Poster

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

Chair: Kosuke Doki, Japan

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[P27-9-7] Comparison of therapeutic efficacy of brand-name allopurinol and its generic medicine by population pharmacodynamic analysis based on electronic medical records

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Background

Since generic medicines are approved for clinical use without human studies evaluating effectiveness and side effects, it is still doubt about their efficacy and safety. Allopurinol, a xanthine oxidase inhibitor, is often used for treatment of hyperuricemia and gout, and some of its generic medicines are also approved to use in clinical situations.

Methods

To construct the population pharmacodynamic (PPD) model, we retrospectively collected the information of patient’ s backgrounds, clinical test values, and prescribed drugs from electronic medical records in two hospitals. We chose patients who were prescribed only one kind of allopurinol for treatment of hyperuricemia or gout in the first case. We constructed a physiological indirect response model to describe the time course of serum uric acid (UA) concentrations. The PPD analysis was performed using NONMEM 7.3 with the first order conditional estimation method with interaction (FOCE-INTER).

Results

An indirect response I_{max} (maximum drug inhibitory effect) model, based on the 634 serum UA concentrations of 148 patients, could describe the time course of serum UA levels in patients during the treatment with brand-name and two generic medicines of allopurinol. Before the initiation of treatment, the basal UA levels were increased in correlation with serum creatinine (SCr) concentrations. The inhibitory effects of allopurinol on the production of UA were attenuated by increasing of the body mass index (BMI), but the I_{max} value was significantly different between male and female patients. The result of simulation analysis revealed that the achievement rate to decrease serum UA concentrations below 6.0 mg/dL (until 180 days after the initiation of treatment) was dependent on both daily dosage of allopurinol and basal UA levels. However, we were unable to find significant difference in anti-hyperuricemic effects of generic and brand-name allopurinol.

Conclusions

Our constructed PPD model described the influence of BMI, SCr, and gender on serum UA levels in patients treated with brand-name of allopurinol or its generic medicines. The results of the population analysis also indicated that anti-hyperuricemic effects was not significantly different between brand-name and generic allopurinol.