27O-ISMS35 **Identification of Novel Pyrrolo[2,3-*d*]pyrimidine Derivatives as Potent HCK and FLT3-ITD Dual Inhibitors**

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Results of our recent structure-activity relationship (SAR) development for HCK and FLT3-ITD dual inhibitors supported by *in silico* docking simulation and X-ray crystallography studies will be presented. Thus, 15 different amino acids were systematically introduced to our core structure: 7-cyclohexyl-5-(4-phenoxyphenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-4-amine, which had been recently reported as a potent HCK inhibitor. Activities of newly synthesized compounds against HCK were predicted by *in silico* docking simulation studies based on a HCK-ligand co-crystal structure. The relationship between predicted and actually measured activities will be discussed using newly obtained co-crystal structures. Compounds with potent *in vitro* activities were evaluated in a viability studies with an acute myeloid leukemia (AML) cell line MV4-11. Our SAR analyses led to the identification of compound **31**, which exhibited potent HCK and FLT3-ITD inhibition and anti-proliferation activity against MV4-11 cell line.