

併用薬剤の調達、用法・用量外の場合における問題点とその解決**

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**Issues Involved in the Use of Unapproved Dosages and
Administration of Combination Drugs**

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Summary

In the field of oncology, it is well known that a combination of different anti-cancer drugs can result in a higher performance than is obtained with either drug separately, and thus may provide a better therapeutic outcome. Recently, clinical studies of combination therapy with standard drugs have also become common. For the use of unapproved combination drugs, the filing of a clinical trial notification (CTN) is required. Most such trials involve dosage or administration routes or schedules that are out of the range of the approved content. In the US, a Cross Reference Letter for the investigational new drug (IND) obtained from the applicant for the combination drug, would suffice. If a similar process were adopted in Japan, it would be easier to start the clinical study at an earlier stage. In a global study, it is often the case that the combination drug is already marketed overseas. Sometimes, the combination drug has to be approved under the Pharmaceutical Affairs Law to be covered by health insurance. Since the supplemental NDA has to be conducted by the company that holds the drug approval, there is an urgent need for a co-development cooperative structure. In the US or EU, the label will indicate that the drug indication is approved in combination with the concomitant drug. There is no need to file a supplemental NDA (SNDA), as there is in Japan. Expectations in Japan are high for a new regulatory framework that does not require a SNDA for a new dosage and/or administration schedule or route when the combination drug already has the same indication as the drug in question.

Key words

Unapproved combination drugs, CTN, Cross Reference Letter, Co-development cooperative structure, Supplemental NDA, New regulatory framework