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Chugai Obtains Approval for Expanded Use of FoundationOne CDx Cancer Genomic Profile as a Companion Diagnostic of Novartis' MET inhibitor, Capmatinib for Non-Small Cell Lung Cancer with *MET* exon 14 Skipping Alterations

- FoundationOne CDx Cancer Genomic Profile obtained approval as a companion diagnostic of Novartis' investigational MET inhibitor capmatinib for advanced and/or metastatic non-small cell lung cancer patients whose tumors have that leads to *MET* exon 14 skipping
- Novartis submitted an application for capmatinib to the Ministry of Health, Labour and Welfare
- It is estimated that 3-4%[1)] of all patients with non-small cell lung cancer have an identified *MET* exon 14 skipping

TOKYO, May 29, 2020 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that it obtained an approval from the Ministry of Health, Labour and Welfare (MHLW) for expanded use of the genomic mutation analysis program, FoundationOne® CDx Cancer Genomic Profile as a companion diagnostic of the Novartis' investigational MET inhibitor, capmatinib (INC280) for the treatment of unresectable advanced and/or metastatic non-small cell lung cancer (NSCLC) with that leads to *MET* exon 14 skipping (METex14).

"We are pleased that FoundationOne CDx Cancer Genomic Profile was approved as a companion diagnostic of an investigational MET inhibitor, capmatinib. Since the standard treatment of NSCLC is decided based on whether the cancer has a driver mutation, we believe NSCLC is one of the cancer types that comprehensive genomic profiling can particularly contribute to its treatment decision," said, Dr. Osamu Okuda, Chugai's President and COO. "By continuing to collaborate with many biopharma partners, we will expand the companion diagnostic functions and are committed to working toward the realization of precision medicine."

The approval aims to expand the program for use as a companion diagnostic to aid in identifying patients who could benefit from capmatinib for the treatment of unresectable advanced and/or metastatic NSCLC with METex14 by detecting mutations that lead to METex14. It is estimated that 3-4% of all patients with NSCLC have an identified METex14[1)] and is said to be a poor prognosis factor[2)]. Capmatinib is a selective MET inhibitor and is confirmed to strongly inhibit the kinase activity of the METex14[3)]. Efficacy and safety of capmatinib are investigated in patients with advanced and/or metastatic NSCLC in the phase II GEOMETRY mono-1 study conducted by Novartis. Novartis Japan K.K. has submitted the regulatory application of capmatinib to the MHLW.

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Developed by Foundation Medicine Inc., FoundationOne CDx Cancer Genomic Profile is a next-generation sequencing based *in vitro* 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 program is available as a companion diagnostic for multiple molecular-targeted drugs approved in Japan.

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

Approval information The underlined part has been 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
EGFR exon 19 deletions and *EGFR* exon 21 L858R 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)
NTRK1/2/3 fusion gene	Solid tumors	entrectinib
BRCA1/2 alterations	Ovarian cancer	olaparib

Reference

1. Salgia R. MET in Lung Cancer: Biomarker Selection Based on Scientific Rationale. Mol Cancer Ther. 2017; 16(4):555-565.

2. Tong JH, Yeung SF, Chan AWH, et al. MET Amplification and Exon 14 Splice Site Mutation Define Unique Molecular Subgroups of Non–Small Cell Lung Carcinoma with Poor Prognosis. Clin Cancer Res. 2016; 22(12):3048-3056.

3. Fujino T, Kobayashi Y, Suda K, et al. Sensitivity and Resistance of MET Exon 14 Mutations in Lung Cancer to Eight MET Tyrosine Kinase Inhibitors In Vitro. J Thorac Oncol: 2019 Oct;14(10):1753-1765

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