Poster

[P26-8] P26-8: Oncologic drugs (4): Pharmacokinetics, TDM practice

Chair: Kohji Naora, Japan

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[P26-8-3] Long term drug interaction between enzalutamide and warfarin after discontinuation of enzalutamide

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Background

Enzalutamide, an androgen receptor signaling inhibitor used in the treatment ofan metastatic castration-resistant prostate cancer, is known as a moderate inducer of CYP2C9 and CYP2C19 and a strong inducer of CYP3A4. In some reports, Since warfarin is mainly metabolized by CYP2C9, it has been shown that enzalutamide is reported to reduced the AUC of oral *S*-warfarin by inducing CYP2C9y 56%. Furthermore, because the average half-life of enzaltamide is 5.8 days, it is also known that this its interaction may could persist long after enzalutamide is withdrawn because of the long half-life of enzalutamide, 5.8 days. However, the duration of its interaction is not studied well.Although, there is no report describing actual duration of this interaction, we We have experiencedreport a case suspected of long-term drug interaction between enzalutamide and warfarin.

Methods

Blood sample was taken when the patient visited hospital. The serum concentration of enzalutamide was measured by LC-MS/MS.

Results

72 years old man was taking 2 mg/day of warfarin for atrial fibrillation. Since the patient started 160 mg/day of enzalutamide, the dose of warfarin was gradually escalated from 2 mg/day to 4.5 mg/day. Enzalutamide was subsequently switched to 1000 mg/day of abiraterone because the concentration of prostate-specific antigen (PSA) increased. Although the dose of warfarin was kept as 3.75 mg/day, the INR increased to 1.8, 2.8 and 5.4 at 29, 43 and 55 days after stopping enzalutamide and . For instance, on day 29 after discontinuation of enzaltamide, the INR was 1.8 and on day 43 the INR was 2.8. On day 55, warfarin was discontinued and vitamin K was administered because the INR increased to 5.4. The serum concentration of enzalutamide was 164 ng/mL on day 43 and 24.4 ng/mL on day 57.

Conclusions

In spite of receiving the keeping the same dose of warfarin, the INR was increased even more than one month after discontinuation of enzalutamide is discontinued. This case suggested that a patients who takes enzalutamide and warfarin requires continuous and frequent attention to the change of INR after discontinuation of enzalutamide.