S01-3 **Evaluation of supersaturation behavior of pazopanib hydrochloride in the presence of HPMC by pH-shift dissolution testing**

○ Hikaru SUGIHARA[1]

[1]Ono Pharmaceutical Co., Ltd.

Salts of weakly basic active pharmaceutical ingredients are widely used to improve aqueous solubility and/or dissolution rate. However, these compounds are prone to precipitation due to the lower solubility of the un-ionized species at the higher pH in the intestinal region. The goal of this study was to investigate the degree of supersaturation achieved following dissolution of different amounts of pazopanib hydrochloride at low pH, followed by rapid pH increase. Using pH solubility profiles, phase boundaries were defined for crystalline and amorphous free base forms. In the presence of a crystallization inhibitor, hydroxypropylmethyl cellulose (HPMC), the degree of supersaturation was found to be very high at pH 6.5. At a dose equivalent to the clinical dose, the maximum free drug concentration observed at pH 6.5 was dictated by the amorphous solubility. Solutions that exceeded the amorphous solubility upon pH increase were found to undergo glass − liquid phase separations (GLPS) with the formation of amorphous colloidal drug-rich particles. Microscopic observations confirmed that HPMC delayed the appearance of pazopanib free base crystals.