博士後期課程

令和 6 年度
武蔵野大学大学院　薬科学研究科　薬科学専攻 博士後期課程　入学試験問題 （3 月 10 日）
［ 英語 ］ 次の文章を読み、各問に答えよ。

This guideline provides recommendation to promote a consistent approach in designing, conducting, and interpreting enzyme- or transporter-mediated in vitro and (A) drug-drug interaction (DDI) studies during the development of a therapeutic product. A consistent approach will reduce uncertainty for pharmaceutical industry to meet the requirement of multiple regulatory agencies and lead to more efficient utilization of resources.

In (A) practice, patients are often prescribed more than one drug which can result in a DDI. Some patients, in particular fragile older patients or patients with serious or multiple health issues, can be prescribed a large number of different drugs (i.e., polypharmacy). The occurrence of DDIs is a common (A) problem that can increase the risk of adverse events, sometimes leading to hospital admissions. Alternatively, some DDIs can reduce treatment efficacy. Hence, it is important to consider an investigational drug's potential to interact with other drugs.

（中略）

The potential for an investigational drug to cause DDIs should be investigated in a stepwise manner during drug development. The potential for a new drug to cause pharmacokinetic interactions both as a *victim* (effect of other drugs on the investigational drug) and as a *perpetrator* (effect of the investigational drug on concomitant drugs) should be evaluated. All aspects mentioned below are further expanded and discussed later in the document.

Evaluating the potential of an investigational drug as a *victim* of a metabolic enzyme- or transporter-mediated DDI involves identification of the principal routes of the drug's elimination. For drugs that are not eliminated predominantly unchanged in urine or that are not biologics eliminated through unspecific catabolism, the keystone of the identification of principal elimination routes is a well performed clinical mass balance study. In some instances, e.g., if a large part of the dose is found as unchanged drug in feces, an absolute bioavailability study can also be a useful complement to aid interpretation. Using data from the mass balance study, the quantitative contributions of the different elimination pathways should be estimated based on the amount of dose excreted as primary

and secondary metabolites along specific routes. For quantitatively important elimination pathways, in vitro and clinical studies should be used to identify the main enzymes or transporter proteins involved in these pathways. The ability to predict interactions affecting the investigational drug is dependent on the identification of these proteins.

Evaluating the DDI potential of an investigational drug as a *perpetrator*, involves characterizing the effect of the drug on enzymes and transporters. This evaluation often starts with in vitro experiments to elucidate potential DDI mechanisms. Identification of DDI risks should then be followed by clinical DDI studies based on mechanistic knowledge, and the results should be translated to appropriate (A) management recommendations for drugs as a *victim* and *perpetrator* of DDIs.

The results of DDI evaluations inform the protocols for (A) studies in patients regarding the use of concomitant drugs. Information about the interaction potential should be gained as early in drug development as practically possible to assure safety and avoid unnecessary restrictions of concomitant medications and/or exclusion of patients who require the concomitant medications in clinical studies, typically phase 2/3 studies. The timing of the different non-clinical and clinical studies is dependent on the context and type of product; some general recommendations are given below. Predictive modeling (see Section 7.3) can also assist evaluation of the DDI potential.

（ICH Harmonised Guideline: Drug Interaction Studies M12 Draft versionより引用）

問1　医薬品開発において薬物相互作用の可能性を評価することが重要である理由について、問題文の記載に基づいて日本語で記しなさい。

問 2　5 か所の (A) に共通に入る語（1 語）を、問題文から抜き出して記載しなさい。

問 3　医薬品開発において、被験薬が薬物動態学的相互作用の victim あるいは perpetrator となる可能性を評価する方法について、問題文の記載に基づいてそれぞれ簡潔に記しなさい（日本語で）。

問 4　下線部を和訳しなさい。