449TiP MASTER KEY project: A basket/umbrella trial for rare cancers in Japan

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Background: Rare cancers have had a challenge in establishing standard therapies for patients compared to major cancers, due to the lack of basis for clinical studies and investigations. We started a biomarker driven basket/umbrella trial using a "master protocol", called the MASTER KEY Project, which aims to find more efficient ways to evaluate treatments for rare cancers and to build a treatment development infrastructure by collaborating with industries. Similar studies including NCI-MATCH trial are ongoing; however, MASTER KEY Project is the first to be reported for such large scale trials that focuses only on rare cancers.

Trial design: The project consists of two main parts: the prospective registry study part and the multiple clinical trials (sub-study) part. Patients with advanced rare cancers (annual incidence less than 6 cases per 100,000 population)/cancers of unknown primary/rare pathological subtypes of major cancers, who have priorly been evaluated by a molecular diagnostic testing, such as a validated next generation sequencing assay, are enrolled into the registry study. The primary objective of the registry study is to collect consecutive data on biomarker, patient background, and prognosis to build a large-scale database highly reliable for use as historical control data in future clinical trials. In the sub-studies, drugs are provided by various industries, who are collaborators. Sub-studies are placed under a "master protocol", allowing new sub-studies to be added at any time. Each sub-study is ordinarily a single arm study and will enroll 5-20 patients with the appropriate biomarker of interest, regardless of histopathologic tumor type. A biomarker-negative sub-study will also be available so that all patients have a chance to be enrolled in a sub-study. The project opened in May 2017. As of April 2018, more than 200 of a planned 100 patients/year have been enrolled in the project. There are three ongoing sub-studies. Two of them are biomarker related studies, which enroll patients harboring BRAF mutation and mismatch repair deficiency, respectively. In addition, three sub-studies are under planning and they will open by fall of 2018.

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