Ⅱ期

平成 31 年度
武蔵野大学大学院　薬科学研究科　薬科学専攻　修士課程　入学試験問題　（1 月 13 日）
［　英語　］ 次の文章を読み、各問に答えよ。

Clinical drug development is often described as consisting of four temporal phases (Phase I-IV). It is important to recogni(z)e that the phase of development provides an inadequate basis for classification of clinical trials because one type of trial may occur in several phases (see Fig 1.). A classification system using study objectives as discussed in section 2.2 is preferable. ① It is important to appreciate that the phase concept is a description, not a set of requirements. It is also important to realis(z)e that the temporal phases do not imply a fixed order of studies since for some drugs in a development plan the typical sequence will not be appropriate or necessary. For example, although human pharmacology studies are typically conducted during Phase I, many such studies are conducted at each of the other three stages, but nonetheless sometimes labelled as Phase I studies. Figure 1 demonstrates this close but variable correlation between the two classification systems. The distribution of the points of the graph shows that the types of study are not synonymous with the phases of development.

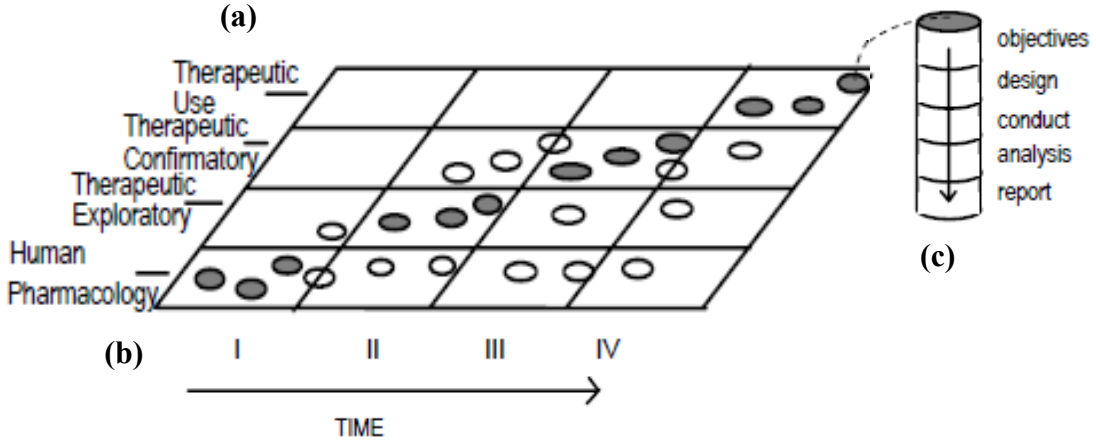

Figure 1 - This matrix graph illustrates the relationship between the phases of development and types of study by objective that may be conducted during each clinical development of a new medicinal product. The shaded circles show the types of study most usually conducted in a certain phase of development, the open circles show certain types of study that may be conducted in that phase of development but are less usual. Each circle represents an individual study. To illustrate the development of a single study, one circle is joined by a dotted line to an inset column that depicts the elements and sequence of an individual study.

②Drug development is ideally a logical, step-wise procedure in which information from small early studies is used to support and plan later larger, more definitive studies. To develop new drugs efficiently, it is essential to identify characteristics of the investigational medicine in the early stages of development and to plan an appropriate development based on this profile.

Initial trials provide an early evaluation of short-term safety and tolerability and can provide pharmacodynamic and pharmacokinetic information needed to choose a suitable dosage range and administration schedule for initial exploratory therapeutic trials. Later confirmatory studies are generally

larger and longer and include a more diverse patient population. Dose-response information should be obtained at all stages of development, from early tolerance studies, to studies of short-term pharmacodynamic effect, to large efficacy studies (see ICH E4). Throughout development, new data may suggest the need for additional studies that are typically part of an earlier phase. For example, blood level data in a late trial may suggest a need for a drug-drug interaction study, or adverse effects may suggest the need for further dose finding and/or additional non-clinical studies. In addition, to support a new marketing application approval for the same drug e.g. for a new indication, pharmacokinetic or therapeutic exploratory studies are considered to be in Phase I or Phase II of development.

（ICH-E8 General Considerations for Clinical Trials より引用）

問1　(a) (b) (c)に入る 1 語を問題文から選んで記しなさい。
問2　下線部①を和訳しなさい。
問3　下線部②を和訳しなさい。
問4　Figure 1 の丸印が何を表すのか、また黒（影付）丸と白丸の違いを記しなさい。
問5　Section2.2 で論じられている試験の目的を下表に示す。(a) (b) (c) (d) に例示する試験は、それぞれ Human Pharmacology、Therapeutic Exploratory、Therapeutic Confirmatory、Therapeutic Use のどれに該当するか。本文の内容を踏まえ、表中に記しなさい。

(a) Dose-response exploration studies
(b) Pharmacoeconomic studies
(c) Adequate, and well controlled studies to establish efficacy
(d) Drug interaction studies

	Objective of Study	Study Examples
Human Pharmacology	・ Assess tolerance ・ Define/describe Pharmacokinetics and Pharmacodynamics ・ Explore drug metabolism and drug interactions ・ Estimate activity	
Therapeutic Exploratory	・ Explore use for the targeted indication ・ Estimate dosage for subsequent studies ・ Provide basis for confirmatory study design, endpoints, methodologies	
Therapeutic Confirmatory	・ Demonstrate/confirm efficacy ・ Establish safety profile ・ Provide an adequate basis for assessing the benefit/risk relationship to support licensing ・ Establish dose-response relationship	
Therapeutic Use	・ Refine understanding of benefit/risk relationship in general or special populations and/or environments ・ Identify less common adverse reactions ・ Refine dosing recommendation	