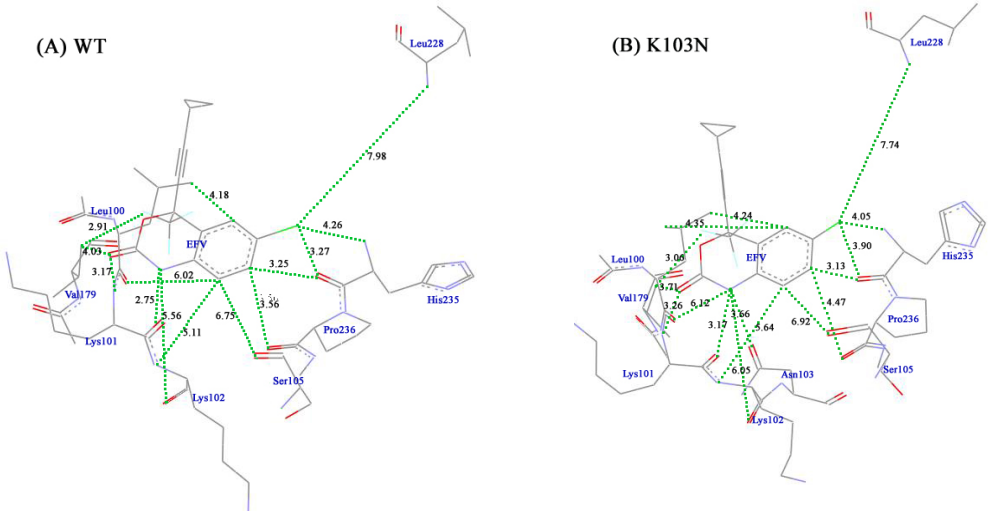

ESI 1. Interatomic distances between EFV and the residues in the binding pocket when cause the significant different binding between WT and K103N mutant type; (A) WT and (B) K103N mutant type (in Å).

ESI 2. The binding energy, interaction energy and deformation energy of EFV bound to the K103N RT binding pocket from ONIOM2A and ONIOM2C calculations.

Energy component (kcal mol^{-1})	ONIOM2A	ONIOM2C
BE	-5.65	-8.87
INT	-10.3	-15.41
DEF	4.64	6.57
DEF_{EFV}	1.51	1.38
DEF_{BP}	3.14	5.18