Poster

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

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[P26-8-4] Everolimus pharmacokinetics and toxicity in Japanese patients with advanced breast cancer

Masaki Hirabatake[1], Tomoyuki Mizuno[2], Rieko Miura[3], Eri Hohokabe[4], Sayaka Takebe[5], Kazuki Hashimoto[6], Yuichiro Kikawa[7], Hironori Kato[8], Thoru Hashida[9] (1.Kobe City Medical Center General Hospital, 2.Cincinnati Children's Hospital Medical Center, 3.Kobe City Medical Center General Hospital, 4.Kobe City Medical Center General Hospital, 5.Kobe City Medical Center General Hospital, 6.Kobe City Medical Center General Hospital, 7.Kobe City Medical Center General Hospital, 8.Kobe City Medical Center General Hospital, 9.Kobe City Medical Center General Hospital)

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Background

Everolimus is a cornerstone drug for advanced breast cancer treatment. However, frequent everolimus-induced adverse effect is a clinical problem in breast cancer treatment, especially in Japanese patients. So far, the optimal target concentration range of everolimus has been characterized in patients with organ transplantation; however, there is limited information on therapeutic drug management of everolimus in breast cancer patients [Shipkova M et al. Ther Drug Monit. 2016]. In this study, we evaluated the everolimus pharmacokinetics (PK) and toxicity in Japanese breast cancer patients.

Methods

Twelve patients were enrolled from November 2015 to November 2016. Seven patients started everolimus at 10 mg once daily, while 5 were administered a reduced dose of 5 mg. Blood samples were collected at pre-dose and 1, 4, and 8 hours post-dose. Everolimus concentration was determined by validated latex-enhanced turbidimetric immunoassay. PK parameters were estimated with Bayesian estimation using MW/Pharm (Mediware). The toxicity was evaluated based on CTCAE Ver. 4.0.

Results

The median (range) age and body weight were 66 (42-85) years and 51.4 (39.0-61.5) kg, respectively. The 50% of dose reduction due to adverse events were observed in 4 out of 7 patients who started at 10mg and 3 out of 5 patients who started at 5mg. Estimated trough concentrations at an initial dose of 10mg and 5mg were 19.1 (13.2-35.7) and 16.0 (11.3-29.2) ng/mL, respectively , which were higher than the documented target range for renal and heart transplantation patients (3-8 ng/mL). The estimated trough concentrations and AUC at an initial dose tended to be higher in patients treated with reduced dose due to adverse events than in other patients (trough concentration (median): 19.9 vs 16.1 ng/mL, AUC (median): 822 vs. 617 ng·h/mL). The main adverse events were mucositis oral (10/12), rash (9/12), malaise (6/12).

Conclusions

This study indicates that everolimus trough concentrations for standard dose of breast cancer treatment were higher than the target range in patients with organ transplantation. Our results suggest that high everolimus concentrations is associated with poor tolerability in breast cancer patients. Further clinical study is being planned to clarify the PK-PD relationship and identify the target concentration range for breast cancer patients.