
Poster

[P27-9] P27-9: Pharmacokinetics and PK/PD

Chair: Kosuke Doki, Japan

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[P27-9-1] Chromatographic determination of serum eltrombopag concentration for the therapeutic drug monitoring in patients with idiopathic thrombocytopenic purpura

Naoya Yanagimachi¹, Naoshi Obara², Mamiko Sakata³, Yuichi Hasegawa⁴, Shigeru Chiba⁵, Kosuke Doki⁶, Masato Homma⁷ (1.University of Tsukuba Hospital and University of Tsukuba, 2.University of Tsukuba Hospital and University of Tsukuba, 3.University of Tsukuba Hospital and University of Tsukuba, 4.University of Tsukuba Hospital and University of Tsukuba, 5.University of Tsukuba Hospital and University of Tsukuba, 6.University of Tsukuba Hospital and University of Tsukuba, 7.University of Tsukuba Hospital and University of Tsukuba)

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Background

Eltrombopag (ETP), a thrombopoietin receptor agonist, is used for the treatment of idiopathic thrombocytopenic purpura (ITP) at the daily dose of 12.5 - 50 mg. Although the dose adjustment of ETP is achieved by monitoring the platelet (PLT), the efficacy (PLT elevation) is different among the patients. It has been unclear whether or not therapeutic drug monitoring (TDM) for ETP is useful for assessing the drug response. We developed a high-performance liquid chromatography (HPLC) for determining serum ETP in TDM for ITP patients under ETP administration.

Methods

Reversed-phase HPLC equipped with ODS column was used for ETP determination. The wavelength for ultra violet was set at 265 nm and the mobile phase consisting of 10 mM 1-pentanesulfonic acid sodium salt, acetonitrile and acetic acid (100:300:2, v/v/v) was pumped at 1.0 mL/min. Serum samples spiked with internal standard (diclofenac) was precipitated with acetonitrile and the supernatant was injected into the HPLC. Serum samples collected from 11 ITP patients (Male/Female: 1/10, 60.2±18.0 year, 53.2±9.7 kg) were analyzed for determining ETP concentration. The relationship between ETP concentration and PLT elevation (PLT ratio: before/after administration of ETP) was examined. The study was approved by the ethical committee of the University of Tsukuba hospital.

Results

The calibration curve was linear at the range of 0.1 - 50 g/mL for ETP concentration ($r = 0.9997$). The recoveries of ETP were greater than 94.5% with the coefficient of variations (CVs) less than 2.8%. The CVs for intra-day and inter-day assay were 1.3 - 3.1% and 3.6 - 7.6%, respectively. Serum ETP concentrations were 0.35 - 7.16 g/mL under the daily dose of 3.6 - 50 mg. There was a positive correlation between ETP concentration and the daily dose ($r=0.76$, $p<0.01$). Higher correlation co-efficient was found between ETP concentration and PLT ratio ($r=0.56$, $p<0.01$) compared with that between daily dose and PLT ratio ($r=0.39$, $p<0.01$).

Conclusions

Present HPLC can be used for determining serum ETP in patients under ETP treatment. TDM for ETP may be

useful for assessing the PLT elevation in the patients with ITP.