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Drug development and translational science of multiple receptor tyrosine kinase inhibitor (RTKI) lenvatinib (E7080) as an anti-cancer agent

◯Yasuhiro FUNAHASHI[1]
[1]Biomarkers and Personalized Medicine Core Function Unit, Eisai Product Creation Systems

Vascular endothelial growth factor (VEGF) is the key molecule in regulation of angiogenesis via binding to their cognate receptors, VEGFR1-3. Bevacizumab, a monoclonal antibody directed against human VEGF, was approved for a treatment of cancer patients and confirmed that blocking VEGF signaling is a feasible approach to develop anti-cancer agents. Since bevacizumab targets only VEGF-A among the various angiogenic factors such as fibroblast growth factor (FGF) and hepatocellular growth factor (HGF), inhibition of multiple receptor tyrosine kinase (RTK) signalings related to angiogenesis is a promising therapeutic strategy. We developed a novel multiple RTK inhibitor, lenvatinib (E7080), which targets VEGFR1-3, FGFR1-4, RET, KIT and PDGFRβ. Lenvatinib is currently in Phase II/ III clinical studies. We investigated the pharmacologic profile of lenvatinib by using VEGF- and FGF-driven angiogenesis assays. To develop predictive/response biomarker hypothesis, we have been challenging in translational science via systems biology, in which pharmacology data was combined with 'Omics' data in preclinical cancer models. A better understanding of the responses of tumor vasculature to anti-angiogenesis therapy will have significant clinical implications for the selection of appropriate patients, who will have more benefits from anti-angiogenesis therapy. In this presentation, we will introduce our recent research for lenvatinib from the aspects of both drug development and translational science.