

レンヌ事件の教訓

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Lessons learned from the tragic case in Renne

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Abstract

Since there are few benefits for subjects participating in a first-in-human trial (FIH), safety for the subjects is the most important concern in the trial. After the case of TGN1412, FIHs had been safely performed, but a world-shaking case occurred at Renne in France. In an FIH of BIA 10-2474, a fatty acid amide hydrolase inhibitor, a subject died and other subjects were suffering from the same symptom at the 5th cohort of the repeated administration part. Retrospective examination of published data gradually revealed specific properties of the compound. The tragedy might be due to some secondary pharmacological action which induced neurological damage in human at the much higher dose level than that of the anticipated primary pharmacological action, and that the compound shows non-linear pharmacokinetics and pharmacodynamics. Several problems have been pointed concerning conduct of the trial. The ratio of dose increments are too high at the later stage of the ascending doses in spite of the fact that non-linear pharmacokinetics is predicted at the dose level and such a high dose may not be necessary. This case shed light again not only on the importance of careful planning of a protocol by strict investigation of the available preclinical data, but also of utilizing all the data available in conducting a trial. The case seems that the primary objective is not confirming the safety, but observing the protocol. It should be noted that the safety of the subjects is the most important in any case.

Key words

BIA 10-2474, Renne, first-in-human trial (FIH), death, fatty acid amide hydrolase inhibitor

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