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CLINICAL STUDY

Quality of life for androgen receptor targeted agents in patients with metastatic castration resistant prostate cancer

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ABSTRACT

BACKGROUND: Few studies have evaluated health-related quality of life (HRQoL) with abiraterone acetate plus prednisone (abiraterone) compared to enzalutamide in metastatic castration resistant prostate cancer (mCRPC). So, this study aimed to assess impact of abiraterone and enzalutamide on patients´ functioning in mCRPC real-world setting.

METHODS: In this 12-month, prospective, observational study, 36 mCRPC patients from Slovakia were included. Patients were treated with abiraterone or enzalutamide according to routine practice. HRQoL was assessed at baseline and 3-/6-/9-/12-month visits using the Functional Assessment of Cancer Therapy–Prostate (FACT-P) and European Quality of Life 5 Dimensions (EQ-5D) questionnaires. Changes from baseline and occurrence of deteriorations/improvements were compared using two-sample t-test/Mann-Whitney test and Pearson's chi-square/Fisher's exact test, respectively. Mixed-effects model for repeated measures was used to evaluate the difference between the two arms in mean changes of quality of life after 12 months.

RESULTS: Frequency of clinically meaningful deterioration of quality of life assessed by FACT-P was similar for abiraterone and enzalutamide: 0%, 14.3%, 23.1%, 16.7% vs. 10%, 26.3%, 22.2%, 40% at 3-, 6-, 9- and 12 months of therapy (p=0.496, 0.670, 1.000 and 0.236, respectively). After 12 months of treatment, no statistically significant difference between the treatment arms was observed in estimated mean changes in FACT-P total scores (p=0.620) and its components, EQ-5D index (p=0.108), and EQ-5D visual analogue scale (p=0.324).

CONCLUSION: According to the results of this study, abiraterone and enzalutamide had a comparable impact on quality of life in chemo-naive mCRPC in routine practice *(Tab. 4, Fig. 4, Ref. 23)*. Text in PDF www.elis.sk

KEY WORDS: quality of life, abiraterone, enzalutamide, castration resistant prostate cancer.

Introduction

Androgen receptor axis-targeted agents (ARTAs), such as enzalutamide and abiraterone acetate, have demonstrated significantly higher efficacy in prolonging the overall survival (OS) of metastatic castration-resistant prostate cancer (mCRPC) compared to androgen deprivation therapy (ADT) alone, and become a treatment standard for mCRPC (1–4). Registration trials of both ARTAs have also evaluated their impact on patients' health-related quality of life (HRQoL). These analyses have shown that HRQoL was maintained during the treatment and both drugs improved patient-related outcomes (5–8).

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HRQoL represents a multidimensional concept consisting of physical, functional, social and emotional domains. Several evaluation instruments have been developed to assess the functioning of patients which could be divided into three groups: prostate-specific, cancer generic and generic instruments (9). Published systematic reviews have shown that the most used questionnaire to assess quality of life in studies with ARTAs was the Functional Assessment of Cancer Therapy–Prostate (FACT-P) instrument that was validated for use in mCRPC patients (9–14). However, due to existing between-studies inconsistencies, such as different time intervals for FACT-P assessment or inconsistent definition of the population eligible for HRQoL-related analysis, it is difficult to compare the outcomes across studies (10). There are currently only a few studies that directly compare the effect of ARTAs on patients´ functioning, either in clinical trials or in real-world settings, and therefore further research in this area, including head-to-head comparisons, is still needed.

We conducted a prospective, observational, three-centre research to evaluate and compare the effect of both ARTAs, abiraterone acetate plus prednisone versus enzalutamide, on quality of life in patients with chemotherapy-naïve mCRPC in a real clinical practice and under local indication conditions in

Slovakia. According to our knowledge, this is a first such research in Slovakia. Herein, we report the results for 12 months.

Patients and methods

Trial design

This was a 12-month, prospective, observational, nonrandomised, three-centre study conducted by hospital-based specialists in urological oncology in Slovakia, assessing the effects of abiraterone acetate 1000 mg and prednisone 10 mg given daily versus enzalutamide 160 mg daily for first-line therapy of mCRPC over 12 months. Evaluation of impact of both drugs on HRQoL and their comparison was a primary objective of the study. The decision to treat the patient with either drug was at the discretion of treating physician and preceded study enrolment. The treatment of patients was not influenced by their participation in the research. All patients meeting enrolment criteria who visited a physician participated in the research, were invited to participate in this research to minimise recruitment bias. Institutional ethics board approval was obtained.

Patients

Key eligibility criteria included the following requirements and were linked to reimbursement conditions defined by the Ministry of Health of the Slovak Republic valid at the time of the research conduct: confirmed mCRPC in adult men who were asymptomatic or mildly symptomatic after failure of ADT, without proven visceral metastases, and for whom chemotherapy was not yet clinically indicated. Patients were required to have Eastern Cooperative Oncology Group (ECOG) performance status of 0–1, PSA level was ≤114 ng/ml, Haemoglobin ≥13 g/dL, and PSA doubling time ≥55 days. The treatment was administered until the clinical progression of the disease (15).

HRQoL assessments

HRQoL was prospectively assessed with patient self-reported questionnaires: Functional Assessment of Cancer Therapy–Prostate (FACT-P) and European Quality of Life 5 Dimensions 5 Level assessment (EQ-5D-5L). FACT-P is a standardized tool that has been validated for use in mCRPC. FACT-P is a 39-item instrument consisting of both a general assessment of quality of life (FACT-General) with four subscales (physical, social/family, emotional, and functional well-being) and Prostate Cancer Subscale (PCS) with 12 items assessing prostate-related problems (11–14). The questionnaire has been used in all the registration trials evaluating both ARTAs in mCRPC (10). Higher score indicates higher quality of life level. The EQ-5D-5L is a generic questionnaire that assesses five dimensions of health (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) with five levels of severity. The EQ-5D-5L includes also a visual analogue scale (VAS) to record the patient´s self-rated general status of health (a scale from 0 to 100) (16–17).

The FACT-P and EQ-5D-5L questionnaires were patient self-administered at baseline, every 3 months while on treatment until 1 year of the therapy, using a validated translation. We included questionnaires completed before June 1, 2023.

Statistical analysis

Categorical variables were described using absolute and relative frequencies (%). Continuous variables were characterized by mean with standard deviation (SD) and median with inter-quartile range (IQR). Differences in continuous parameters were tested between treatment groups using the two-sample t-test or the non-parametric Mann–Whitney test (if normality rejected). Normality was assessed using the Shapiro–Wilk test. Differences in categorical variables were assessed using Pearson's chi-square test or Fisher's exact test (if assumptions are not met). The level of statistical significance was set at 5%. Quality of life deterioration (improvement, respectively) was assessed as a decrease (increase, respectively) in the score compared to baseline value at given time point after entry by a pre-defined threshold. The cutoffs were based on existing evidence on the range of changes in individual scores that are clinically meaningful for patients (10). EQ-5D summary index values were calculated using Dutch weights (18). Mixed effects model for repeated measures was used to estimate mean changes in FACT-P and its components, EQ-5D summary index and EQ VAS compared to baseline values. Covariates (fixed effects) included: treatment (abiraterone vs. enzalutamide), baseline value of the given quality of life parameter, time (3/6/9/12 months) and interaction between treatment and time point. Individual patients entered the model as random effects. An unstructured covariance matrix was set as a part of the model specification. Estimated mean changes together with confidence intervals were presented for both treatment groups in the form of graphs. Estimates of the magnitude of change in quality of life and the difference in change between treatment groups at twelve-month follow-up are presented as well. Missing data were not imputed and all patients with long-term follow-up were included in the analysis. There may be different numbers of patients in the sub-analyses. Analyses were performed using SAS statistical software (version 9.4).

Results

Baseline data

A total of 45 patients were enrolled into the research, of which 9 were excluded due to lack of follow-up. Twenty patients included in the analysis were treated with enzalutamide 160 mg daily and 16 patients were treated with abiraterone acetate (hereafter abiraterone) 1000 mg and prednisone 10 mg given daily. Baseline characteristics were well balanced between both study arms and no statistically significant difference in the baseline characteristics was observed between abiraterone (n=16) and enzalutamide (n=20). Also, the occurrence of comorbidities was not statistically significantly different between the studied treatment arms. Bone disease treatment was present in all analysed patients. Among comorbidities, hypertension (81.3% with abiraterone and 90% with enzalutamide) and cardiac comorbidities (62.5% with abiraterone and 60% with enzalutamide) had the highest prevalence (Tab. 1).

The median baseline FACT-P scores were similar in both arms (Tab. 2). The median baseline FACT-P total score in the enzalutamide cohort was 91.8 (70.4–102.8) and in the abiraterone one was 98.2 (79.3–113.0). No statistically significant difference was

Tab. 1. Baseline characteristics.

Parameter	Statistics	Total (n=36)	Abiraterone (n=16)	Enzalutamide (n=20)	p
Age (years)	Median (IQR)	74.0 (71.0–78.5)	73.0 (71.0–78.0)	74.5 (70.5–79.5)	0.468[a]
	Mean (SD)	73.8 (7.0)	72.9 (8.1)	74.6 (6.0)	
Weight (kg)	Median (IQR)	82.0 (75.5–94.0)	84.5 (78.0–95.0)	78.0 (74.0–91.5)	0.189[b]
Baseline PSA (ng/mL)	Median (IQR)	27.00 (10.10–75.80)	34.07 (9.56–93.38)	18.35 (10.27–64.50)	0.479[b]
Baseline Hemoglobin (g/L)	Median (IQR)	132.5 (124.5–136.0)	131.0 (125.5–134.0)	133.5 (124.0–137.5)	0.478[b]
Time since prostate cancer diagnosis (months)	Median (IQR)	36.5 (24.0–84.0)	29.0 (19.5–90.0)	43.0 (29.0–78.0)	0.386[b]
Time since diagnosis of mCRPC stage (months)	Median (IQR)	2.5 (1.8–7.5)	2.5 (2.0–7.0)	2.5 (1.0–7.5)	0.736[b]
Gleason Score	Median (IQR)	8.0 (7.0–9.0)	8.0 (7.5–9.0)	8.0 (7.0–9.0)	0.716[b]
Metastatic sites					
M1b	n (%)	27 (75.0%)	12 (75.0%)	15 (75.0%)	1.000[d]
M1a + M1b	n (%)	9 (25.0%)	4 (25.0%)	5 (25.0%)	
Comorbidities					
Bone therapy at baseline	n (%)	36 (100.0%)	16 (100.0%)	20 (100.0%)	-
Cardiac disorders	n (%)	22 (61.1%)	10 (62.5%)	12 (60.0%)	0.879[c]
Hypertension	n (%)	31 (86.1%)	13 (81.3%)	18 (90.0%)	0.637[d]
Musculoskeletal disorders	n (%)	9 (25.0%)	4 (25.0%)	5 (25.0%)	1.000[d]
Diabetes mellitus	n (%)	8 (22.2%)	3 (18.8%)	5 (25.0%)	0.709[d]
Neurological disorders	n (%)	4 (11.1%)	1 (6.3%)	3 (15.0%)	0.613[d]
COVID-19	n (%)	6 (16.7%)	3 (18.8%)	3 (15.0%)	1.000[d]

IQR – interquartile range, SD – standard deviation. Differences in continuous variables between the study arms were tested using a) the two-sample t-test or b) the Mann–Whitney test. Differences in frequencies between the study arms were tested using c) the Pearson's chi-squared test or d) the Fisher's exact test

observed in the comparison of EQ-5D VAS values between the treatment arms. At entry, however, we could observe a numerically slightly higher mean value of the EQ-5D VAS in patients with abiraterone compared to patients with enzalutamide (72 vs 64) (Tab. 3).

The overall FACT-P and EQ-5D-5L questionnaire response rates of the analysed sample were above 90%, which represents a high level of compliance in real-world setting. The most common reason for treatment discontinuation was the disease progression.

Tab. 2. Baseline FACT-P scores by treatment.

Parameter	Statistics	Total (n=36)	Abiraterone (n=16)	Enzalutamide (n=20)	p[1]
FACT-P: PWB	n / n missing	35/1	15/1	20/0	0.236[a]
	Mean (SD)	17.5 (5.5)	18.8 (5.0)	16.6 (5.7)	
	Median (IQR)	17.0 (15.0–22.0)	18.0 (17.0–23.0)	17.0 (14.0–20.0)	
FACT-P: SWB	n / n missing	35/1	15/1	20/0	0.868[b]
	Mean (SD)	19.4 (5.2)	19.4 (6.0)	19.4 (4.7)	
	Median (IQR)	20.0 (16.3–23.0)	21.0 (16.3–23.0)	20.0 (17.5–22.6)	
FACT-P: EWB	n / n missing	35/1	15/1	20/0	0.443[a]
	Mean (SD)	13.1 (5.7)	13.9 (6.2)	12.4 (5.5)	
	Median (IQR)	14.0 (8.0–18.0)	16.0 (8.0–19.0)	12.5 (8.5–15.5)	
FACT-P: FWB	n / n missing	35/1	15/1	20/0	0.396[a]
	Mean (SD)	15.6 (6.2)	16.7 (7.2)	14.9 (5.3)	
	Median (IQR)	17.0 (11.0–21.0)	20.0 (11.0–22.0)	14.0 (10.5–20.0)	
FACT-P: PCS	n / n missing	35/1	15/1	20/0	0.292[a]
	Mean (SD)	25.1 (7.0)	26.6 (5.4)	24.1 (7.9)	
	Median (IQR)	26.0 (21.0–30.0)	27.0 (23.0–32.0)	26.0 (17.5–27.5)	
FACT-P: TOI	n / n missing	35/1	15/1	20/0	0.238[a]
	Mean (SD)	58.3 (16.2)	62.1 (15.3)	55.5 (16.7)	
	Median (IQR)	58.0 (48.0–71.0)	63.0 (55.0–78.0)	56.5 (46.0–68.5)	
FACT-P Total Score	n / n missing	35/1	15/1	20/0	0.298[a]
	Mean (SD)	90.8 (22.6)	95.4 (22.8)	87.3 (22.4)	
	Median (IQR)	93.0 (75.2–112.7)	98.2 (79.3–113.0)	91.8 (70.4–102.8)	

[1]Statistical significance of differences between the study arms was calculated using (a) the two-sample t-test or (b) the Mann–Whitney test. SD = standard deviation; IQR = inter-quartile range; FACT-P = Functional Assessment of Cancer Therapy–Prostate; PWB = Physical well-being; SWB = Social and family well-being; EWB = Emotional well-being; FWB = Functional well-being; PCS = Prostate cancer subscale; TOI = Trial outcome index

Tab. 3. Baseline EQ-5D values: VAS and utility index.

Parameter	Total (n=36)	Abiraterone (n=16)	Enzalutamide (n=20)	p[1]
EQ-5D VAS at baseline, n / n missing	35 / 1	15 / 1	20/0	
Mean (SD)	67.4 (13.6)	72.0 (13.2)	64.0 (13.1)	0.096[b]
Median (IQR)	70.0 (50.0–80.0)	75.0 (65.0–80.0)	62.5 (50.0–77.5)	
EQ-5D utility index at baseline, n / n missing	36 / 0	16 / 0	20 / 0	
Mean (SD)	0.67 (0.24)	0.71 (0.22)	0.64 (0.26)	0.307[b]
Median (IQR)	0.74 (0.57–0.82)	0.75 (0.65–0.87)	0.70 (0.55–0.80)	

EQ-5D = European Quality of life 5-Domain Scale; SD = standard deviation; IQR = interquartile range; VAS = visual analogue scale; n = number of patients in the treatment arm; n = number of available values; n missing = number of missing values. Differences between the treatment arms were tested using b) the Mann–Whitney test

Analysis of minimally important difference (MID) from baseline

HRQoL improvement was defined as an increase in the score at defined time points by predetermined thresholds compared with baseline. Thresholds were based on existing evidence of score range changes that are clinically meaningful to patients. For the purposes of this analysis, the upper limit of the minimally important difference (MID) range was used consistently with the PREVAIL HRQoL analysis (8). Clinically meaningful improvements in EQ-5D VAS and EQ-5D utility index are defined as an increase of ≥11 and ≥0.14 points compared to baseline values. Clinically meaningful improvement in FACT-P Total is defined as an increase of ≥10 points compared to baseline values, and in PWB, SWB, WEB, FWB, PCS and TOI as an increase of ≥3 points compared to baseline values (8). A HRQoL deterioration was defined similarly, but as a decrease in the score by the thresholds versus baseline scores.

Similar clinically meaningful improvement of quality of life assessed by FACT-P was observed in 20%, 21.4%, 23.1% and 33.3% of patients treated with abiraterone in comparison to 15%, 26.3%, 22.2% and 26.7% of patients treated with enzalutamide at 3-, 6-, 9- and 12 months of therapy, respectively. Conversely, clinically meaningful improvement in EQ-5D VAS scores over time from baseline was more common in enzalutamide-treated patients (0%, 7.1%, 7.7% and 8.3% vs. 10%, 10.5%, 16.7% and 20% for abiraterone arm vs. enzalutamide arm at 3-, 6-, 9- and 12 months of therapy, respectively), however the differences were not statistically significant (p=0.496, p=1.000, p=0.621, p=0.605, respectively) The proportion of patients with HRQOL improvement, both in FACT-P total scores EQ-5D VAS score at 12-month of treatment is shown in Figure 1. These differences in proportions between the two drugs were not statistically significant (p=1.000 and p=0.605, respectively).

Clinically meaningful deterioration of quality of life assessed by FACT-P was observed in 0%, 14.3%, 23.1% and 16.7% of patients treated with abiraterone in comparison to 10%, 26.3%, 22.2% and 40% of patients treated with enzalutamide at 3-, 6-, 9- and 12 months of therapy, respectively. These differences were not statistically significant (p=0.496, 0.670, 1.000 and 0.236, respectively). Proportions of patients with HRQoL deterioration by domains and subscales in both treatment arms at 12 months of therapy are shown in Figure 2. A higher proportion of patients in enzalutamide group reported worsening in TOI (Trial Outcome Index) score compared to abiraterone group (60% vs. 40%, p=0.047).

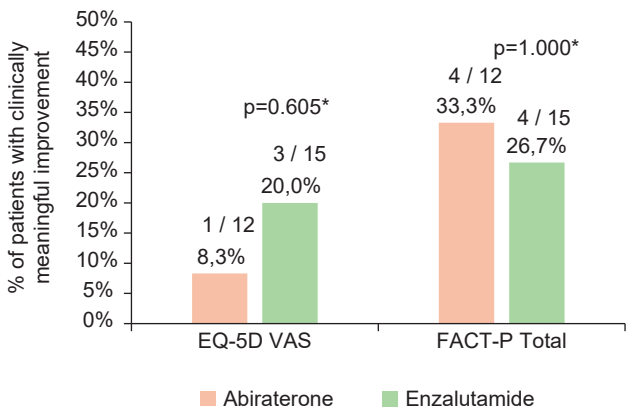

Fig. 1. Percentage of patients with a clinically meaningful improvement in EQ-5D VAS and FACT-P Total score at 12-month. FACT-P = Functional Assessment of Cancer Therapy–Prostate; VAS = visual analogue scale. Above the individual bars, the number of patients with clinically meaningful improvement / the number of patients with available data at given time point are presented. *p-values were obtained using the Fisher exact test.

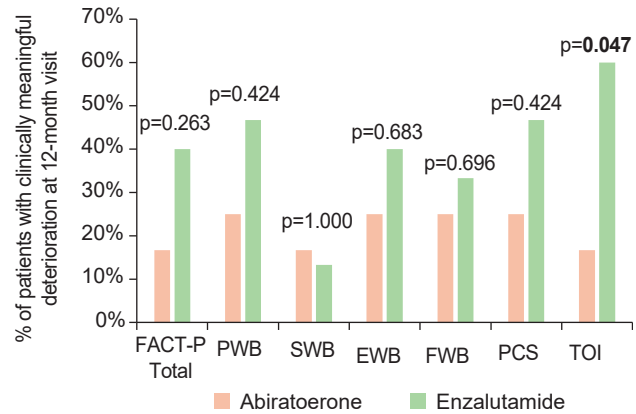

Fig. 2. Percentage of patients with a clinically meaningful deterioration in FACT Total score, FACT-P domains and subscales at 12-month. FACT-P=Functional Assessment of Cancer Therapy–Prostate; PWB = Physical well-being; SWB=Social and family well-being; EWB = Emotional well-being; FWB = Functional well-being; PCS = Prostate cancer subscale; TOI = Trial outcome index. Occurrence of clinically meaningful deterioration between arms was compared using the Pearson chi-squared test or Fisher exact test.

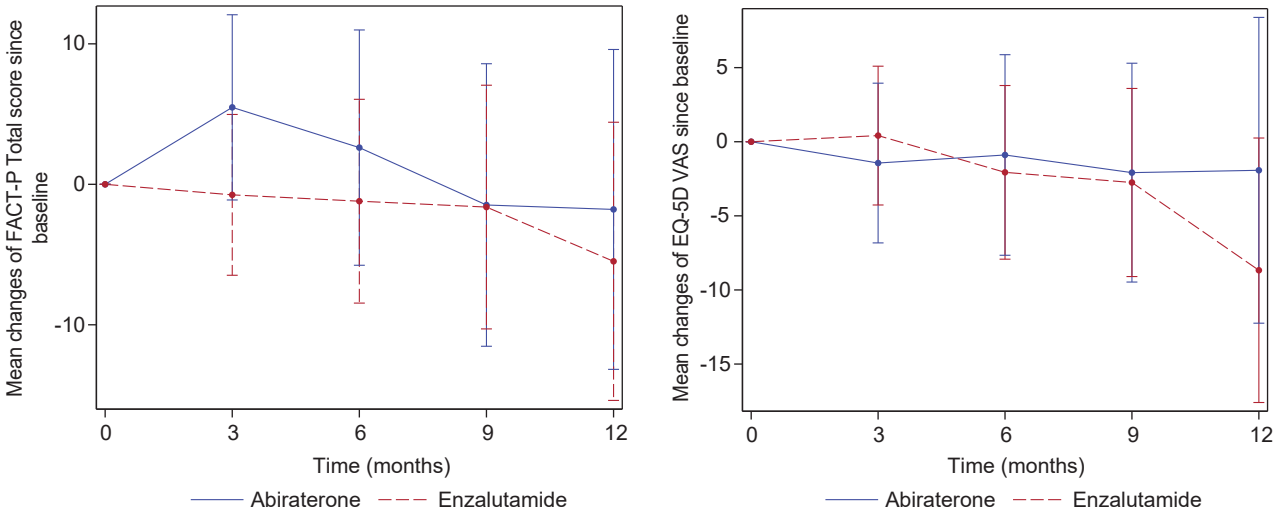

Fig. 3. Adjusted mean changes (95% CI) in FACT-P Total score and EQ-5D VAS over 12 months using mixed model for repeated measures analysis.

3.3 Mixed model for repeated measures

In the analysis, we modelled mean changes from baseline in FACT-P and its components, EQ-5D utility index, and EQ-5D VAS in both treatment arms using a repeated-measures mixed-effects model while simultaneously adjusting for baseline value of modelled parameter, time, and the interaction between time and treatment. After 12 months of treatment, no statistically significant difference between the treatment arms was observed in estimated mean changes in FACT-P total scores (p=0.620) and its components, EQ-5D index (p=0.108), and EQ-5D VAS (p=0.324) (Figs 3 and 4, Tab. 4). Abiraterone-treated patients showed numerically greater improvements in all the studied parameters (except SWB at 12 months), however, the differences were not statistically significant.

Discussion

Abiraterone and enzalutamide are the standard first-line therapy for mCRPC and have been shown to have comparable efficacy. Our research was performed as prospective, observational, head-to-head comparison of HRQoL of abiraterone and enzalutamide in real clinical practice of mCRPC treatment management in Slovakia. The patient-reported outcomes were assessed by FACT-P and EQ-5D-5L questionnaires, the same tools that were used in registration trials of both ARTAs, as well as in some of a few comparative studies (2, 4–6, 20–21). The questionnaires' completion rates were high, allowing for longitudinal analysis of patient-reported outcomes while adjusting for confounders. Owing to the inclusion criteria defined by the Slovak health authority, the study cohort was representative of the real-world mCRPC population in Slovakia which might differ from populations of other countries where the limiting indication criteria are missing.

Patients included in the research were elderly with a median age of 73 years in the abiraterone cohort and 74.5 years in the enzalutamide one and had frequent anamnesis of existing comorbidities. Cardiac disorders were present in 62.5% and hypertension in 81.3% of patients receiving abiraterone, and in 60% and 90% of patients receiving enzalutamide, respectively, which is a higher

Tab. 4. Analysis of changes in FACT-P and EQ-5D from baseline to month 12.

HRQoL Parameter	Abiraterone (A)	Enzalutamide (E)	Difference between arms (A–E)	p
FACT-P Total Score	–1.79 (–13.17; 9.60)	–5.48 (–15.38; 4.42)	3.70 (–11.42; 18.81)	0.620
FACT-P: PWB	–0.68 (–4.54; 3.19)	–3.26 (–6.64; 0.13)	2.58 (–2.58; 7.73)	0.311
FACT-P: SWB	0.26 (–1.81; 2.34)	0.40 (–1.40; 2.21)	–0.14 (–2.89; 2.61)	0.919
FACT-P: EWB	0.51 (–2.50; 3.51)	–0.28 (–2.88; 2.32)	0.78 (–3.19; 4.76)	0.691
FACT-P: FWB	1.28 (–1.52; 4.07)	–1.76 (–4.17; 0.65)	3.04 (–0.67; 6.74)	0.105
FACT-P: PCS	–1.98 (–5.84; 1.87)	–2.33 (–5.70; 1.05)	0.34 (–4.80; 5.48)	0.892
FACT-P: TOI	–2.75 (–11.45; 5.94)	–5.75 (–13.32; 1.82)	3.00 (–8.57; 14.57)	0.598
EQ-5D utility index	–0.04 (–0.15; 0.06)	–0.16 (–0.26; –0.07)	0.12 (–0.03; 0.26)	0.108
EQ VAS	–1.93 (–12.24; 8.39)	–8.67 (–17.59; 0.25)	6.74 (–6.98; 20.47)	0.324

Adjusted least squares mean changes (95% confidence intervals) between baseline and 12-month visits are presented. Positive values represent improvement in quality of life, negative values represent worsening. Covariates included baseline parameter value, treatment type, timepoint and interaction between time and treatment type. Random effects associated with subjects are included. Enzalutamide was a reference group for the difference estimate. FACT-P = Functional Assessment of Cancer Therapy–Prostate; VAS = Visual Analogue Scale. PWB = Physical well-being; SWB = Social and family well-being; EWB = Emotional well-being; FWB = Functional well-being; PCS = Prostate cancer subscale; TOI = Trial outcome index; EQ-5D = European Quality of Life 5-Domain Scale

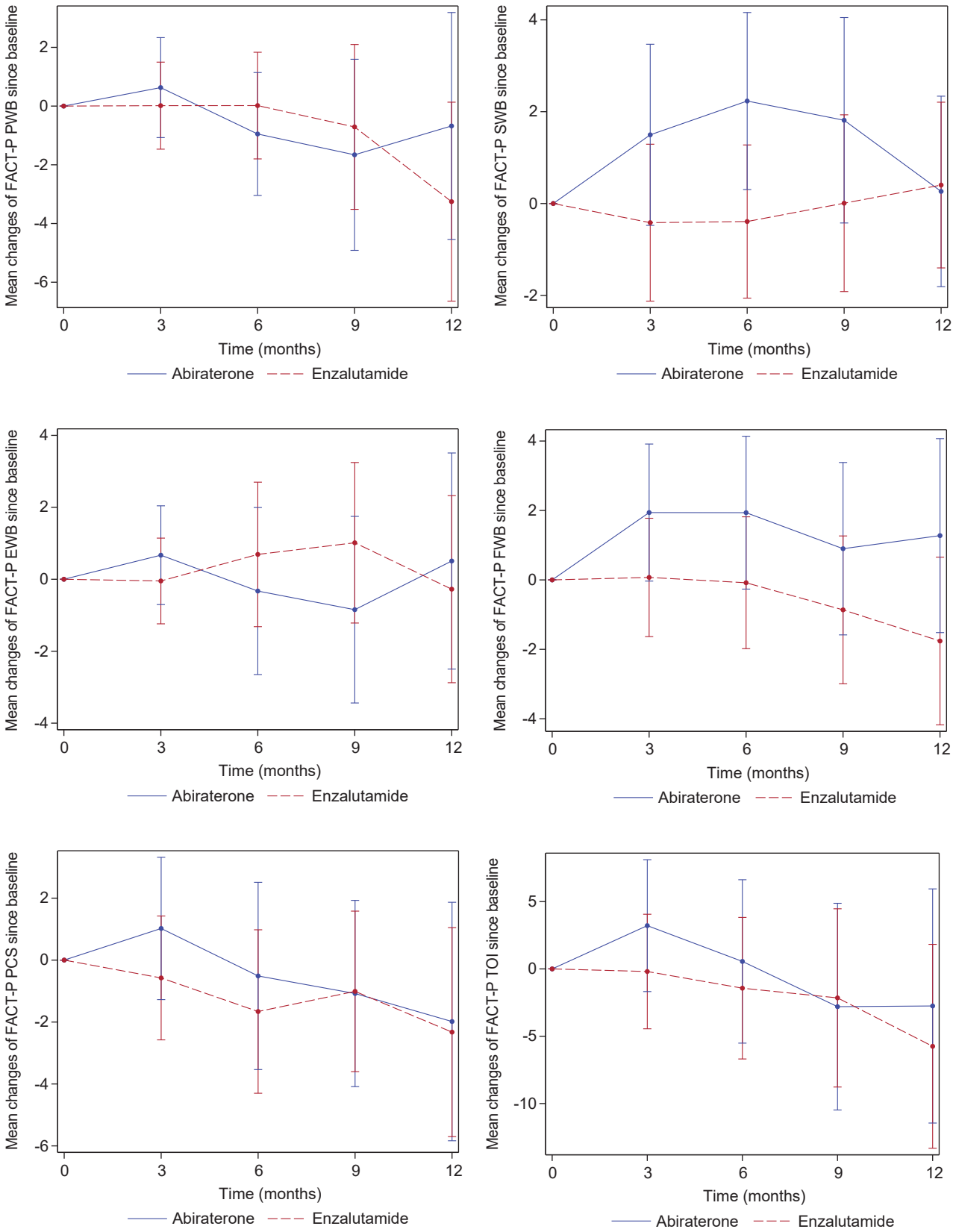

Fig. 4. Adjusted mean changes (95% CI) in FACT-P domains and subscales over 12 months using mixed model for repeated measures analysis.

percentage than in other studies from real-world setting. In the AQUARIUS, a prospective, 12-month, observational comparative study in patients with mCRPC from Denmark, France, and the UK, 48% of patients treated with abiraterone and enzalutamide reported cardiovascular abnormalities at the study entry (19). Similarly, in the HEAT trial, a randomized study comparing fatigue, HRQoL and metabolic changes in men treated with enzalutamide or abiraterone plus prednisone in mCRPC, a frequency of cardiovascular diseases was lower (cumulatively, approximately 22% and 14% of patients in the enzalutamide arm and abiraterone arm had medical history of cardiovascular disease, and 64% of patients in both arms used antihypertensives) (20).

The median PSA of both cohorts in our study was comparable to PSA levels in other comparative trials assessing HRQoL (19, 21). Median time since mCRPC diagnosis to ARTA initiation in Slovakia was 2.5 months in both subgroups which is longer than in a similar comparative trial, the AQUARIUS, with the median of 1.4 and 1.5 months for abiraterone and enzalutamide, respectively (19). The longer period might be partially explained by a need for an individual approval of ARTA therapy by payers which usually takes several days to weeks (up to 4 weeks from an individual treatment request submission).

Baseline FACT-P scores in both arms were numerically lower than those in other trials: median FACT-P total score was 98.2 for abiraterone and 91.8 for enzalutamide while it was 116.5 and 114.0 for abiraterone and enzalutamide, respectively, in the comparative trial published by Khalaf et al (21). Similarly, expressed by mean values, baseline FACT-P scores (95.4 in the abiraterone subgroup and 87.3 in the enzalutamide subgroup) were also lower than in the HEAT trial (mean FACT-P total score was 118.4 in the enzalutamide arm and 115.2 in the abiraterone arm) (20). Chemo-naive mCRPC cohort of the VITAL study population reported median baseline FACT-P score at the level of 114.3 (22). We assume that the low initial FACT-P total score in patients of our study might relate to a higher frequency of present comorbidities and later initiation of ARTA therapy. However, other unknown and not studied factors might play their role, such as COVID-19 pandemic era with its negative impact on healthcare and on patients´ everyday lives.

Our research showed that treatment with abiraterone and enzalutamide had a comparable impact on HRQoL in the first line mCRPC setting in routine clinical practice in Slovakia. There were no statistically significant differences in the frequency of clinically meaningful worsening or improvement of HRQoL between the two treatment groups over 12 months in FACT-P total scores, majority of its domains´ scores and EQ-5D VAS level. A proportion of patients with a clinically meaningful deterioration in TOI score at 12-month was lower in the abiraterone group than in the enzalutamide one (p=0.047). After 1 year of treatment, no statistically significant difference between the two arms was observed in estimated mean changes in FACT-P total scores (p=0.620) and its components, EQ-5D index (p=0.108), and EQ-5D VAS (p=0.324). Quality of life of mCRPC patients remained maintained throughout 1 year of treatment with either of the two drugs.

There is a limited number of head-to-head trials comparing the impact of both ARTAs on efficacy and quality of life. From those few available, some proved favourable effect of abiraterone on patients´ functioning compared to enzalutamide, some have not shown between-group differences. Important is to emphasize that assessment tools, as well as studies´ designs differed. In a comparative study published by Khalaf et al., changes in FACT-P scores over time from baseline were more favourable in the abiraterone group versus the enzalutamide group in patients ≥75 years (p=0.003) with no significant difference in younger patients. A significantly higher proportion of patients treated with enzalutamide experienced clinically meaningful worsening in the physical and functional domains compared to abiraterone (37% vs 21%, p=0.013; 39% vs 23%, p=0.015) (21). The HEAT trial compared the difference in the HRQoL of mCRPC patients treated with abiraterone or enzalutamide assessed by the FACT-P tool. Between-group differences in quality-of-life measurement were not clinically significant (20). Quality of life in the AQUARIUS study was evaluated by the EORTC QLQ-C30 (European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire C30) questionnaire, and the results showed that cognitive functioning and fatigue items were significantly in favour of abiraterone over enzalutamide (19). Similarly, the real-world phase 4 study of enzalutamide and abiraterone with prednisone tolerability (REAAcT) assessed the patients´ functional status with the EORTC QLQ-30 questionnaire. However, the overall mean changes from baseline for the EORTC QLQ-C30 assessment were similar in both treatment groups (23).

The limitations of our study included lack of randomization, although baseline characteristics were well-balanced, relatively small sample size (making it difficult to demonstrate statistical significance), low number of treatment centres involved in the research and open-label design. Furthermore, there was no formal correction for multiple testing, thus, significant results have to be interpreted with extreme caution. The positives of the research included a collection of data based on validated questionnaires with a high completion rate throughout the study. The assessment periods were preplanned. We have provided data from real clinical practice in Slovakia which represents the general population, including elderly patients and patients with comorbidities, which is an advantage compared to clinical trials which usually include a more selected population.

Conclusion

In conclusion, the results of our research showed that treatment with abiraterone and enzalutamide had a comparable impact on quality of life in the first line mCRPC setting in routine clinical practice in Slovakia. Clinically meaningful worsening or improvement of HRQoL between the two treatment groups over 12 months in FACT-P total scores, majority of its domains' scores and EQ-5D VAS level was similar. We observed that the baseline FACT-P total score was lower, the time since the diagnosis of mCRPC to the initiation of ARTA treatment was relatively longer than in similar studies, and mCRPC patients in Slovakia showed a higher frequency of comorbidities. However, the quality of life of mCRPC patients remained maintained throughout 1 year of treatment with either of the two drugs.

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