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Chugai Obtains Regulatory Approval for FoundationOne CDx Cancer Genomic Profile to Identify TMB-High Tumors

TOKYO, November 16, 2021 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that it obtained approval from the Ministry of Health, Labour and Welfare (MHLW) on November 15, 2021, for FoundationOne® CDx Cancer Genomic Profile to be used to identify advanced/recurrent tumor mutation burden-high (TMB-High; ≥10 mutations/megabase (mut/Mb)) solid tumors. An application for a humanized anti-human PD-1 monoclonal antibody, pembrolizumab (genetical recombination) [Product name: Keytruda®] in TMB-High solid tumors that have progressed following prior chemotherapy was submitted by MSD K.K. on March 11, 2021 and is currently under review with the MHLW.

“The approval may enable physicians to make treatment suggestions based on TMB measurement. TMB is the third tumor-agnostic biomarker following *NTRK* fusion and high microsatellite instability,” said Dr. Osamu Okuda, Chugai’s President and CEO. “We will continue to encourage the proper use of this test to support treatment decision-making, and therefore enable better access to targeted therapies by evaluating many potential gene alterations at one time.”

With this approval, FoundationOne CDx Cancer Genomic Profile will help identify patients with TMB-High advanced/recurrent solid tumors.

As a leading company in the field of oncology, Chugai is committed to realizing advanced personalized oncology care, and contributing to patients and healthcare professionals through improving access to comprehensive genomic profiling of cancers.

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Approval information (underlined indicates newly added)

Intended uses or indications

- The Product is used for comprehensive genomic profiling of tumor tissues in patients with solid cancers.
- The Product is used for detecting gene mutations and other alterations to support the assessment of drug indications listed in the table below.

Alterations	Cancer type	Relevant drugs
Activated *EGFR* alterations	Non-small cell lung cancer (NSCLC)	afatinib dimaleate, erlotinib hydrochloride, gefitinib, osimertinib mesylate
EGFR exon 20 T790M alterations		osimertinib mesylate
ALK fusion genes		alectinib hydrochloride, crizotinib, ceritinib
ROS1 fusion genes		entrectinib
MET exon 14 skipping alterations		capmatinib hydrochloride hydrate
BRAF V600E and V600K alterations	Malignant melanoma	dabrafenib mesylate, trametinib dimethyl sulfoxide, vemurafenib
ERBB2 copy number alterations (HER2 gene amplification positive)	Breast cancer	trastuzumab (genetical recombination)
KRAS/*NRAS* wild-type	Colorectal cancer	cetuximab (genetical recombination), panitumumab (genetical recombination)
Microsatellite instability high		nivolumab (genetical recombination)
Microsatellite instability high	Solid tumors	pembrolizumab (genetical recombination)
Tumor mutational burden-high		pembrolizumab (genetical recombination)*
NTRK1/2/3 fusion gene		entrectinib, larotrectinib sulfate
BRCA1/2 alterations	Ovarian cancer	olaparib
BRCA1/2 alterations	Prostate cancer	olaparib
FGFR2 fusion genes	Biliary tract cancer	pemigatinib

* Application under review and not yet approved for the drug indication as of November, 2021

About FoundationOne CDx Cancer Genomic Profile

Developed by Foundation Medicine Inc., FoundationOne CDx Cancer Genomic Profile is a next-generation sequencing based *in vitro* companion diagnostic device for the detection of substitutions,

insertion and deletion alterations, and copy number alterations in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin-fixed, paraffin-embedded (FFPE) tumor tissue specimens. The device is available as a companion diagnostic for multiple molecular-targeted drugs approved in Japan.

About tumor mutational burden

Tumor mutational burden (TMB) is a measure of the number of somatic mutations per coding region within a tumor's genome. Levels are measured by the number of non-inherited mutations occurring per megabase (1 million DNA base pairs) of the tumor genome, and with a status of 10 mutations per megabase or more defined as TMB-High by the FoundationOne CDx Cancer Genomic Profile. More neoantigen is induced in TMB-High tumors, and such tumors may respond better to immune-checkpoint inhibitors. TMB-High tumors are reported to be relatively common in malignant melanoma, non-small cell lung cancer, colorectal cancer, and endometrial cancer[1)].

[Reference]

1. Vanderwalde, A. et al.: Microsatellite instability status determined by next-generation sequencing and compared with PD-L1 and tumor mutational burden in 11,348 patients. Cancer Med. 7(3): 746-756, 2018

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