Poster

[P26-7] P26-7: Oncologic drugs (3): Pharmaometrics, PK/PD, special population

Chair: Shiro Fukumori, Japan

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[P26-7-1] Bayesian prediction of myelosuppression profiles based on routine clinical data after gemcitabine and cisplatin treatment

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Keywords: myelosuppression, population pharmacodynamic, NONMEM, modeling and simulation

Background

In the cancer chemotherapy, hematological toxicity is one of the serious adverse events and is often a dose-limiting factor. In the clinical practice, a monitoring of the counts of the blood cells such as platelet (PLT), red blood cell (RBC) and white blood cell (WBC) is necessary to prevent the toxicity. We have already proposed a population pharmacodynamic modeling approach to explain myelosuppression profiles based on routine clinical data[1)]. In this study, we aimed to develop a modeling and simulation (M&S) procedure for Bayesian prediction of time course profiles of blood cell counts that reflect myelosuppression profiles[2)].

Methods

The population model[1)] is based on an equation for Erlang distribution, which was applied to explain time course profiles of PLT, RBC and WBC. In addition, one-point Bayesian prediction was performed using data from optimal day (e.g. Day 8) and evaluated predictabilities of nadir values and times to nadir (T_{nadir}) after gemcitabine and cisplatin (GC) treatment. Population pharmacokinetic analyses were performed using NONMEM, and the empirical Bayesian prediction was applied using the POSTHOC option in NONMEM.

Results

PLT, RBC and WBC counts were retrospectively collected from 61 time courses (a total of 472 points) of 27 cancer patients. Predictive performance by a one-point Bayesian prediction was evaluated using data from Day 8 in consideration of practical applicability to outpatients. Some good predictability was obtained for nadir values with some exceptions for PLT and RBC, whereas the predictability of T_{nadir} was insufficient.

Conclusions

We designed and implemented a pharmacodynamic model based on an Erlang statistical distribution functions, and proposed its application to routine predictions of nadir values for myelosuppression after treatment with GC regimens. Some good predictability was obtained for nadir values with some exceptions for PLT and RBC, whereas the predictability of T_{nadir} was insufficient for PLT, RBC and WBC. Although the strategy may have to be improved, our current M&S approach could be used for supportive care during cancer chemotherapy.

1) Y. Yano et al., J. Pharm. Sci., 98: 4402-4412 (2009)
2) Y. Chisaki et al., Pharmacology, 98: 284-293 (2016)