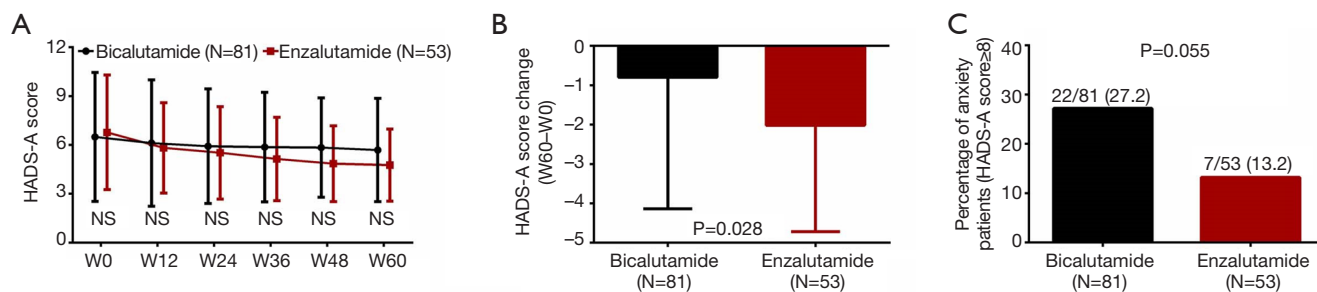


Figure 2 Assessment of anxiety performed by HADS-A in Enzalutamide group and Bicalutamide group. Enzalutamide group presented with similar HADS-A score compared to Bicalutamide group at each visit (A); the reduction of HADS-A score (W60–W0) in Enzalutamide group was elevated compared with Bicalutamide group (B) percentage of anxiety patients in Enzalutamide group was numerically reduced compared to Bicalutamide group, but no statistical significance (C); comparison between two groups was determined by *t* test, Wilcoxon rank sum test or Chi-square test. $P < 0.05$ was considered as significant. HADS-A, Hospital Anxiety and Depression Scale-anxiety.

obviously (W60–W0) in Enzalutamide group compared with Bicalutamide group ($P < 0.001$, *Figure 6D*). In addition, subgroup analysis in Enzalutamide group between patients with good response and bad response were shown in *Table S1*.

Discussion

In the current study we found that (I) enzalutamide

presented with better efficacy in alleviating anxiety and depression compared with bicalutamide; (II) enzalutamide was more effective on improving QoL compared to bicalutamide in mCRPC patients.

Enzalutamide is a novel NSAA that binds to AR with 5–8 folds higher affinity than bicalutamide and displays no agonistic effect to mutant AR protein (W741C) in castration-resistant LNCaP/AR human prostate cancer

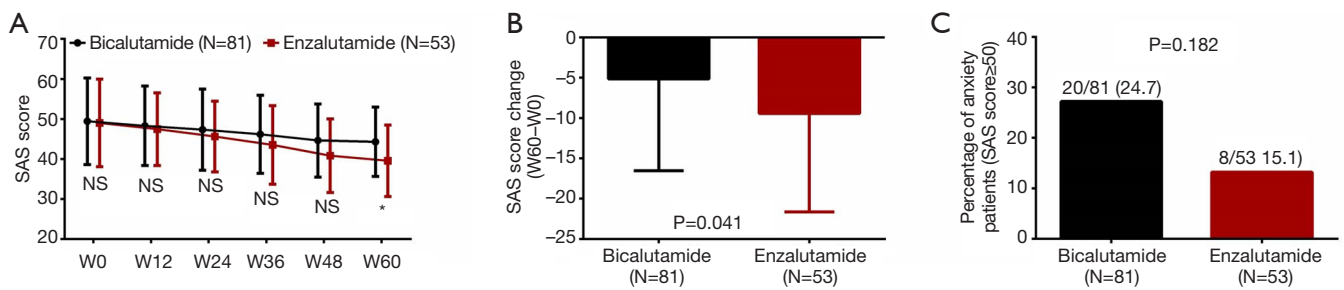


Figure 3 Assessment of anxiety performed by SAS in Enzalutamide group and Bicalutamide group. SAS score in Enzalutamide group was reduced compared to Bicalutamide group at W60, whereas the score was similar between two groups at W12, W24, W36 and W48 (A); reduction of SAS score (W60–W0) in Enzalutamide group was larger than that in Bicalutamide group (B), while percentage of anxiety patients between two groups was of no difference (C); comparison between two groups was determined by *t* test, Wilcoxon rank sum test or Chi-square test. *P*<0.05 was considered as significant. *, *P*<0.05. SAS, Zung Self-Rating Anxiety Scale.

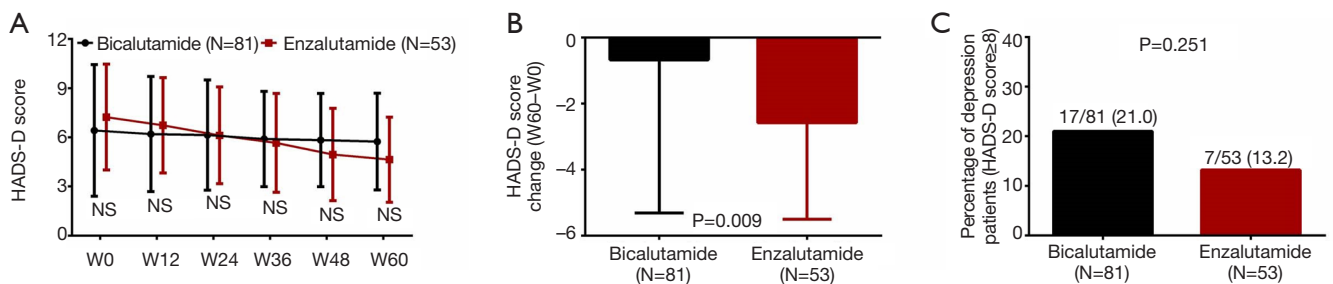


Figure 4 Assessment of depression performed by HADS-D in Enzalutamide group and Bicalutamide group. HADS-D score was similar between Enzalutamide group and Bicalutamide group at W12, W24, W36, W48 and W60 (A); HADS-D score reduction (W60–W0) was greater in Enzalutamide group compared to Bicalutamide group (B); as to percentage of depression patients, no difference was found between two groups (C); comparison between two groups was determined by *t* test, Wilcoxon rank sum test or Chi-square test. *P*<0.05 was considered as significant. HADS-D, Hospital Anxiety and Depression Scale-depression.

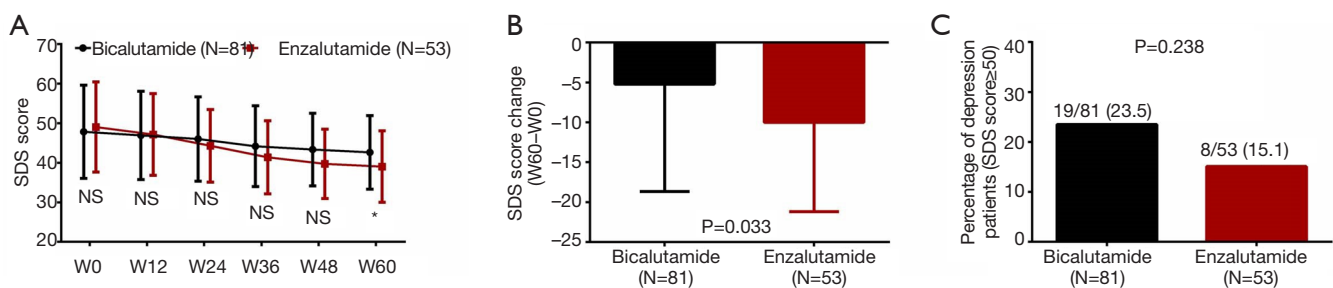


Figure 5 Assessment of depression performed by SDS in Enzalutamide group and Bicalutamide group. SDS score was decreased in Enzalutamide group compared to Bicalutamide group at W60, while it was of no difference between two groups at W12, W24, W36 or W48 (A); enzalutamide group presented with more SDS score decrement (W60–W0) compared to Bicalutamide group (B); percentage of depression patients between two groups was similar (C); comparison between two groups was determined by *t* test, Wilcoxon rank sum test or Chi-square test. *P*<0.05 was considered as significant. *, *P*<0.05. SDS, Zung Self-Rating Depression Scale.

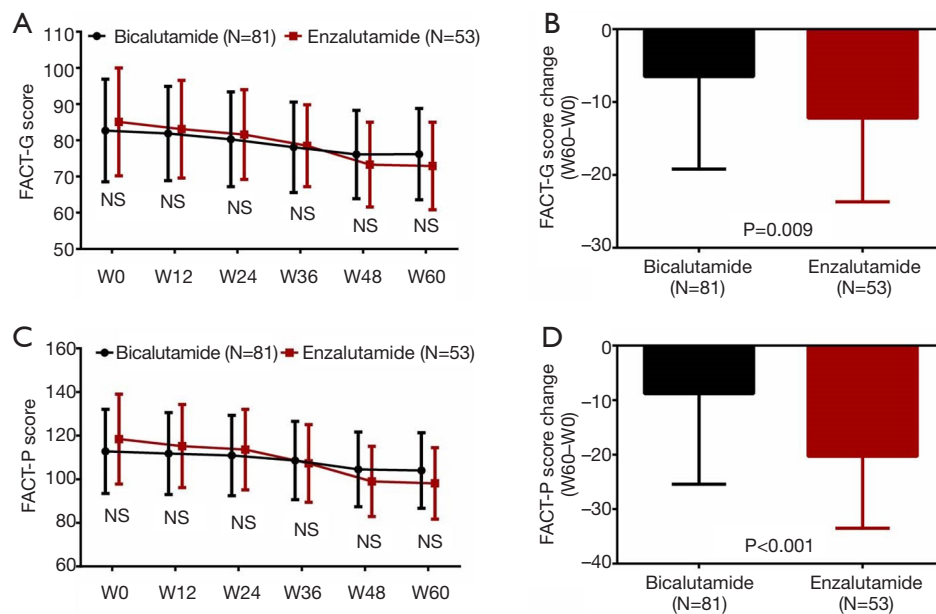


Figure 6 Assessment of QoL performed by FACT-G as well as FACT-P in Enzalutamide group and Bicalutamide group. FACT-G score was of no difference between Enzalutamide group and Bicalutamide group at each visit (A); whereas the reduction of FACT-G score (W60–W0) was larger in Enzalutamide group compared to Bicalutamide group (B); as to FACT-P score, it was also similar between two groups at W12, W24, W36, W48 and W60 (C); while FACT-P score in Enzalutamide group was decreased more obviously (W60–W0) compared to Bicalutamide group (D). Comparison between two groups was determined by *t* test or Chi-square test. $P < 0.05$ was considered as significant. QoL, quality of life; FACT-G, Functional Assessment of Cancer Therapy-General; FACT-P, Functional Assessment of Cancer Therapy-Prostate.

cells (19,20). According to several studies, enzalutamide is capable of delaying initial time to chemotherapy, reducing risk of first skeletal-related event and prolonging PFS as well as OS in mCRPC patients (16–18). Whereas limited information is discovered related to the influence of enzalutamide on mental status, just one interesting study discloses that mCRPC patients who received enzalutamide present with better mental states compared to patients who received bicalutamide at W13 (21). Considering that previous study evaluates patients' psychological states via European Quality of Life 5-Domain Scale (EQ-5D), but not specific assessment tools (such as HADS or SAS/SDS), the efficacy of enzalutamide on mental status in mCRPC patients remains to be further explored. In the current study, we used HADS-A/HADS-D and SAS/SDS specifically to assess the anxiety and depression in mCRPC patients received enzalutamide or bicalutamide at each visit, and validated that enzalutamide relieved anxiety and depression more effectively compared with bicalutamide in mCRPC patients. The possible reason might be that: (I) enzalutamide presented with better anti-tumor effect

compared with bicalutamide, thereby indirectly alleviated anxiety and depression than bicalutamide in mCRPC patients; (II) enzalutamide might directly improve anxiety and depression via greatly regulating androgen which resulted in dysregulated homeostasis, while this hypothesis should be further verified in future studies. To our knowledge, this is the first study to specifically and comprehensively compare the efficacy on anxiety as well as depression between enzalutamide and bicalutamide in mCRPC patients, which might provide more information for the utilization of enzalutamide in clinical practices.

As for QoL, it is the general well-being of individuals' daily life, and its assessment is commonly conducted in mCRPC patients via different self-reports (such as FACT-G and FACT-P) from different aspects (including emotional, social and physical aspects) (17,19,22). Based on a limited number of studies, enzalutamide is disclosed to contribute to the improvement of QoL in mCRPC patients (23,24). For instance, a clinical study illustrates that enzalutamide presents with higher rate of QoL improvement and longer median time to QoL deterioration (assessed by FACT-P

questionnaire) compared to placebo group in mCRPC patients who have previously received chemotherapy (docetaxel) (24). In addition, increased percentage of patients achieving QoL improvement and median time to QoL deterioration (assessed by FACT-P and EQ-5D questionnaires) is also observed in enzalutamide group compared with placebo group in chemotherapy-naïve mCRPC patients (23). However, the comparison of QoL between enzalutamide and bicalutamide is seldom illuminated. In our study, we found that enzalutamide better improved QoL assessed by FACT-G and FACT-P compared with bicalutamide in mCRPC patients. This result might be explained by that: Firstly, enzalutamide presents with better efficacy in relieving clinical symptoms and improving survival, thereby directly improving QoL in mCRPC patients. Secondly, enzalutamide might reduce mental stress and elevate confidence through its good treatment efficacy on delaying disease progression, thereby resulting in the remission of anxiety and depression, which indirectly improved QoL in mCRPC patients (16,17,19,20).

There were some limitations in this study: (I) since this was a cohort study, several baseline characteristics including disease duration, previous history of antiandrogen therapy or radiation therapy between Enzalutamide group and Bicalutamide group were different, which might cause confounding bias. However, we separately compared baseline anxiety status, depression status and QoL between the two groups, and we observed that no difference existed, which indicated these assessments were comparable between two groups; (II) the relative small sample size in this study with 53 patients in Enzalutamide group and 81 patients in Bicalutamide group might decrease statistical power. And considering that quite a few patients withdrew during the studies in both groups, we utilized intention to treat analysis to avoid decreasing statistical power although this was an observational study. However, randomized trials with larger sample size needed to be conducted in the future.

In conclusion, enzalutamide presents with better efficacy on alleviating anxiety and depression, as well as improving QoL in mCRPC patients compared to bicalutamide.

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Footnote

Conflicts of Interest: Both authors have completed the

ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/tcr.2019.09.12>). The 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 Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Review Board of The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology with the ethical approval ID of No. 2015-2, and all patients provided written informed consents.

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Supplementary

Table S1 Subgroup analysis in Enzalutamide group between patients with good response and bad response

Parameters	Good response patients (PSA decline $\geq 50\%$ from baseline, N=34)	Bad response patients (PSA decline $< 50\%$ from baseline, N=19)	P value
HADS-A Score			
W0	7.4 \pm 3.4	5.7 \pm 3.6	0.218
W60	5.0 \pm 2.2	4.3 \pm 2.3	0.568
Change (W60–W0)	–2.4 \pm 2.8	–1.4 \pm 2.4	0.232
Anxiety patients (W60) (HADS-A Score ≥ 8 , n/%)	5 (14.7)	2 (10.5)	0.666
SAS Score			
W0	51.3 \pm 11.8	44.8 \pm 7.7	0.074
W60	38.4 \pm 9.3	41.6 \pm 8.1	0.400
Change (W60–W0)	–12.9 \pm 12.9	–3.2 \pm 7.8	0.004
Anxiety patients (W60) (SAS Score ≥ 50 , n/%)	5 (14.7)	3 (15.8)	0.916
HADS-D Score			
W0	7.8 \pm 3.4	6.2 \pm 2.8	0.174
W60	4.6 \pm 2.8	4.6 \pm 2.2	0.999
Change (W60–W0)	–3.2 \pm 3.1	–1.5 \pm 2.4	0.047
Depression patients (W60) (HADS-D Score ≥ 8 , n/%)	6 (17.6)	1 (5.3)	0.202
SDS Score			
W0	49.7 \pm 11.2	47.8 \pm 12.0	0.999
W60	36.8 \pm 7.5	43.1 \pm 10.3	0.028
Change (W60–W0)	–12.9 \pm 11.7	–4.7 \pm 8.1	0.009
Depression patients (W60) (SDS Score ≥ 50 , n/%)	2 (5.9)	6 (31.6)	0.012
FACT-G Score			
W0	85.5 \pm 13.8	84.4 \pm 14.2	0.999
W60	69.4 \pm 10.1	79.2 \pm 11.3	0.004
Change (W60–W0)	–16.1 \pm 12.0	–5.2 \pm 9.2	0.001
FACT-P Score			
W0	119.5 \pm 21.1	116.4 \pm 19.4	0.924
W60	92.7 \pm 19.8	107.5 \pm 20.6	0.026
Change (W60–W0)	–26.8 \pm 14.4	–8.9 \pm 13.8	<0.001

Data were presented as mean \pm standard deviation or count (percentage). Comparison was determined by *t*-test (Bonferroni correction) or Chi-square test. HADS-A, Hospital Anxiety and Depression Scale-Anxiety; SAS, Zung Self-Rating Anxiety Scale; HADS-D, Hospital Anxiety and Depression Scale-Depression; SDS, Zung Self-Rating Depression Scale; FACT-G, Functional Assessment of Cancer Therapy-General; FACT-P, Functional Assessment of Cancer Therapy-Prostate.