Present Aspects of Single Microdose and Preclinical Studies

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Exploratory clinical studies using microdose (MD) techniques were adopted by OECD in July of 2003. Although the U.S. FDA accepted this concept, they had some concerns concerning Phase I screening studies. Therefore, the draft CDER guidance of April 2005, concerning exploratory IND studies, was revised to place more emphasis on screening Phase I trials compared to previous FDA guidance. In the present race to develop new drugs, if new drug candidates, even unique ones, are discontinued in clinical trials, pharmaceutical companies will waste a great deal of time and effort and suffer substantial economic burden. In an attempt to avoid such situations, it is now believed that a "go" or "no-go" decision can be made if human drug safety is anticipated in the early stages of development. I discussed the merits and advantages of 2-week repeated dose toxicity studies over extended single-dose studies for conducting clinical microdose studies in a forum at the annual meeting of the Japanese Society for the Study of Xenobiotics (JSSX) in Kanazawa in November 2004 and at the annual meeting of the Japanese Society of Toxicology (JSOT) in 2005. At these meetings, I stressed that techniques which permit early clinical trials could narrow down the number of new drug candidates. If the purpose of preclinical studies is only to detect adverse drug reactions (ADR), it is sufficient to conduct step-by-step clinical studies. The development of an infrastructure of clinical trials and innovation of consistent investigation techniques from clinical trials through regulatory approval are essential for implementation of MD studies in Japan. Therefore, although the international trend is to employ MD studies for rapid pharmaceutical development, I propose that we reconsider the experimental design of pre-clinical studies focusing on insuring the safety from common sense of Japanese who are wary of clinical trials.