Case Report

Changing the enzalutamide form from a capsule to a tablet improves the adherence of medicine intake: A case of a significant decrease in the prostate-specific antigen level and improvement in radiographic findings

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Introduction: In June 2018, enzalutamide began to be sold in a tablet form in Japan and Germany. We herein report the case of an improvement in prostate cancer progression due to changing enzalutamide dosage form from a capsule to a tablet.

Case presentation: A 76-year-old man was initially referred to our hospital for the further examination of his elevated prostate-specific antigen level (3664.0 ng/mL). He had developed castration-resistant prostate cancer 10 months after initial treatment. Treatment with enzalutamide (capsule form) was subsequently initiated. In June 2018, drug form of enzalutamide was changed from a capsule to a tablet. After switching to an enzalutamide tablet, his prostate-specific antigen level decreased significantly from 493.0 to 26.5 ng/mL.

Conclusion: While the reason for this prostate-specific antigen response is unclear, changing the enzalutamide form from a capsule to a tablet may have improved the adherence of drug intake and thereby resulted in castration-resistant prostate cancer control.

Key words: dosage form, enzalutamide, enzalutamide capsule, enzalutamide tablet.

Keynote message

While the reason for this PSA response is unclear, changing the ENZ form from a capsule to a tablet may have improved the adherence of drug.

Introduction

ENZ prolongs the survival and reduces skeletal-related events both in pre- and post-chemotherapy CRPC and is now used in more than 90 countries.1,2 However, despite this effectiveness, a fair number of patients experience adverse events, including fatigue and nausea. The PREVAIL and AFFIRM trials reported fatigue in 25.3% and 13.3% of cases and nausea in 13.3% and 20.1% of cases, respectively.1,2 Most cases showed adverse events of Common Terminology Criteria for Adverse Events Grade ≤2. Ogawa et al. managed adverse effects using traditional Chinese medicine, noting a decrease in the cancer fatigue scale.3 Other reports have suggested changing the timing of ENZ intake from morning to night in order to reduce the incidence of these adverse event.4 A temporary drug holiday or dose reduction has often helped patients maintain their ENZ intake.

In June 2018, ENZ began to be sold in a tablet form in Japan and Germany. We herein report the first case of an improvement in prostate cancer progression due to changing the ENZ dosage form from a capsule to a tablet.

Abbreviations & Acronyms
ALP = alkaline phosphatase
BSI = bone scan index
CRPC = castration-resistant prostate cancer
ENZ = enzalutamide
LUTS = lower urinary tract symptoms
OD = orally disintegrating
PSA = prostate-specific antigen

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Case presentation

A 76-year-old man was initially referred to our hospital for the further examination of his elevated PSA level (3664.0 ng/mL) in December 2016. He received initial hormonal therapy of leuprorelin acetate and bicalutamide for 10 months. In October 2017, he developed CRPC. He initially received dexamethasone, but his PSA remained elevated at 122.9 ng/mL. Although he took ENZ (160 mg) in capsule form for 2 months, his PSA and ALP levels remained high at 493.0 ng/mL and 450 IU/L, respectively.

In June 2018, the drug form of ENZ was changed from a capsule to a tablet (160 mg). After switching to the tablet form, his PSA significantly decreased from 493.0 to 26.5 ng/mL in the first month. The levels had decreased even further to 0.33 ng/mL by November 2018. A bone scan showed the same phenomenon, and his BSI decreased from 5.88 to 2.25 (Figs 1,2). Of note, no other drugs were changed when changing the dosage form of ENZ from a capsule to a tablet. During a careful interview to assess his adherence to medication, he noted that he forgot to take the ENZ capsules once or twice a week. Changing the medication to tablet form encouraged better adherence.

Discussion

Risk factors for drug intake difficulties in elderly patients are thought to include oral dryness, esophagus movement, water

![Clinical course](image)

Fig. 1 Clinical course.

![Bone scan](image)

Fig. 2 A bone scan at the time of (a) ENZ capsule intake and (b) ENZ tablet intake.
intake, drug form, drug size, and number of drugs. A large drug size and capsule format allows for easy attachment to the esophagus mucosa, subsequently necessitating a large amount of water for drug intake. Yamada et al. showed that, when patients were ≥70 years old, taking drugs with 15 mL water requires a significantly longer time to pass the esophagus than in patients <70 years old. In addition, elderly patients usually have several complicating diseases, requiring them to take several drugs at a time. Indeed, at our institute, the patients who had been prescribed ENZ were also taking an additional seven tablets for other complications on average (unpublished data).

Masumori et al. reported that changing the dosage form of silodosin from a capsule (2 and 4 mg; 15.5-mm-diameter capsule for both) to a tablet (2 and 4 mg: 6.4- and 11.0-mm-diameter pill, respectively) improved the adherence. However, the efficacy for LUTS did not change. In healthy volunteers, changing the silodosin drug form from a capsule to a tablet did not change the pharmacokinetics. Other studies have shown that changing the drug form did not alter the effectiveness in LUTS patients with regard to a tamsulosin capsule versus an OD tablet and a naftopidil capsule versus an OD tablet.

This case showed both a decrease in PSA and radiographic improvement. In radiotherapy or the initial administration of luteinizing hormone-releasing hormone agonists, PSA bounce or temporary PSA elevation is sometimes observed. In contrast, PSA bounce has not been reported in association with ENZ treatment. Thus, the likelihood of an association between ENZ and PSA bounce is considered to be lower. In this case, changing to an ENZ tablet encouraged the patient to take his medicine more steadfastly. Despite its effectiveness, he had previously been taking his ENZ capsule only moderately. While detailed mechanism underlying the improvement in his prostate cancer is unclear, he undoubtedly obtained a benefit from changing the dosage form. He had also taken dexamethasone and lansoprazole. These drugs have not been reported to affect the blood concentrations of ENZ and no drug interactions between these drugs and ENZ has been reported. According to the interview form of ENZ, pharmacokinetic data revealed that the C max of ENZ capsule was 4.8 ± 0.9 (µg/mL) and ENZ tablet was 3.5 ± 0.8 (µg/mL). These differences might have influenced the patient’s fatigue.

In conclusion, we herein report the first case of a significant improvement in both the PSA level and radiographic findings in a case of CRPC after changing the ENZ dosage form from a capsule to a tablet.

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Conflict of interest

The authors declare no conflict of interest.

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