# 28AB-ISMS18 Best-in-Class ALK Inhibitor: Alectinib

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It has been revealed that various gene alterations in tumors contribute to a process of the tumorigenesis and the growth of neoplastic cells due to the rapid development of the recent molecular biologic analysis technologies. In innovative drug development and the development of the anti-tumor agent, a concept of the personalized healthcare to choose the most suitable treatment drug for each patient is realizing based on molecules and the genetic information of the individual patient, and some of these molecular-targeted drugs actually exhibit a maximum effect with a minimum side effect.

Anaplastic lymphoma kinase (ALK) was firstly identified as the fused gene which constituted NPM-ALK resulting from the chromosome translocation in an undifferentiated large cells type lymphoma in 1994. Following the discovery of an ALK fused gene for an inflammatory muscular fiber blast cell tumor and the diffuse large-B-cell lymphoma, EML4-ALK was identified as a new fusion oncogene in the non-small cell lung (NSCLC) cancer in 2007 by Soda *et. al*.. Since it was the first report of the gene alteration as an oncogene in solid tumor, promptly we initiated a high-throughput screening using Chugai-Roche small-molecule library. In the course of chemical modification campaign focusing on the strength of anti-tumor activity and the kinase selectivity to identify clinical compound, we lastly produced Alectinib (CH542802/RO542802). Because of the high selectivity of Alectinib in various preclinical experiments including kinase and tumor cell panels and also mouse xenograft models[1)], we started the phase I/II limited to the NSCLC patient segment which had ALK variation in 2010 in Japan. Based on the results[2)], new drug application was filed for the treatment of ALK fusion gene positive unresectable, recurrent / advanced NSCLC in October, 2013. After receiving the designation of the orphan drug in September of the year, and the approval was obtained by the Japanese Ministry of Health, Labour and Welfare (MHLW) on July, 2014. As for the development in foreign countries including EU and US, F. Hoffmann-La Roche AG carries out clinical trials (Roche Cord: RG7853).

In this presentation, the process of Alectinib development where we perform PHC (Personalized healthcare) strategy will be summarized, and we will also discuss the current issues on the patient screening, simultaneous development diagnostic agent (CDx), and the clinical designs for basket/umbrella trials.

1) Sakamoto H, Tsukaguchi T, Hiroshima S, et al.: CH5424802, a selective ALK inhibitor capable of blocking the resistant gatekeeper mutant. Cancer Cell 2011; 19:679-90.
2) Seto T, Kiura K, Nishio M, et al.: CH5424802 (RO5424802) for patients with ALK-rearranged advanced non-small-cell lung cancer (AF-001JP study): a single-arm, open-label, phase 1–2 study. Lancet Oncol 2013; 14:590-90