Corticosteroid switch from prednisone to dexamethasone in metastatic castration-resistant prostate cancer patients with biochemical progression on abiraterone acetate plus prednisone

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Abstract

**Background:** To assess the efficacies and potential predictors of a corticosteroid switch in metastatic castration-resistant prostate cancer (mCRPC) patients with biochemical progression on abiraterone acetate plus prednisone (A + P).

**Methods:** Patients with mCRPC treated between April 2016 and August 2020, who experienced biochemical progression on A + P and then switched to A plus dexamethasone (D), were retrospectively identified. The primary endpoint was progression-free survival (PFS), and the secondary endpoints were PSA response, overall survival (OS), and safety.

**Results:** One hundred and thirty consecutive cases were enrolled. The median PFS and OS on A + D were 5.0 and 18.7 months, respectively. The best PSA decline of ≥50% (PSA50) and ≥30% (PSA30) were observed in 29.2 and 46.2% patients, respectively. Lower PSA at corticosteroid switch (≤20 ng/mL; median PFS, HR 0.63, p = 0.019; median OS, HR 0.38, p = 0.001) and longer mCRPC-free survival (≥18 months; median PFS, HR 0.61, p = 0.013; median OS, HR 0.51, p = 0.015) were identified as independent prognostic predictors associated with longer PFS and OS. A risk stratification tool was developed to select candidates for corticosteroid switch based on the independent prognostic predictors of PFS and OS.

**Conclusions:** A corticosteroid switch from prednisone to dexamethasone is effective for mCRPC which progressed on A + P treatment. Patients with lower PSA at corticosteroid switch and/or longer mCRPC-free survival may gain more benefits by the corticosteroid switch.

**Keywords:** Abiraterone, Castration-resistant prostate cancer, Prednisone, Dexamethasone, Corticosteroid switch
Background
Metastatic castration-resistant prostate cancer (mCRPC) is one of the leading causes of death among men worldwide [1]. Although novel therapeutic options were developed for mCRPC, no therapy is curative, and patients with mCRPC have a short overall survival (OS) [2–5].

Abiraterone (A) is a potent inhibitor of CYP17, which blocks gonadal and non-gonadal androgen steroidogenesis [6]. Continuous CYP17 inhibition also blocks adrenal glucocorticoid synthesis and results in elevated adrenocorticotropic hormone levels, which may lead to secondary mineralocorticoid excess characterized by fluid retention, hypertension, hypokalemia and cardiovascular events [7]. Therefore, A is administered in combination with 5 mg prednisone (P) twice daily for mCRPC patients to prevent these side effects [3].

The OS of mCRPC patients is prolonged by the treatment with A plus P (A + P) [3, 8]. However, the survival benefit of ~4 months is still limited. Notably, P is not the only concomitant corticosteroid used with A. Dexamethasone (D) 0.5 mg once daily was used in a trial of A reported by Reid et al. [9]. Their study showed a prostate-specific antigen (PSA) decline of ≥50% (PSA50) in 51% of patients, whereas a PSA50 rate of 43% was observed in another trial with 5 mg P twice daily [10]. Moreover, A + P at 5 mg twice daily or D at 0.5 mg once daily was compared in a trial reported by Attard et al. [11]. Therein, a median radiographic progression-free survival (PFS) of 26.6 and 18.5 months were observed in patients treated with D and P, respectively. Interestingly, several studies have reported that the switch from P to D in mCRPC would achieve secondary responses [12–18]. These studies reported PFS of 2.5–11.8 months and PSA50 in 11–55% of patients. The differential responses suggested that not all patients who progressed on A + P could benefit from the corticosteroid switch. However, previous studies with a relatively small cohort (< 48 cases) did not distinguish candidates who may have OS benefits from a corticosteroid switch [12–18].

The aim of our study was therefore to assess the efficacies and potential predictors based on PFS and OS of a corticosteroid switch from A to D in mCRPC patients with PSA progression on A + P.

Materials and methods

Patients
Data of mCRPC patients with Eastern Cooperative Oncology Group (ECOG) performance status score ≤2 subject to a corticosteroid switch from A + P to A + D between April 2016 and August 2020 at West China Hospital (Chengdu, China) and Sun Yat-sen University Cancer Center (Guangzhou, China) was retrospectively analyzed. Report of these data was approved by the institutional review board and ethical committee of the two institutions. However, due to the retrospective nature of this study, ethical committee of West China Hospital and Sun Yat-sen University Cancer Center waived the informed consent for this study. All methods were performed in accordance with the Declaration of Helsinki. Patients that had PSA progression on A + P were switched from P to D. The PSA progression was defined by PCWG3 criteria [19].

Treatments and outcomes
In this study, the corticosteroid switch from P 5 mg twice daily to D 0.5 mg once daily was performed after PSA progression. Abiraterone 1000 mg once daily was continued. All patients had castrate levels of testosterone < 50 ng/dL. The A + D treatment was maintained until biochemical progression. Biochemical progression was evaluated according to PCWG3 criteria [19]. Biological and Clinical evaluations were performed monthly for the first 3 months, and every 1–3 months thereafter, or any time in case of clinical symptoms. Imaging assessments were performed every 3–6 months, or any time in case of clinical and/or biological progression.

The primary endpoint of this study was PFS, which was defined as the time interval from corticosteroid switch to PSA progression according to PCWG3 criteria [19]. The secondary endpoints of this analysis included OS, PSA response and safety. In this context, OS was defined as the time interval between the corticosteroid switch and death from any causes. PSA response was defined as the best PSA decline of ≥50% (PSA50) and ≥30% (PSA30). Any adverse events were evaluated according to the National Cancer Institute Common Terminology Criteria version 5.0.

Statistical analysis
The continuous variables are expressed as median values, and the categorical variables are presented as frequency (%). Factors predicting PFS and OS were determined by Univariate Cox regression. Those factors with p < 0.05 were further tested in multivariate Cox models. Different risk groups were developed according to the multivariate Cox models. The survival curves were generated by the Kaplan-Meier method, and differences were assessed by a log-rank test. All reported p values in this study were assessed with statistical significance defined as p < 0.05 were two-sided. Statistical analyses were carried out with GraphPad Prism version 7 and SPSS version 22.

Results

Patient characteristics
One hundred and thirty eligible patients were included in this study; among them, 79 were from one hospital and 51 from another. The clinical characteristics of these patients are shown in Table 1. Eighteen patients received...
Table 1 Baseline characteristics of patients at the time of corticosteroid switch

| Characteristics                              | No. of patients (%) |
|----------------------------------------------|---------------------|
| Median age (range), years                    | 73 (50–91)          |
| ISUP grading at diagnosis                   |                     |
| ≤ 4                                          | 43 (33.1)           |
| > 4                                          | 75 (57.7)           |
| NA                                           | 12 (9.2)            |
| Median time to mCRPC (range), months         | 13.7 (2.0–168.5)    |
| Chemotherapy before A + P                   |                     |
| Yes                                          | 18 (13.8)           |
| No                                           | 112 (86.2)          |
| ECOG performance status at corticosteroid switch |                     |
| 0                                            | 76 (58.5)           |
| 1, 2                                         | 54 (41.5)           |
| Metastasis at corticosteroid switch         |                     |
| Bone                                         | 123 (94.6)          |
| Lymph node                                   | 35 (26.9)           |
| Visceral                                     | 21 (16.1)           |
| Median PFS of A + P (range), months          | 6.6 (1.0–48.3)      |
| PSA response to A + P                        |                     |
| PSA decline ≥50%                             | 71 (54.6)           |
| PSA decline ≥30% and < 50%                   | 12 (9.2)            |
| No response                                  | 47 (36.1)           |
| Median PSA level (range), ng/mL              |                     |
| At diagnosis                                 | 100.1 (3.7–11,640.0) |
| At A + P initiation                          | 36.7 (1.2–3126.0)   |
| At corticosteroid switch                    | 21.1 (2.2–2893.0)   |
| PSA nadir after corticosteroid switch        | 140 (0.02–3133.0)   |
| Hemoglobin, g/dL                             |                     |
| ≥ 13                                         | 39 (30.0)           |
| < 13                                         | 62 (47.7)           |
| NA                                           | 29 (22.3)           |
| ALP, U/L                                     |                     |
| Normal                                       | 68 (52.3)           |
| High                                         | 27 (20.8)           |
| NA                                           | 35 (26.9)           |
| LDH, U/L                                     |                     |
| Normal                                       | 69 (53.1)           |
| High                                         | 24 (18.5)           |
| NA                                           | 37 (28.5)           |

A: abiraterone acetate; ALP: alkaline phosphatase; CRPC: Castration-resistant prostate cancer; D: dexamethasone; ECOG: Eastern Cooperative Oncology Group; ISUP: The International Society of Urological Pathology; LDH: lactate dehydrogenase; NA: not available; P: prednisone; PFS: progression-free survival; PSA: prostate-specific antigen

docetaxel therapy after diagnoses with mCRPC. The median age (range) was 73 (50–91) years. The median (range) PSA level at corticosteroid switch was 21.1 (2.2–2893.0) ng/mL.

PSA and survival outcomes

At the time of data cut-off, 20 patients (15.4%) were still responding on A + D; 110 patients (84.6%) had biochemical progression, and 78 (70.9%) of them received further treatments. PSA50 and PSA30 were observed in 38 (29.2%) and 60 patients (46.2%), respectively. The median follow-up was 15.0 months (95% CI, 12.2–15.8). At the last follow-up, 60 patients (46.2%) died from various causes. The observed median PFS of A + D treatment was 5.0 months (95% CI, 3.9–6.1 months), and median OS was 18.7 months (95% CI, 15.7–21.5 months). The median PFS was 8.9 and 3.2 months among patients with and without PSA50 (Fig. 1A), 8.1 and 2.9 months among those with and without PSA30 (Fig. 1C), respectively. The median OS was 29.8 and 17.3 months among patients with and without PSA50 (Fig. 1B), 28.3 and 17.0 months among those with and without PSA30 (Fig. 1D), respectively.

Univariate and multivariate prognostic analyses

The univariate Cox analyses of factors predicting PFS and OS for the corticosteroid switch are shown in Table 2. Due to lack of data for some patients, ALP, LDH and hemoglobin were not analyzed. Among all the tested factors, two factors were found associated with both longer PFS and OS, including lower PSA level (≤ 20 ng/mL) at corticosteroid switch and longer mCRPC-free survival (≥ 18 months). Patients with better ECOG performance status score (0) also had longer OS. In multivariate analyses, PSA level (≤ 20 ng/mL) at corticosteroid switch and mCRPC-free survival (≥ 18 months) were identified as independent factors in predicting both PFS and OS (Table 3). PFS curves are shown in Fig. 2A and C, while OS curves are shown in Fig. 2B and D.

Prognostic risk stratification

Because ECOG performance status itself may affect survival, three risk groups were further defined based on only two factors (PSA at corticosteroid switch and mCRPC-free survival) which can predict both PFS and OS independently in multivariate Cox analysis: low-risk group (n = 28), with two favorable prognostic predictors (PSA at corticosteroid switch ≤20 ng/mL and mCRPC-free survival ≥18 months); intermediate-risk group (n = 61), with one unfavorable prognostic predictor (PSA at corticosteroid switch ≤20 ng/mL and mCRPC-free survival < 18 months; PSA at corticosteroid switch > 20 ng/mL and mCRPC-free survival ≥18 months); and high-risk group (n = 41), with two unfavorable prognostic
predictors (PSA at corticosteroid switch > 20 ng/mL and CRPC-free survival < 18 months). Univariate Cox analyses indicate that patients in the intermediate-risk and high-risk groups featured 2.01- and 2.73-fold risk of progression, and 2.83- and 5.62-fold risk of death, respectively (Table 4), compared with patients with low-risk. Survival curves of PFS and OS for these groups are shown in Fig. 3. The PFS of low-risk group was significantly longer than intermediate-risk group (median 8.7 vs 4.5 months, \( p = 0.003 \)) and high-risk group (median 8.7 vs 3.0 months, \( p < 0.001 \)), whereas the PFS between intermediate-risk and high-risk were not significantly different (median 4.5 vs 3.0 months, \( p = 0.160 \)). This risk stratification was able to separate the OS (median NA vs 28.5 vs 18.7 months in low-, intermediate- and high-risk groups, respectively, \( p < 0.05 \)) of all groups. Rates of PSA50 were 35.7, 32.7 and 19.5% for low-, intermediate- and high-risk groups, respectively.

Safety
A + D treatment was well-tolerated after the corticosteroid switch for all patients in this study. No adverse events grade 3/4 were observed, and no dose reduction of D was required. No treatment-related death happened. Fluid retention (\( n = 6, 4.6\% \)), fatigue (\( n = 4, 3.1\% \)), hypokalaemia (\( n = 3, 2.3\% \)), hypertension (\( n = 3, 2.3\% \)), and hyperglycaemia (\( n = 2, 1.5\% \)) were the most common adverse events. All of these adverse events were grade 1/2.

Discussion
A switch of corticosteroid from 5 mg P twice daily to 0.5 mg D once daily after progression on A + P was able to reverse biochemical resistance, as reported by several studies [12–18]. The corticosteroid switch could prolong PFS of 2.5–11.8 months, and result in PSA50 and PSA30 of 11–55% and 40–45%, respectively. In the present study, PSA50 and PSA30 were observed in 28.5 and 46.2% of patients, respectively; the median PFS and OS were 5.0 and 18.7 months, respectively, after the corticosteroid switch. These results further support the benefits from this corticosteroid switch. Long-term use of dexamethasone may result in some adverse events. Considering that dexamethasone is inexpensive and relative short-term use is safe, patients can easily and safely obtain A + D treatment after progression on A + P. This can be helpful especially for patients who cannot afford other effective sequential therapies, or when few sequential agents are available.

Although all previous studies have attributed a positive clinical value to corticosteroid switch, its efficacy appears not completely consistent. For example, PSA50 ranged...
### Table 2 Univariate Cox analyses predicting PFS and OS of corticosteroid switch

| N   | PFS, months | OS, months |
|-----|-------------|------------|
|     | Median (95%CI) | HR (95%CI) | p value | Median (95%CI) | HR (95%CI) | p value |
| Age at corticosteroid switch, years | | | | | | |
| ≥ 70 | 81 | 5.5 (4.4–6.6) | 0.75 (0.51–1.10) | 0.139 | 18.1 (16.7–19.5) | | |
| < 70 | 49 | 3.2 (0.7–5.7) | | | 23.5 (13.5–33.5) | | |
| ISUP grading at diagnosis | | | | | | |
| > 4 | 75 | 4.8 (3.5–6.1) | 1.01 (0.67–1.53) | 0.946 | 20.1 (14.3–25.9) | | |
| ≤ 4 | 43 | 5.5 (2.9–8.1) | | | 17.3 (13.4–21.2) | | |
| ECOG at corticosteroid switch | | | | | | |
| 0 | 76 | 5.6 (4.2–7.0) | 0.75 (0.51–1.10) | 0.140 | 23.5 (17.3–29.7) | | |
| ≥ 1 | 54 | 3.7 (2.2–5.2) | | | 17.4 (13.8–21.0) | | |
| PSA at diagnosis, ng/mL | | | | | | |
| ≥ 100 | 76 | 4.8 (3.7–5.9) | 1.09 (0.71–1.65) | 0.703 | 19.0 (14.2–23.8) | | |
| < 100 | 41 | 5.9 (5.0–6.8) | | | 18.1 (14.2–22.0) | | |
| PSA at corticosteroid switch, ng/mL | | | | | | |
| ≤ 20 | 64 | 6.9 (5.8–8.0) | 0.60 (0.41–0.87) | 0.007 | 25.9 (21.7–30.1) | | |
| > 20 | 66 | 3.7 (2.8–4.6) | | | 15.6 (13.3–17.9) | | |
| mCRPC-free survival, months | | | | | | |
| ≥ 18 | 53 | 6.9 (5.2–8.6) | 0.58 (0.40–0.85) | 0.005 | 23.6 (17.7–29.5) | | |
| < 18 | 77 | 3.2 (2.0–4.4) | | | 17.1 (15.1–19.1) | | |
| Time to progression on A + P, months | | | | | | |
| ≥ 8 | 50 | 6.2 (4.5–7.9) | 0.75 (0.51–1.10) | 0.144 | 17.5 (15.3–19.7) | | |
| < 8 | 80 | 4.2 (2.6–5.8) | | | 19.0 (14.9–23.1) | | |
| PSA response on A + P | | | | | | |
| Decline ≥ 50% | 72 | 4.9 (3.8–6.0) | 1.11 (0.75–1.62) | 0.608 | 17.4 (16.2–18.7) | | |
| Decline < 50% | 58 | 5.4 (3.6–7.2) | | | 28.3 (14.9–41.7) | | |

A: abiraterone acetate; CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; HR: hazard ratio; ISUP: The International Society of Urological Pathology; mCRPC: metastatic castration-resistant prostate cancer; OS: overall survival; P: prednisone; PFS: progression-free survival; PSA: prostate-specific antigen

### Table 3 Multivariate Cox analyses predicting PFS and OS of corticosteroid switch

| N   | PFS | OS |
|-----|-----|----|
|     | HR (95%CI) | p value | HR (95%CI) | p value |
| ECOG at corticosteroid switch | | | | |
| 0   | 76 | 0.58 (0.35–0.97) | 0.040 |
| ≥ 1 | 54 | | |
| PSA at corticosteroid switch, ng/mL | | | | |
| ≤ 20 | 64 | 0.63 (0.43–0.93) | 0.019 | 0.38 (0.22–0.66) | 0.001 |
| > 20 | 66 | | | |
| mCRPC-free survival, months | | | | |
| ≥ 18 | 53 | 0.61 (0.41–0.90) | 0.013 | 0.51 (0.30–0.88) | 0.015 |
| < 18 | 77 | | | |

CI: confidence interval; D: dexamethasone; HR: hazard ratio; mCRPC: metastatic castration-resistant prostate cancer; OS: overall survival; PFS: progression-free survival; PSA: prostate-specific antigen
from 11 to 55%, and median PFS was 2.5–11.8 months in these studies [12–18]. In our cohort, no PSA decline happened in 33.1% patients, while 20 patients presented PFS ≤ 2 months. These results indicate that not all patients show a satisfactory response to corticosteroid switch, and emphasizes the importance of candidate selection for corticosteroid switch in clinical practice. Fenioux et al. [12] developed a prognostic score to distinguish patients with longer PFS for A + D based on independent favorable prognostic factors predicting PFS. However, the study involved only a small cohort (48 patients) with 14 and 9 patients in low- and high-risk groups, respectively. Besides, whether longer PFS of patients corresponded with OS benefits was not clear, since OS was not reported therein.

In this study, two factors favorable for both PFS and OS of corticosteroid switch were considered: lower PSA (≤ 20 ng/mL) at corticosteroid switch and longer mCRPC-free survival (≥ 18 months). Longer mCRPC-free survival, which is associated with longer PFS after corticosteroid switch, was shown by previous studies, as reported by Fenioux et al. [12] and Rivero-Belenchón et al. [16]. Furthermore, lower PSA at corticosteroid switch indicated longer PFS after corticosteroid switch [12]. Fenioux et al. [12] reported that short PFS for A + P is a favorable factor predicting PFS after corticosteroid switch; however, Romero-Laorden et al. [14] had contrasting results. Interestingly, PFS for A + P was not an independent factor predicting the effect of the corticosteroid switch in our study and the study reported by Rivero-Belenchón et al. [16]. Further prospective studies with more enrolled patients are therefore needed to clarify the association between PFS for A + P and the efficacy of corticosteroid switch.

A risk stratification tool was developed based on the two independent prognostic predictors of PFS and OS in

**Table 4** Results of univariate Cox analyses in the prognostic risk stratification

| Risk group | N | PFS | OS |
|------------|---|-----|----|
|            |   | Events | HR (95% CI) | p value | Events | HR (95% CI) | p value |
| Low        | 28 | 20 | 1 |  | 6 | 1 |  |
| Intermediate | 61 | 52 | 2.01 (1.19–1.37) | 0.009 | 27 | 2.83 (1.16–6.87) | 0.022 |
| High       | 41 | 38 | 2.73 (1.58–4.72) | < 0.001 | 27 | 5.62 (2.30–13.78) | < 0.001 |

CI: confidence interval; HR: hazard ratio; OS: overall survival; PFS: progression-free survival
our study, including PSA at corticosteroid switch and mCRPC-free survival, to select candidates for the corticosteroid switch. Although the PFS was not different significantly between patients in intermediate- and high-risk groups, patients in all risk groups were well-separated based on OS. Furthermore, PSA50 was better in low- (35.7%) and intermediate-risk (32.7%) groups, as compared with high-risk group (19.5%). Therefore, patients with low- and intermediate-risk may be appropriate candidates to receive a corticosteroid switch after biochemical progression on A + P treatment, as they may gain more survival benefits from the switch. On the other hand, patients with high-risk may be not suitable to receive the switch due to poor responses and low survival benefits.

To date, the exact mechanism underlying the corticosteroid switch to reverse A + P resistance remains unclear. Several hypotheses have been proposed to explain this effect [20]. First, the activation of glucocorticoid receptor (GR) leads to resistance. Dexamethasone 0.5 mg has lower equivalent glucocorticoid activity when compared with prednisolone 10 mg, thus fewer GRs are activated by Dexamethasone [21]. Second, AR point mutations of AR can be activated by prednisone, rather than by dexamethasone [22]. Third, pharmacodynamic and pharmacokinetic differences between prednisone and dexamethasone lead to higher efficacy of dexamethasone in suppressing the adrenocorticotropic hormone [23]. Fourth, resistance due to the activation of mineralocorticoid receptors, for which dexamethasone has lower affinity [24]. Nevertheless, none of these hypotheses have been fully verified, thus further research is needed to uncover the mechanism of the corticosteroid switch.

The activity of D itself may be involved in the antitumor effect; it has been shown that D can suppress lymphangiogenesis in prostate cancer [25]. A was administered without steroids in a phase I/II study, and D 0.5 mg once daily was added to A after PSA progression, which treatment resulted in PSA50 in 33% of patients [26]. In another phase I/II trail that prior to the clinical use of enzalutamide and A in mCRPC patients, D monotherapy was found more effective than P [27]. These results may explain why PFS for A + P treatment is not a predictive factor of the efficacy of corticosteroid switch. Whether it is A + D treatment or D monotherapy that leads to the antitumor effect after progression on A + P treatment needs to be elucidated by further research.

The limitations of current study include the retrospective nature of this study, which may lead to potential bias. Moreover, a control group that D monotherapy was administered when corticosteroid switch was carried out was also lacking. Thus, the possibility of the antitumor effect being related to D monotherapy cannot be excluded. A + D treatment was terminated due to PSA progression in most patients, hence A + D treatment length was less than three months for some patients. Furthermore, LDH, Hb and ALP were not included in univariate and multivariate analyses due to lack of data, which may be significant prognostic factors; and only patients with ECOG≤2 were included, this could have impact on OS. Finally, sequential treatments after progression on A + D could influence OS, and this was not analyzed in this study.

**Conclusions**

The present study adds to evidence that the corticosteroid switch from prednisone to dexamethasone is a feasible and effective alternative for mCRPC patients who failed from A + P treatment. Patients with lower PSA at corticosteroid switch and/or previous longer mCRPC-free survival may gain more treatment benefits after this type of corticosteroid switch.

**Abbreviations**

A: abiraterone acetate; D: dexamethasone; ECOG: Eastern Cooperative Oncology Group; mCRPC: metastatic castration-resistant prostate cancer;
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Authors’ contributions
Zhenyu Yang drafted the manuscript. Zhenyu Yang, Yuchao Ni, Diwei Zhao, Yijun Zhang, Jun Wang, Lijuan Jiang, Dong Chen, Zhiming Wu, Yanjun Wang, Zhenyu Yang

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Yonghong Li supervised the study. All authors approved the final submitted draft.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Approval to report these data was obtained from the institutional review board and ethical committee of West China Hospital and Sun Yat-sen University Cancer Center. However, due to the retrospective nature of this study, ethical committee of West China Hospital and Sun Yat-sen University Cancer Center waived the informed consent for this study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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References
1. Sun H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021; 71(3):209–49.
2. Beer TM, Armstrong AJ, Rathkopf DE, Liorit Y, Sternberg CN, Higano CS, et al. Enzalutamide in metastatic prostate cancer before chemotherapy. N Engl J Med. 2014;371(5):24–33. https://doi.org/10.1056/NEJMoa1405085.
3. Ryan CJ, Smith MR, Fizazi K, Saad F, Mulders PF, Sternberg CN, et al. Abiraterone acetate plus prednisone versus placebo plus prednisone in chemotherapy-naive men with metastatic castration-resistant prostate cancer (COU-AA-302): final overall survival analysis of a randomised, double-blind, placebo-controlled phase 3 study. Lancet Oncol. 2015;16(3):52–60. https://doi.org/10.1016/S1470-2045(14)71205-7.
4. de Wit R, de Bono J, Sternberg CN, Fitzki K, Tombal B, Wulfing C, et al. Cabazitaxel versus Abiraterone or Enzalutamide in Metastatic Prostate Cancer. N Engl J Med. 2019;381(26):2506–18. https://doi.org/10.1056/NEJMoa1911206.
5. Parker C, Nilsson S, Heinrich D, Helle SI, O’Sullivan JM, Fossa SD, et al. Alpha emitter radium-223 and survival in metastatic prostate cancer. N Engl J Med. 2013;369(3):213–23. https://doi.org/10.1056/NEJMoa1213755.
6. Yin L, Hu Q. CYP17 inhibitors–abiraterone, C17,20-lyase inhibitors and multi-targeting agents. Nat Rev Urol. 2014;11(1):32–42. https://doi.org/10.1038/nr urol.2013.274.
7. Attard G, Reid AH, Yap TA, Raynaud F, Dowsett M, Settatee S, et al. Phase I clinical trial of a selective inhibitor of CYP17, abiraterone acetate, confirms that castration-resistant prostate cancer commonly remains hormone driven. J Clin Oncol. 2008;26(28):4563–71. https://doi.org/10.1200/JCO.2007.1 9.749.
8. Fizazi K, Scher HI, Molina A, Logothetis CJ, Chi KN, Jones RL, et al. Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-303 randomised, double-blind, placebo-controlled phase 3 study. Lancet Oncol. 2012;13(10): 983–92. https://doi.org/10.1016/S1470-2045(12)70379-0.
9. Reid AH, Attard G, Danila DC, Oommen NB, Olmos D, Fong PC, et al. Significant and sustained antitumor activity in post-docetaxel, castration-resistant prostate cancer with the CYP17 inhibitor abiraterone acetate. J Clin Oncol. 2010;28(9):1489–95. https://doi.org/10.1200/JCO.2009.246819.
10. Danila DC, Morris MJ, de Bono JS, Ryan CJ, Denneheade SR, Smith MR, et al. Phase II multicenter study of abiraterone acetate plus prednisone therapy in patients with docetaxel-treated castration-resistant prostate cancer. J Clin Oncol. 2010;28(9):1496–501. https://doi.org/10.1200/JCO.2009.25.9259.
11. Attard G, Menseburger AS, Arlt W, Sternberg CN, Feysenbend S, Berti A, et al. Assessment of the safety of glucocorticoid regimens in combination with Abiraterone acetate: a randomized, open-label phase 2 study. JAMA Oncol. 2019;5(8):1159–67. https://doi.org/10.1001/jamaoncol.2019.1011.
12. Ferlinius C, Louvet C, Charton E, Rozet F, Ropert S, Prapoinch D, et al. Switch from abiraterone plus prednisone to abiraterone plus dexamethasone at asymptomatic PSA progression in patients with metastatic castration-resistant prostate cancer. BJU Int. 2019;123(2):300–6. https://doi.org/10.1111/bju.14515.
13. Lorente D, Omlin A, Ferraleschi R, Pezaro C, Perez R, Mateu J, et al. Tumour responses following a steroid switch from prednisone to dexamethasone in castration-resistant prostate cancer patients progressing on abiraterone. Br J Cancer. 2014;111(12):2248–53. https://doi.org/10.1038/bjc.2014.531.
14. Romero-Laorden N, Lozano R, Jayaram A, Lopez-Campos F, Saez M, Montesa A, et al. Phase II pilot study of the prednisone to dexamethasone switch in metastatic castration-resistant prostate cancer patients with limited progression on abiraterone plus prednisone (SWITCH study). Br J Cancer. 2018;119(9):1052–9. https://doi.org/10.1038/s41416-018-0123-9.
15. Roviello G, Petrioli R, Bonetta A, Conca R, Rodriquenz MG, Aieta M. Corticosteroid switch after abiraterone plus prednisone (SWITCH study). Br J Cancer. 2014;111(12):2248–53. https://doi.org/10.1038/bjc.2014.531.
16. Roviello G, Sobhani N, Corona SP, D’Angelo A. Corticosteroid switch after abiraterone plus prednisone (SWITCH study). Br J Cancer. 2014;111(12):2248–53. https://doi.org/10.1038/bjc.2014.531.
17. Zanardi E, Soldato D, Latorca MM, Catrini C, Boccardo F. To switch or not to switch? A real-life experience using dexamethasone in combination with abiraterone. Ther Adv Urol. 2019;11:1756287219845908.
18. Fang WY, Wang PF, Fan YC, Shih HJ. Clinical experience of steroid switch from prednisone to dexamethasone in patients with metastatic castration-resistant prostate cancer treated with Abiraterone acetate. Urol Int. 2021; 105(6):380–5.
19. Scher HI, Morris MJ, Stadler WM, Higano C, Rasch E, Fizazi K, 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(14):1402–18. https://doi.org/10.1200/JCO.2015.64.2702.
20. Roviello G, Sobhani N, Corona SP, D’Angelo A. Corticosteroid switch after progression on abiraterone acetate plus prednisone. Int J Clin Oncol. 2020; 25(2):240–5. https://doi.org/10.1007/s10147-019-00157-w.
21. Arora VK, Schenkein E, Murali R, Subudhi SK, Wongvipat J, Balbas MD, et al. Glucocorticoid receptor confers resistance to antiandrogens by bypassing androgen receptor blockade. Cell. 2013;155(5):639–22. https://doi.org/10.1016/j.cell.2013.11.012.
22. Richards J, Lim AC, Hay CW, Taylor AE, Wingate A, Nowakowski K, et al. Interactions of abiraterone, epalutamone, and prednisolone with wild-type Glucocorticoid receptor.
and mutant androgen receptor: a rationale for increasing abiraterone exposure or combining with MDV3100. Cancer Res. 2012;72(9):2176–82. https://doi.org/10.1158/0008-5472.CAN-11-3980.

23. Diederich S, Scholz T, Eigendorff E, Burnke-Vogt C, Quinkler M, Exner P, et al. Pharmacodynamics and pharmacokinetics of synthetic mineralocorticoids and glucocorticoids: receptor transactivation and prereceptor metabolism by 11beta-hydroxysteroid-dehydrogenases. Horm Metab Res. 2004;36(6):423–9. https://doi.org/10.1055/s-2004-814578.

24. Lan NC, Graham B, Barter FC, Baxter JD. Binding of steroids to mineralocorticoid receptors: implications for in vivo occupancy by glucocorticoids. J Clin Endocrinol Metab. 1982;54(2):332–42. https://doi.org/10.1210/jcem-54-2-332.

25. Yano A, Fuji Y, Iwai A, Kawakami S, Kageyama Y, Kihara K. Glucocorticoids suppress tumor lymphangiogenesis of prostate cancer cells. Clin Cancer Res. 2006;12(20 Pt 1):6012–7. https://doi.org/10.1158/1078-0432.CCR-06-0749.

26. Attard G, Reid AH, A’Hern R, Parker C, Oommen NB, Folkerd E, et al. Selective inhibition of CYP17 with abiraterone acetate is highly active in the treatment of castration-resistant prostate cancer. J Clin Oncol. 2009;27(23):3742–8. https://doi.org/10.1200/JCO.2008.20.0642.

27. Venkitaraman R, Lorente D, Murthy V, Thomas K, Parker L, Ahiabor R, et al. A randomised phase 2 trial of dexamethasone versus prednisolone in castration-resistant prostate cancer. Eur Urol. 2015;67(4):673–9. https://doi.org/10.1016/j.eururo.2014.10.004.

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