28AB-ISMS04 **Lenvatinib Suppresses Angiogenesis Driven by VEGF and FGF through the Inhibition of both VEGFR and FGFR Signaling Pathways**

○Kenji ICHIKAWA[1], Saori WATANABE-MIYANO[1], Yusuke ADACHI[1], Yuji YAMAMOTO[1], Yoichi OZAWA[1], Yasuhiro FUNAHASHI[1], Kiyoshi OKAMOTO[2], Kenichi NOMOTO[3], Junji MATSUI[1]
[1]Eisai Co., Ltd., Tsukuba, Japan, [2]Eisai Co., Ltd., Tokyo, Japan, [3]Eisai Co., Ltd., Woodcliff Lake, NJ, USA

Lenvatinib mesilate (lenvatinib) is a selective tyrosine kinase inhibitor targeting VEGFR1-3, FGFR1-4, PDGFR α, KIT, and RET. Recently, lenvatinib showed a highly statistically significant improvement of progression free survival compared to placebo control in patients with radioiodine-refractory differentiated thyroid cancer and has been approved in thyroid cancer. To elucidate the mechanism of action in antitumor effect by lenvatinib, we examined the antiangiogenic activity of lenvatinib in preclinical models. Our data indicated that lenvatinib showed potent antiangiogenic activity driven by VEGF and FGF, respectively both *in vitro* and *in vivo* models. Inhibition of FGF and VEGF signaling pathways with lenvatinib were also supported by increase of plasma FGF23 levels and VEGF level to show an inhibition in FGF- and VEGF-driven *in vivo* angiogenesis model. Therefore, the significant clinical outcome might be based on the unique antiangiogenesis activity of lenvatinib, in particular VEGFR and FGFR inhibition, which should be further investigated.